



IMPACT

RESEARCH MAKING A DIFFERENCE **2016**



INTRODUCTION

Message from our Director	4
Our Research at a Glance	6
Discover. Prevent. Cure.....	12



TRANSLATION 2015

Folate win for Aboriginal babies	16
Global research for rare disorder	19
Extra whooping cough shot to protect bubs.....	22
Sun safe: balancing the risks and benefits.....	24
Making the right decision on air travel.....	26
Building the best communities for early child development	28
Starting and staying on track.....	32
Boosting literacy in Aboriginal kids.....	34



PARADIGM SHIFT

A new approach for research with Aboriginal communities.....	38
Young minds really do matter	40
On a quest for kids with cystic fibrosis.....	44
Making FASD history in the Fitzroy Valley	48



IN THE PIPELINE

Taking on a common respiratory infection in kids.....	54
A new job for a specialised drug	56
New app helps teens think twice	58



COLLABORATING FOR IMPACT

Global war on brain cancer.....	62
Collaborating to prevent killer diseases in PNG.....	66
Improving the lives of kids with Type 1 diabetes	68

Our special thanks to those who have contributed to this report:
 Tammy Gibbs, Elizabeth Chester, Marnie McKimmie, Stephanie Pegler, Carolyn Monaghan, Jasmine Raisbeck, Caroline Wise, Ashley Schoof, Nicky Lewis, Tobias Schoep, Amy Sewell and the researchers and families whose stories we have shared.



KIDS are at the ❤️
of everything we do



MESSAGE FROM OUR DIRECTOR

What would you discover to help a child?

When we asked some kids, they had some good ideas – medicine that tastes like icecream and a cap to take away the confusion of autism were just a couple of suggestions.

In many ways, it's the question that drives so much of our research. What new knowledge can we generate that will make a real difference to child health and wellbeing?

I am very proud to present the outcomes of that style of thinking in this years IMPACT Report.

While we haven't yet put our minds to making medicine taste better, you will see that we are tackling many important issues to find ways to prevent, treat or cure the most common and devastating diseases and issues affecting children and young people.



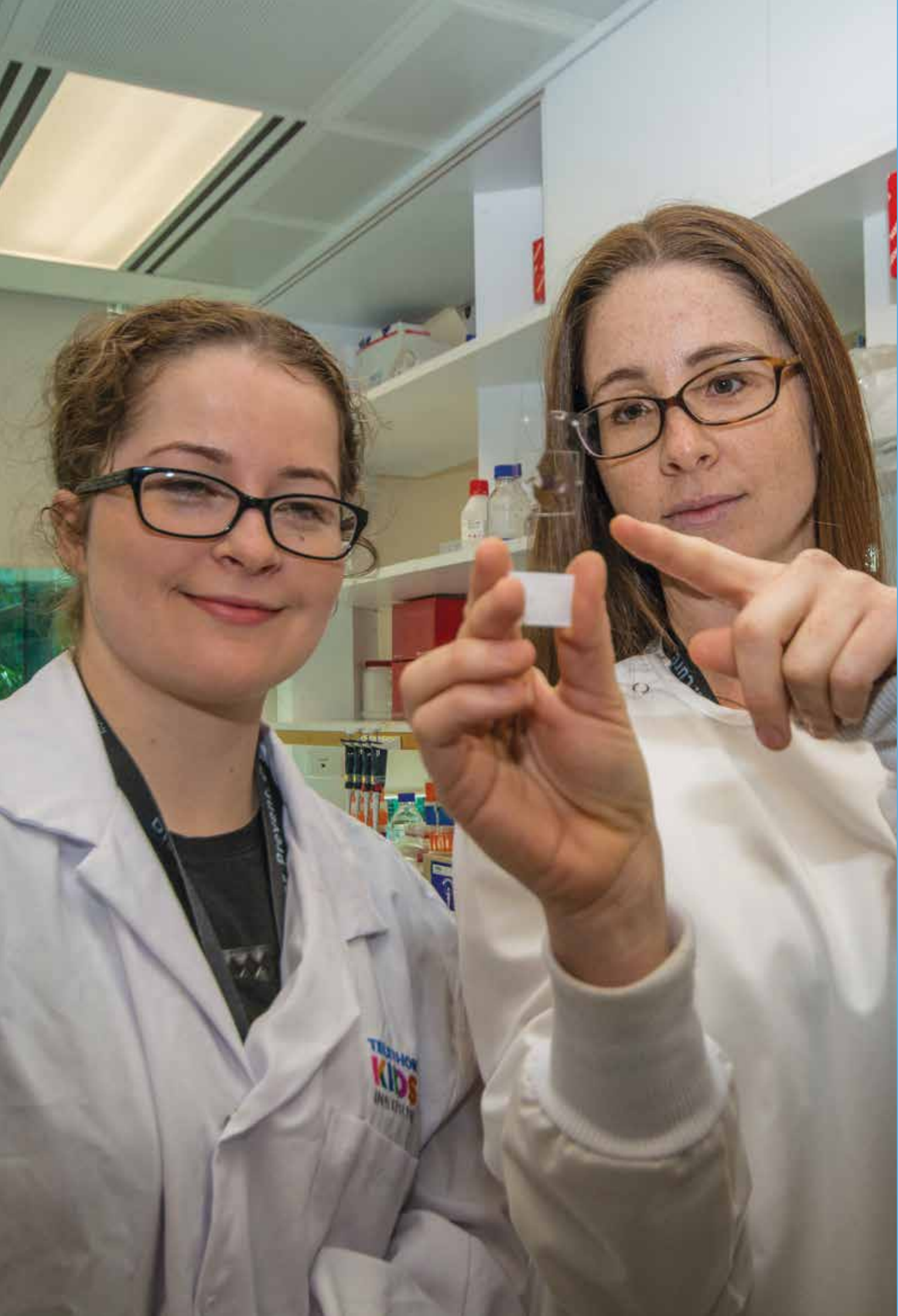
Research impact happens in many ways that extends beyond academia – the influence on policy, clinical guidelines and practice. It includes partnerships with industry and the community.

As you'd expect, impact doesn't happen overnight or in isolation from other research efforts around the world. That's why, in these pages, we celebrate research projects that are at different stages along the pipeline from idea to outcome, the collaboration that makes all of them possible, as well as those that have arrived at the ultimate destination – making a real and measurable difference for children and their families

If you'd like to see more about what the kids suggested, take a look at telethonkids.org.au/discover

In the meantime, I hope you're as inspired as I am by the IMPACT that our research delivers every day.

Jonathan Carapetis
Director

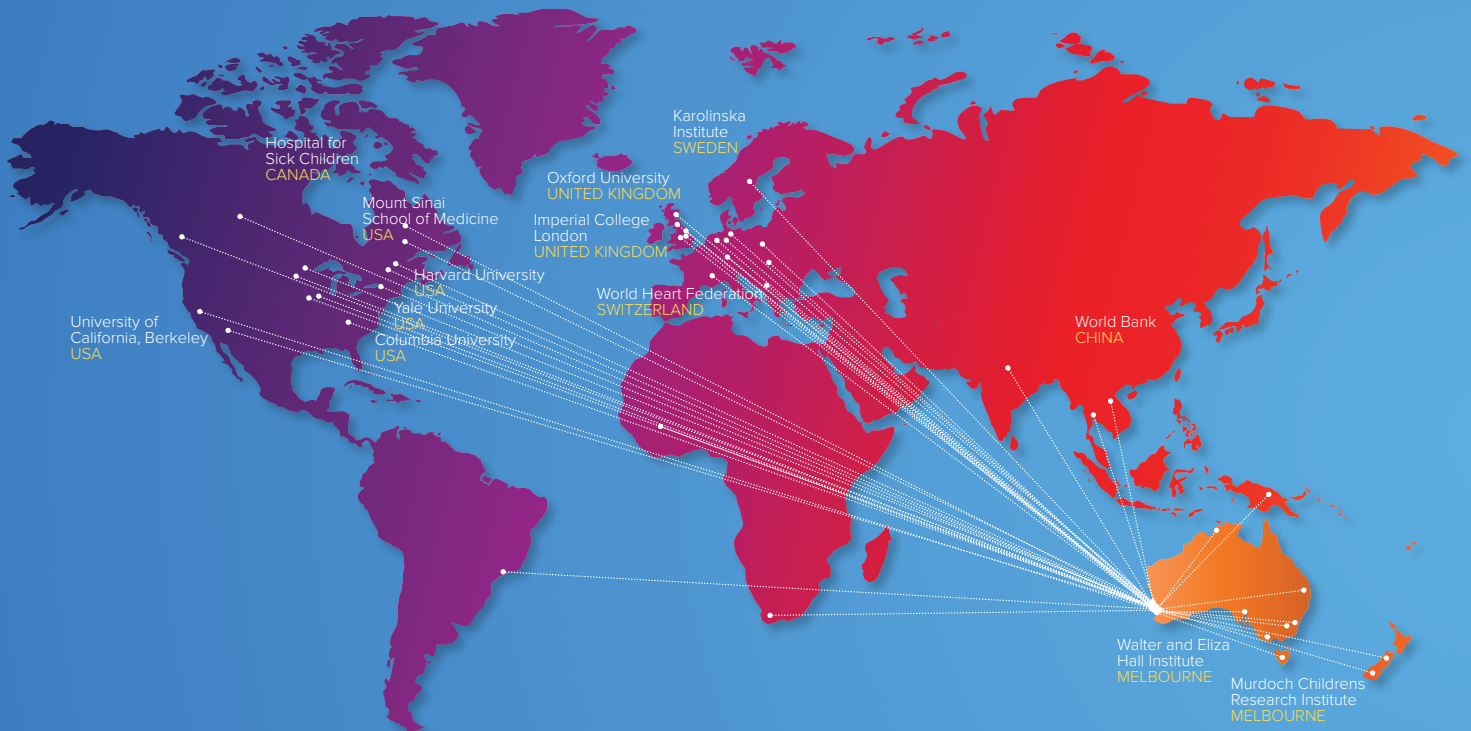


OUR RESEARCH AT A GLANCE

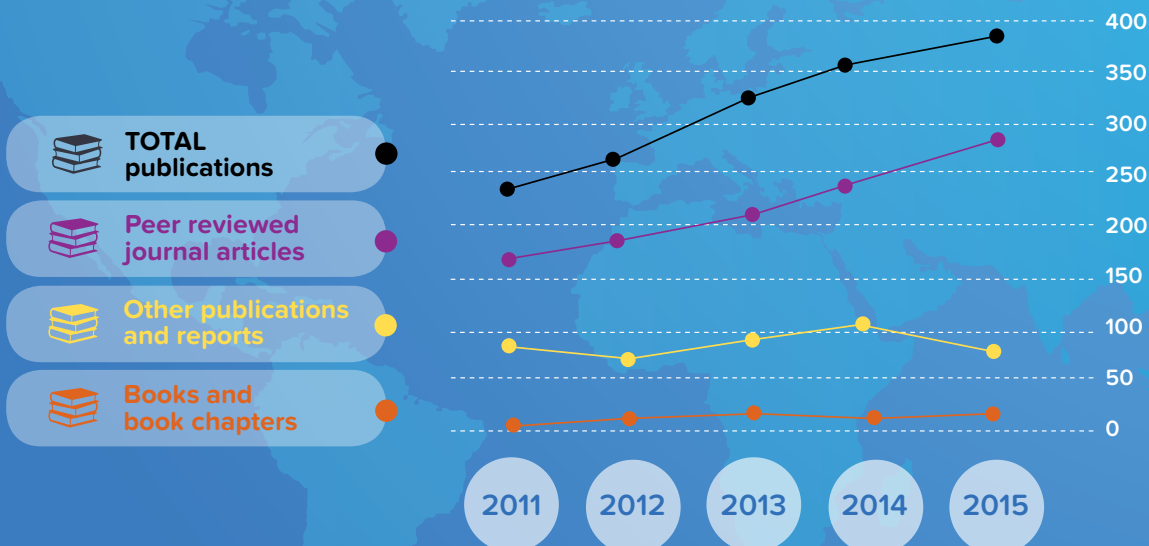
ADVANCING KNOWLEDGE

Our researchers are contributing significantly to the global bank of information on child health and wellbeing

We are **ACTIVELY COLLABORATING** with **colleagues and institutions** around the world

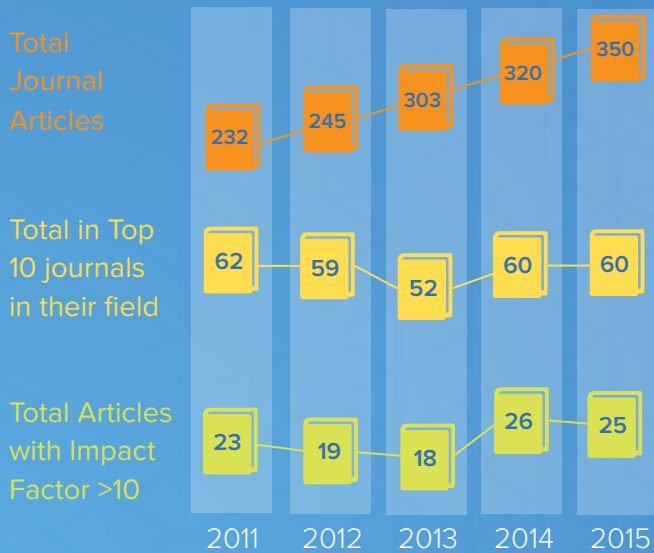


Our knowledge benefits **CHILD HEALTH AND WELLBEING RESEARCHERS** worldwide



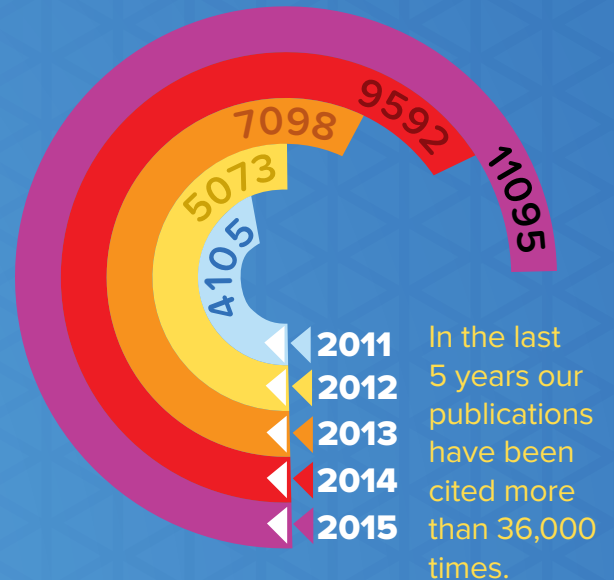
WE PUBLISH in the most **INFLUENTIAL JOURNALS** around the world

Publications over the past 5 years



SCIENTISTS AROUND THE WORLD use our work on child health and wellbeing to advance their **knowledge and research**

Number of Citations



Citation refers to a quotation or reference in a scientific article written by other researchers around the world

Our researchers are regarded as **INTERNATIONAL LEADERS IN THEIR FIELD**



7

of our **RESEARCHERS** have a **Scopus H-index GREATER than 40**

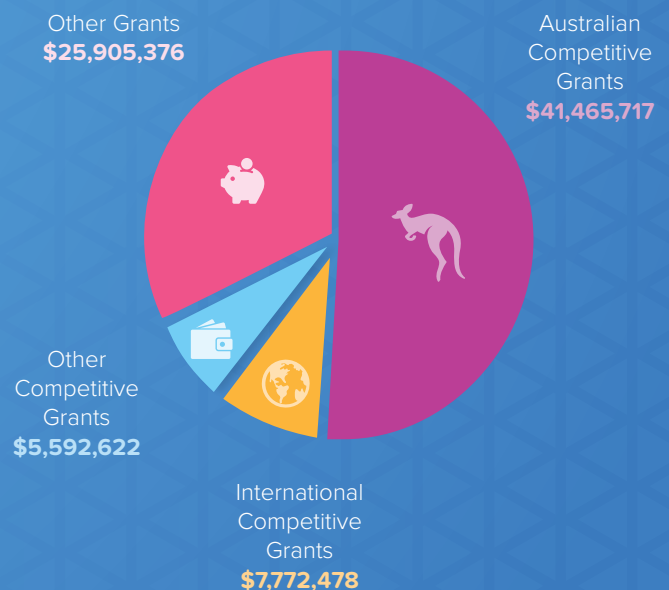
*H-index of 40 is proposed to characterise outstanding scientists likely to be found only at the top universities or major research laboratories (Hirsch 2005 PNAS)

Over the **past 5 years**, we have been awarded over



\$86 million

in **RESEARCH FUNDING** for our research



We are working with the most relevant people around the world to ensure we make a difference for kids and families

THE COMMUNITY is involved in **INFORMING THE WORK** that we do, ensuring it remains **relevant and translatable**

At Telethon Kids we have:



179
consumers

ON



22 **committees**
projects
programs

supported by the Consumer and Community Involvement Program

We are working with 7 of the Top 10 international pharmaceutical companies



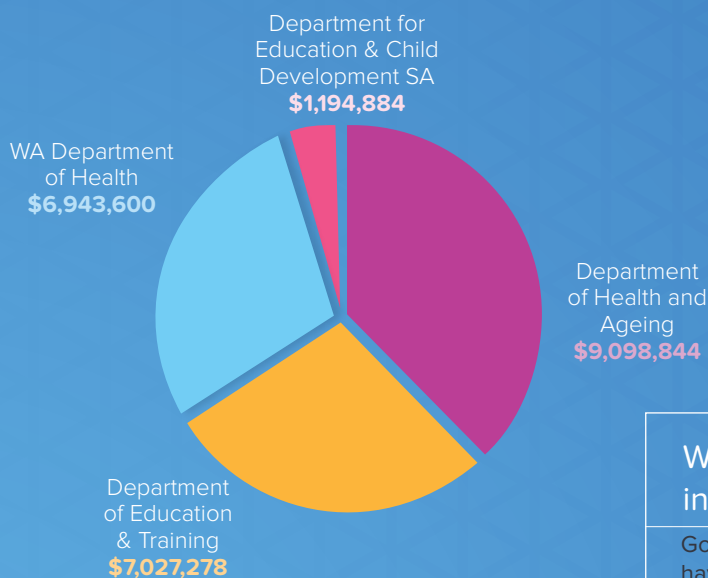
Our research has direct **commercial relevance**, which we protect to ensure that the inventions have the potential to make it to the clinic



23 active
patents



We work closely with government to ensure **OUR RESEARCH** is able to have an **IMPACT** on **GOVERNMENT POLICY**



12

reports provided to government on topics such as **mental health**, **fetal alcohol spectrum disorder** and **early years**

We have received over **\$22 million** in **government contracts** between 2011-2015

Government Departments providing contracts <\$400K/5 years have been given a cumulative \$ value

Our clinical research includes improving the diagnosis of diseases and testing new therapies and devices **TO ENSURE** children receive the **BEST TREATMENT** for their conditions



UNDERSTANDING HUMAN DEVELOPMENT & DISEASE

- Infections & Vaccines
- Ear Disease
- Language Development
- Newborn Encephalopathy
- Obesity
- Nutrition
- Hypospadias
- Asthma

DIAGNOSIS

- Cystic Fibrosis
- Biomarkers of Obesity
- Diabetes
- Rare Diseases

PREVENTION

- Vaccines including:
 - Influenza
 - Hib
 - Meningococcal
 - Pneumococcal
- Allergic Disease
- Asthma

DEVICES

- Diabetes
- Obesity
- Autism

THERAPY

- Asthma
- Bronchiolitis
- Dermatitis
- Cystic Fibrosis
- Autism Spectrum Disorders
- Gastroenteritis
- Mental Health
- Infectious Diseases
- Allergy

RESEARCH CAPACITY BUILDING

We are committed to training the next generation of researchers and ensuring we build collaborative networks to support child health research in Western Australia and beyond

Students from around Australia choose to **STUDY** at the Telethon Kids Institute



In 2015, we had
123 students

13

Honours

11

Masters

8

MD

91

PhD

Over the past 5 years



66 PhD
STUDENTS

have successfully obtained their **DOCTORATE**

Enrolled through:

1	Australia National University
4	Charles Darwin University
8	Curtin University
3	Edith Cowan University
8	Murdoch University
1	University of New South Wales
1	University of Queensland
1	University of Notre Dame Australia
96	University of Western Australia

Our researchers were members of more than **200** external research committees during 2015



65

94



53

People actively involved in our **RESEARCH FOCUS AREAS**

77



**ABORIGINAL
HEALTH**

115



**CHRONIC AND
SEVERE DISEASES**

289



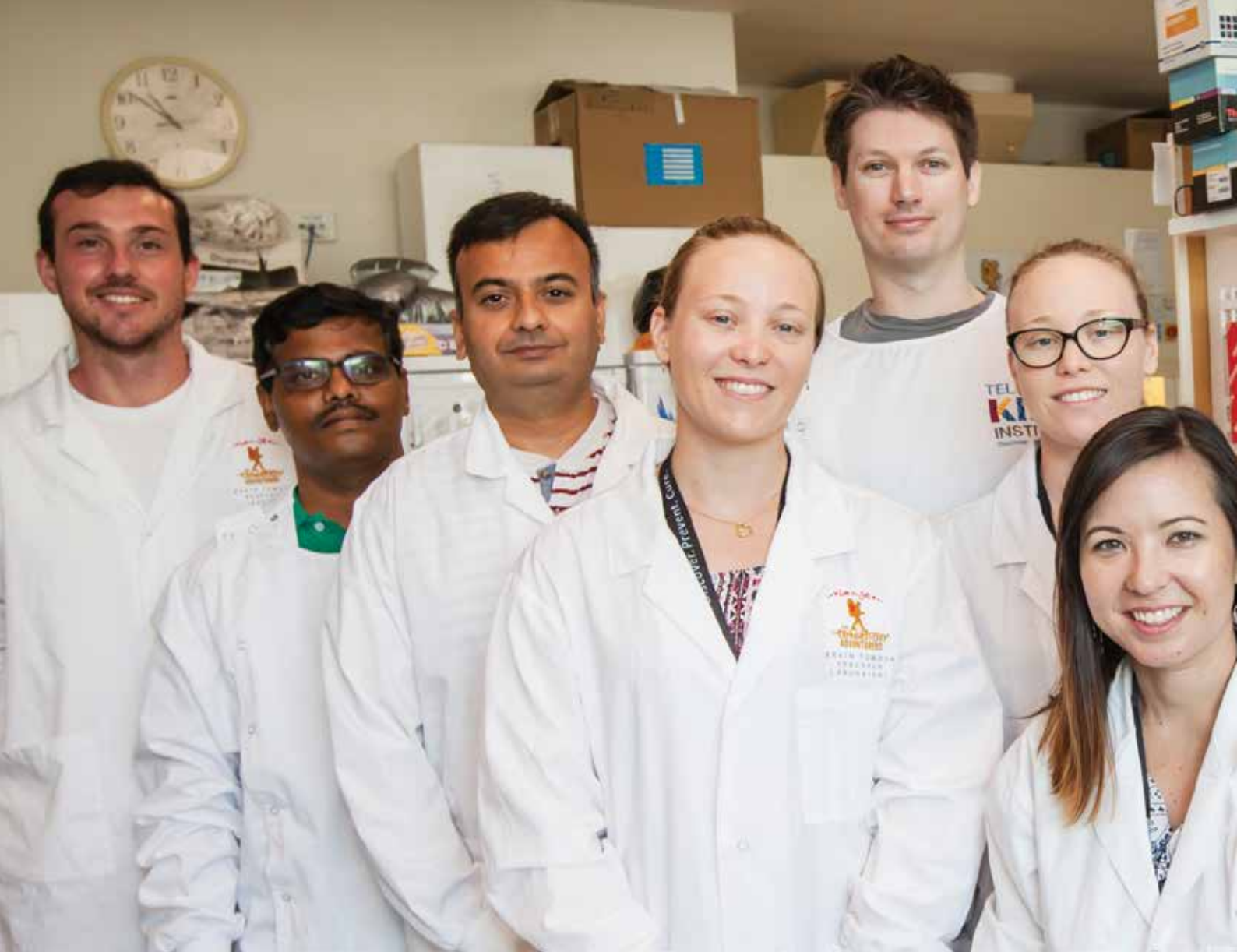
**BRAIN AND
BEHAVIOUR**

220



**EARLY
ENVIRONMENT**





Discover. Prevent. Cure.

Discoveries in health and medicine don't happen overnight.

In the real world of research, eureka moments are few and far between.

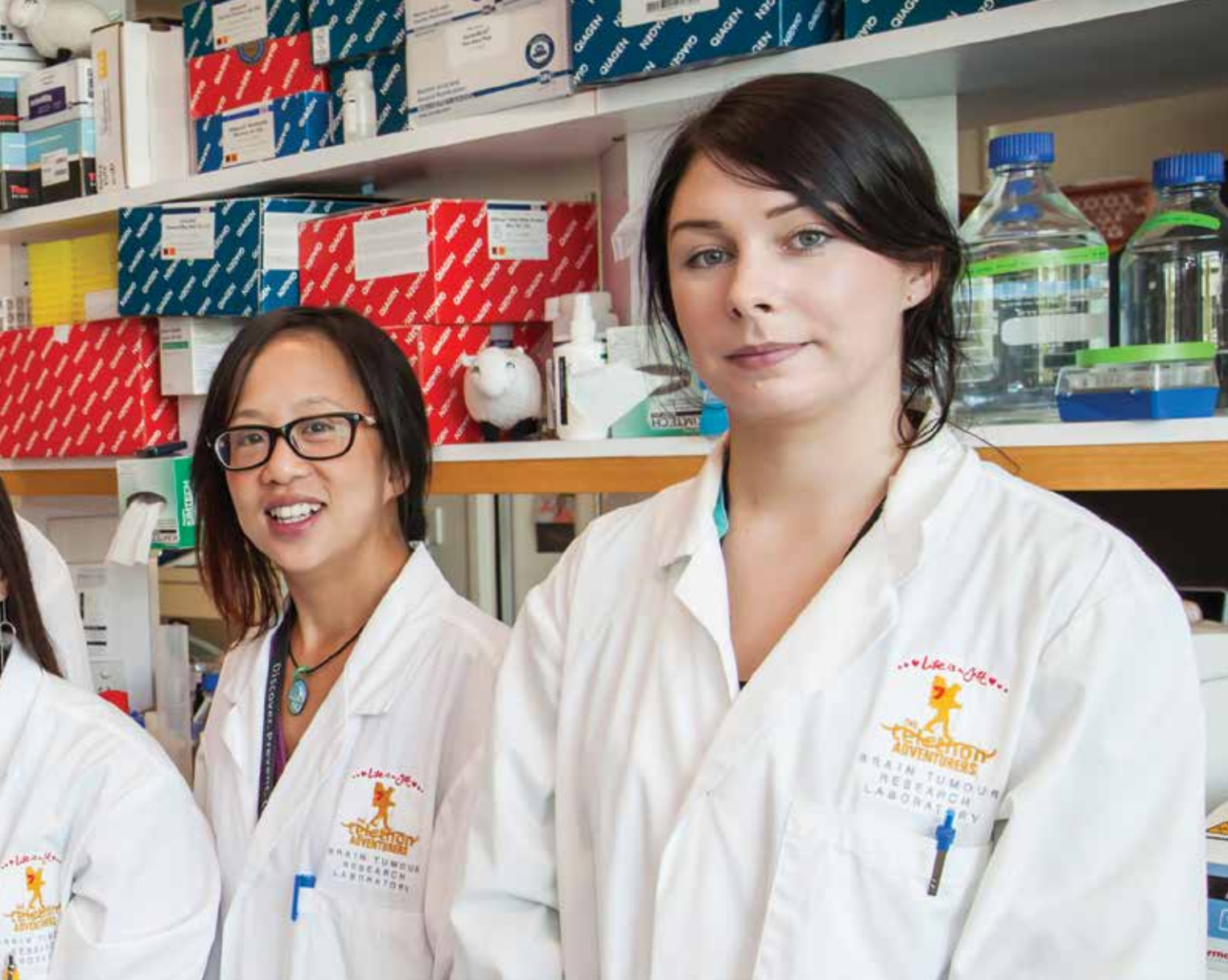
Instead, there is a pipeline of research over many years to build understanding of disease, find out how we might tackle it and then ongoing evaluation to see if cures, treatments or interventions have worked.

It's an incremental process with many milestones along the way, all of which contribute to the global effort to give our kids and families the best possible health and happiness.

Here at Telthon Kids, our dedicated researchers are passionate about discovering causes, cures and treatments for the illnesses and diseases that target our kids and young people.

Our laboratory-based researchers are discovering the mechanisms behind how disease develops.

Our population health researchers are using surveys, questionnaires and databases to find patterns and trends of disease in populations of people.



In the clinic, we are testing new therapies and interventions as well as ways to better manage disease.

We create and foster collaboration with researchers, practitioners, service providers, our partners and the community, to translate our research into the next steps on the research pipeline to deliver tangible benefits to kids and families.

Our IMPACT Report provides a snapshot of research at Telethon Kids. Find out more about how our researchers are making a difference at telethonkids.org.au

TRANSLATION

This research has been actively translated into policy or practice

PARADIGM SHIFT

This research changes the very way scientists think

IN THE PIPELINE

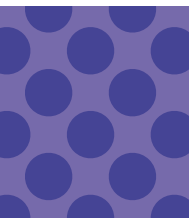
This research is in the pipeline towards translation

COLLABORATING FOR IMPACT

And this research shows how we work with others to make a difference



TRANSLATION



FOLATE WIN FOR ABORIGINAL BABIES

After 30 years of hard work, Telethon Kids Institute researcher Carol Bower is celebrating the final confirmation of all that she ever dared hope for.

Numbers have been crunched and revealed that the mandatory fortification of wheat flour for bread-making with the vitamin folic acid has done its job extremely well.

Lobbied for vigorously by the Institute and introduced across the country in September 2009, it's been hugely successful at increasing folate levels and dramatically reducing the rates of serious birth defects in the Aboriginal population.

The fall-off in spina bifida and other neural tube defects (NTD) has been significant, with a 68 per cent reduction in prevalence in the WA Aboriginal population data recorded by the WA Register for Developmental Anomalies. This comes on top of a 15 per cent reduction recorded for the WA population as a whole.

With the gains reported recently in the *Australian and New Zealand Journal of Obstetrics and Gynaecology*, after the analysis of data on 52,919 Aboriginal births from 1980 to 2014, this is the first scientific paper to show the real and tangible impact of fortification in Australia - a Federal Government decision which Professor Bower and Institute Founding Director and Patron Professor Fiona Stanley fought hard for.

Not only did their research help confirm the link between inadequate levels of folate and neural tube defects, they personally led a number of promotional campaigns encouraging women to increase their folate intake and raising awareness of the effectiveness of bread fortification.

"It's great news," said Professor Bower. "Neural tube defects are devastating birth defects of the brain or spinal cord, which can cause serious disability and even death.

"And the Aboriginal population was at a higher level to start with – with the defects being almost twice as common – so there was more benefit to be gained there."

Folate levels have traditionally been much lower in Aboriginal communities, where there is less access to fresh fruit and vegetables which contain the essential vitamin.

Yet adequate folate levels in the diet of women before conception is essential to reducing the risk of disruptions in the baby's neural tube as it closes within the first few weeks following conception.

Concerns were raised a decade ago when promotion of the use of folic acid supplements (from 1992) and voluntary fortification of several



The folate story

1980

WA birth defects register established by Fiona Stanley and Jane Seward

1981

Smithells et al publish a paper that suggests maternal vitamin supplementation may reduce the risk of neural tube defects, providing a stimulus for similar research in WA

1982-1985

Using the register, a WA case control study of folate intake and neural tube defects confirms the link that adequate maternal folate before and in early pregnancy reduces neural tube defects by around 70%



Professor Carol Bower

1992

We established the first health promotion program in Australia to inform health professionals and women of childbearing age about the benefits of folate

1995

Australia approves voluntary fortification of some foods with folic acid

1996

Voluntary fortification begins

1996+

Using register data, compared births from 1980-1995, a 30% fall in neural tube defects seen in births from 1996 onwards

1997 - 2000

Using the register, a WA case control study shows the health promotion program is not reaching all segments of the target population and voluntary fortification is only reaching half the target population

foods (from 1995), failed to bring the same gains to WA's Aboriginal communities as seen in the general population.

An increasing disparity in the birth prevalence of NTDs between Aboriginal and non-Aboriginal infants then emerged, increasing from a 42 per cent excess in 1980–1992 and reaching an almost twofold difference in 1996–2000.

“And very sadly a lot of these Aboriginal babies were stillborn or died at birth from anencephaly,” said Professor Bower. “So, unless you have got something like the WA register to be tracking these cases, the higher prevalence doesn't reach consciousness in the population as a problem.”

In addition to the reduction in NTDs, the increase in folate levels brought by fortified bread is expected to lead to gains in the general health of both Aboriginal men and women.

“Aside from pregnancy and preventing neural tube defects, this could be a big plus for the Aboriginal population as whole because being folate deficient can cause anaemia and ill health,” said Professor Bower.

In the Institute study analysing blood samples taken at Derbarl Yerrigan Health Service in Maddington and the WA Country Health Service in the Goldfields, for the 95 Aboriginal men and non-pregnant women aged 16–44, no participant was folate-deficient post-fortification. Yet in earlier pre-fortification samples, 10 per cent of women and 26 per cent of men had deficient red cell folate levels. Also there was no evidence of B12 deficiency.

Most ate fortified shop-bought bread at least weekly and half ate it every day.

“From the two Aboriginal groups that participated and Aboriginal researchers involved in the study, we have had some good feedback,” said Professor Bower.

“We were told that there are ‘all these little bits’ that contribute to closing the gap in life expectancy and that this is one of those.

“It's important.”



What's next?

▶ Professor Bower has now re-focused her efforts on to alcohol research and Fetal Alcohol Spectrum Disorders (FASD).

“My interest is primary prevention, and alcohol is one of the things that we can do something about,” she said.

“Folate was a ‘good news’ message, something you can do. Whereas alcohol is something you should not do, so I think that it may be just a little bit harder.”

2001

An evaluation of voluntary fortification shows relatively few foods had been fortified (only 104 foods by 1999, mostly different brands of breakfast cereals)

2004

Assessment for mandatory fortification with folate in Australia began

2007

Australia approves mandatory fortification of bread making flour with folic acid

2009

Fortification of bread making flour with folic acid becomes mandatory

2015

Using the register, research shows spina bifida and other neural tube defects have dropped by 68% in the WA Aboriginal population and by 15% for the WA population as a whole, since mandatory fortification instituted



GLOBAL RESEARCH FOR RARE DISORDER

Fuelled by a determination to fight back against a rare incurable genetic disorder that emerged in seemingly healthy baby girls and began robbing them of their developmental milestones, Telethon Kids Institute researchers set out on a worldwide search to find out all they could about Rett syndrome.

Looking well beyond the 30 families affected in WA, they established an Australian population-based longitudinal study group (AussieRett) and a world-first international database of thousands (InterRett) that have highlighted crucial similarities and differences.

Insights were revealed through extensive parent questionnaires on the challenges of daily living as regression occurs, when ability to talk and walk may be lost. Also through DNA sampling, video footage and health and wellbeing updates.

Collected with the aim of improving quality of life, these have already contributed significantly to the on-going quest to find a cure and prevent the severe disability.

Parent and carer feedback has continued to steer the research of Dr Helen Leonard and Dr

Jenny Downs and the Institute team to uncover unmet needs, reasons for misdiagnosis and links between genetic findings and clinical characteristics.

Also, it has led to them formulating comprehensive guidelines for the clinical assessment and management of complications such as scoliosis, gastrointestinal issues and poor growth, nutrition and bone health.

Focused on better treatment, care and comfort, these well-circulated guidelines are already showing the potential to contribute to improving life expectancy. Institute-collected data has revealed that girls with severe scoliosis who have a spinal fusion are usually healthier and have a longer life expectancy than those who do not have a fusion. Scoliosis has a squashing down effect on the lungs that compromises respiratory function.

Other important findings have come from research collaboration between the Telethon Kids Institute and Israel, which led to the identification of a genetic variation that influences the severity of Rett syndrome symptoms. The discovery was made of a correlation between the severity of clinical symptoms and a common brain-derived neurotrophic factor (BDNF) polymorphism.

“We have listened to what families have told us are their concerns and exactly what they wanted to know,” Dr Downs said.

“And what we have produced really is world-first material.”



Dr Jenny Downs



Rebecca and Jon Watson with daughters Marlee & Maddie

Amongst all of this, Dr Leonard and Dr Downs have still found time to act as advocates for their Rett syndrome families, informing physicians and surgeons of their needs and producing easy-to-read guides to treatment and care. Also, they personally answer, between them, an average of two to three phone calls a week from parents and carers with questions on research insights into vital day-to-day matters such as sleep and feeding.

“We have been told that we have put Rett syndrome on the map and that is fantastic,” said Dr Downs.

Only twenty years ago, Rett syndrome was a relatively unknown disorder. Around this time, Dr Leonard was inspired to switch her focus to investigating rare conditions, when witnessing the distress of a family that only had a small paragraph in a medical text to guide the care of their child.

“When I started my research in 1993, we did not even know that it was a genetic disorder,” said Dr Leonard.

“And until it was clinically defined, girls with Rett syndrome were often misdiagnosed as having a physical disability such as cerebral palsy or a developmental disorder like autism.

“When diagnostic testing became available, for a couple of years we went back and collected DNA on all the children and identified if they had a mutation or not.

“Through this, we found that children who had a milder form of Rett syndrome and milder mutations were often being missed until they were much older, 10 to 14 years, and, on occasion, until adulthood.

“And whilst Rett syndrome is associated with a gene on the X chromosome, our research has shown that boys can also develop the disorder.”

When Dr Downs joined the study 10 years ago, she knew she was in for the long haul.

“There were many very beautiful girls who were being looked after so well by their families in homes all around Australia, and there were

characteristics about this situation that had an extraordinary impact on me,” she said.

“That the girls were developing fairly normally and then their lives turned upside down with the onset of regression, when skills were lost. And I could not believe that that could happen.

“It really inspired me to get very involved, to understand more about this condition and help out.”

What's next?

- ▶ Working in China on an intervention project that looks at whether an early enriched environment can limit disability and aid brain development by impacting on levels of BDNF proteins.
- ▶ Raising awareness among clinicians about the presentation of Rett syndrome *MECP2* abnormalities in baby boys.
- ▶ Collecting information on individuals with a mutation in the *CDKL5* gene which may have some clinical features similar to Rett syndrome.

RETT SYNDROME: THE NUMBERS

- Occurs in 1 in 9000 baby girls.
- Around 15 babies born a year across Australia.
- One a year, on average, born in WA.
- In WA, about 30 families now affected.
- More than 400 people on national database
- Over 2000 people on international database
- Institute now working with 200 families in China.
- About 1000 babies born in China every year.

Rett syndrome

A severe neurodevelopmental disorder mostly affecting females. Those with the condition appear to develop normally until 6 to 18 months of age when they enter a period of regression, lose speech and motor skills and develop repetitive hand movements. Common problems include seizures, irregular breathing patterns, spinal curvature, low bone density and gastrointestinal and sleeping issues. In 1999, a mutation in the *MECP2* gene on the X chromosome was found to be associated with the disorder. Most mutations are sporadic (not inherited).

Marlee

Telethon Kids Institute proved to be a “lifeline” for parents Rebecca and John Watson as Rett syndrome “trapped” their precious 5-year-old daughter Marlee and robbed her of the ability to walk and talk.

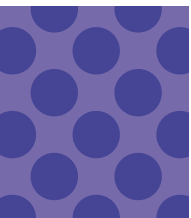
It is through Dr Leonard and Dr Downs, that they have learnt how to ensure she lives her life “to the fullest”. Now, the parents are armed with much-needed medical and communications strategies and life stories of others who achieved their desired goals.

“They are only a phone call away and are always available,” said Rebecca.

And in the first few months of “stumbling in the wilderness” after diagnosis, the researchers had calmed the family and strengthened their determination.

“After talking to them, I came away thinking, ‘Yes, we can do this,’” said John.





EXTRA WHOOPING COUGH SHOT TO PROTECT BUBS

Toddlers now get an additional whooping cough vaccine to protect them against the potentially deadly disease.

The change to the National Immunisation Schedule for whooping cough (also called pertussis) comes as a result of work by researchers at the Wesfarmers Centre of Vaccines and Infectious Diseases at the Telethon Kids Institute.

Telethon Kids researchers recently completed a study in collaboration with the National Centre of Immunisation Research and Surveillance, which showed the protection children receive from their three baby doses of the acellular (aP) whooping cough vaccine starts to wear off after a couple years.

Lead researcher and paediatrician Dr Tom Snelling says this means that children are at increased risk of whooping cough before they have their booster dose at four years of age.

"This is important because three year olds with whooping cough can infect any baby siblings," he says. "As a result of this research, Australian parents will now be given the opportunity to have their child boosted against whooping cough at 18 months, rather than having to wait until four years."

Telethon Kids Institute researchers also collaborated on another project which assessed whether vaccinating parents against whooping cough helps to protect their newborn babies.

The idea is that if parents are protected then their babies will be unlikely to come into contact

with infection," says Dr Snelling from the Telethon Kids Institute.

"This could be especially helpful in the first few months of life when a baby is too young to be fully protected by their own immunisations."

Researchers found that babies born to immunised parents were indeed half as likely to be infected with whooping cough compared with babies born to parents who had never received a whooping cough booster.

However, waiting until after the baby is already born for parents to receive this booster dose appears to be too late, probably because it takes a few weeks for the booster dose to take effect.

"We now know from subsequent research from overseas that the optimal time to provide booster doses of whooping cough vaccine is in the last few months of pregnancy," says Tom.

"This strategy protects both the mother and also provides protective antibodies to the newborn through the placenta."

"Fathers who have not received a booster should also receive one, preferably before their baby is born."

A whooping cough booster has recently become available for all WA women who are pregnant.

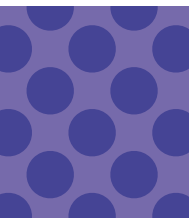


What's next?

- ▶ Telethon Kids researchers are leading a nationwide case-control study which is examining whether children who receive the whole cell pertussis vaccine in infancy are at lower risk of developing food allergies compared with infants who have not. This study should be finished by the middle of 2018.
- ▶ We also plan to pilot the use of whole cell pertussis vaccines in a mixed whole/acellular vaccine schedule, with the expectation this will result in longer lasting protection against whooping cough and might also be a feasible way of lowering the risk of allergic diseases. Currently the acellular vaccine is the only one used in Australia.



Dr Tom Snelling



SUN SAFE: BALANCING THE RISKS AND BENEFITS

Australians are taught to be cautious about sun exposure because of the risk of skin cancer. But recent publicity about vitamin D deficiencies has left us confused about whether we should stay out of the sun or seek out its rays.

The Telethon Kids Institute's D-Light program, set up in 2014 as a collaboration between multi-disciplinary researchers, aims to shed light on the amount of sun exposure that will promote good health in children and adolescents.

Professor Prue Hart, head of the Inflammation Laboratory, is looking into the effects of ultraviolet radiation and vitamin D on the immune system.

"We know sun exposure can give you skin cancers but there are very significant internal health benefits of sun exposure, including improvements in our mental, bone, metabolic, respiratory and general health," Professor Hart said.

"We must better understand where the balance lies. We must better understand the molecules involved in the health benefits and perhaps find agonists or pharmacological mediators that can replicate the effects."

D-Light members are investigating the effects of UV radiation exposure (as in sunlight) and vitamin D on allergic reactions and asthma, obesity and the eye disorder myopia. There is also an ongoing trial giving narrow-band UVB phototherapy to people with an early form of multiple sclerosis.

"Our work also shows that one of the most important roles of vitamin D may be in development, stimulating optimal development of lungs, brain and bone, and perhaps other organs," Professor Hart said.

"It has been proposed that most childhood conditions can benefit from sunlight exposure

and/or vitamin D, including both type 1 and 2 diabetes, cardiovascular disease, allergies, asthma, autism and other brain developmental disorders, respiratory infections and bone development."

Professor Hart said recent studies suggested that pill popping with vitamin D was not the answer for regulating your immune health.

"Supplementation trials with vitamin D have not shown the hoped-for benefits," she said. "Instead, we realise that your vitamin D level is really a marker of recent exposure to sunlight but that it is all the other molecules formed in skin upon sun exposure that may be the active mediators of the benefits to our health."

Professor Hart and her colleague, Professor Robyn Lucas, also worked with the Cancer Council WA to update its guidelines on safe sun exposure in winter months.

But she said the recommendations were still based on research completed in adults. "We need to better understand the consequences of sun exposure for children and where the safe balance of sun exposure may lie," she said.

"It is easy to say that in winter, schools should have sport lessons in the middle of the day so that children take off their jumpers. In summer, responsible sun advice is not clear. At present, we support current Cancer Council recommendations for West Australians as they are built on the best evidence that we have. However, more research is needed and more knowledge of the biologically active molecules produced by cells in the skin of children and adolescents."

Institute researchers are also developing a mobile phone app that will take a photo of your skin and give appropriate sun advice for your skin type.

“It is so important for Australians to understand the checks and balances of exposure to their greatest environmental influence,” Professor Hart said. “We propose that a personalised determination of the optimum level of sun exposure for you will allow you to avoid skin cancer development but maintain optimal homeostasis of your immune system, and allow optimal metabolic, lung and brain health.”

How much sun should we get?

According to Cancer Council guidelines, most West Australians get enough vitamin D through incidental sun exposure. But during June and July, people living in the southern part of the State - Perth or below - should go outside without protection for 30 minutes a day around midday.

What's next?

- ▶ Search for pathways and downstream molecules involved in the beneficial health benefits of sun exposure: “We are entering an exciting era where vitamin D is considered only one of many molecules induced by sun exposure that may benefit our health. We need to better understand the other molecules induced in skin by UV exposure. If we can dissect the good from the bad, we will seek to pharmacologically replicate the beneficial effects.”
- ▶ Develop better evidence supporting sun exposure advice for children.



Professor Prue Hart

MAKING THE RIGHT DECISION ON AIR TRAVEL

Professor Graham Hall is looking at the effect of air travel on premature babies, with his research already contributing to international guidelines.

Baby Ryker, who was born at 34 weeks, has already been up in the air multiple times.

When his mum Sarah went into labour prematurely, she was airlifted from Hopetoun to Perth to give birth to her 2.2 kilogram son. Four months later, the family wanted to visit Melbourne and Adelaide for Christmas so they could introduce Ryker to extended family, but as with most pre-term babies, there were concerns about his lung development.

“I found out that oxygen tanks were very expensive and thought about cancelling, which would have really disappointed his grandparents,” Sarah said.

“Fortunately we were able to participate in the research at Princess Margaret Hospital, which meant the oxygen bottle was free and we were told exactly what to do if Ryker’s oxygen levels dropped. We documented his condition on the flights.”

“I was definitely worried, but Ryker was fine all the way. It was a great trip and I hope the research helps other mums in the same situation.”

The research into hypoxia, which is a drop in oxygen saturation during air travel, is currently underway at the Telethon Kids Institute, led by Professor Graham Hall, in conjunction with Princess Margaret Hospital.

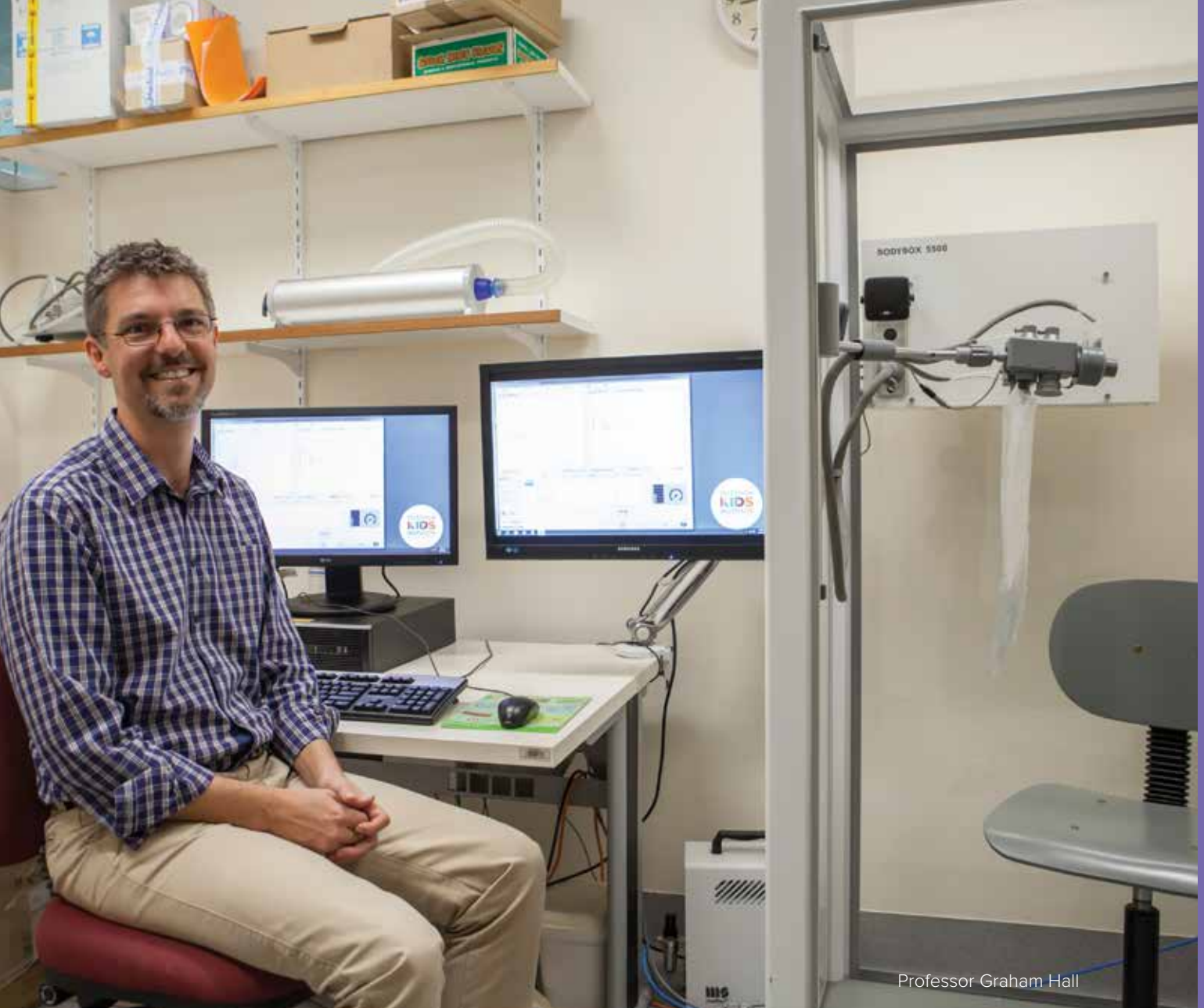
“Due to the effects of altitude, air travellers are breathing less oxygen than normal, leading to lower oxygen levels in the blood, or oxygen saturation,” Professor Hall explains. “While this is perfectly safe for healthy adults, children and babies, the lungs of pre-term babies are not always mature enough to cope with changes in oxygen levels.”

The research uses pre-flight testing on the babies by lowering oxygen levels in simulated conditions on the ground, at Princess Margaret Hospital. The babies are also monitored during the actual flight and given oxygen if it’s required.

Professor Hall, who is head of Paediatric Respiratory Physiology at Telethon Kids, said his passion for the project began several years ago when premature babies who’d reached their due date were being tested and assessed before their flight home to a regional area.

“At the beginning, the tests we did were only based on evidence from adults with respiratory problems, so it all started because I wanted to know if this was the right test for these very small babies,” Professor Hall said.





Professor Graham Hall

“Our latest work is looking at whether babies who were born pre-term can fly without oxygen once they’re one month to 12 months old. Flights are often necessary for medical appointments as well as families, like Sarah and Ryker, wanting to travel for holidays.

“For our research we do the flight test on the ground and then we teach families how to use a monitor and oxygen tank in the air if the child’s oxygen saturation drops below 85%. Flying with babies is already challenging so we appreciate the help from families who are carrying oxygen and taking notes from the monitor,” he said.

Professor Hall says their participation in this work is making a real difference because the test results will help all doctors to give evidence-based advice about flying with prematurely born infants.

Professor Hall’s latest study is due to be completed at the end of 2016.

- ▶ Professor Hall’s work is already creating an important international reference for clinicians such as GPs, who need to give advice to families with pre-term babies.
- ▶ International guidelines on air travel for premature babies are now based on this research by the Telethon Kids Institute, Princess Margaret Hospital and King Edward Memorial Hospital.

BUILDING THE BEST COMMUNITIES FOR EARLY CHILD DEVELOPMENT

Every child deserves the best possible start in life. But what is essential for this? and who needs help the most? - these are the big questions.

The Telethon Kids Institute has invested more than a decade in finding the answers, with its work leading to the roll-out across Australia of the world's first ongoing "proven and reliable measure" of early childhood development.

Known as the Australian Early Development Census (AEDC), the data uncovered and analysed from this not only underpins most major early years initiatives launched in Australia, it continues to steer policy direction in education and health, future research and the decisions of local governments, schools and community groups.

Australia now relies on it to expose and map unmet needs, work out how to respond, guide resource allocation and reveal what makes a difference and what has failed to do so.

Early work by Institute researchers, piloting a Canadian-developed Early Development Index (EDI) in Perth more than 10 years ago, attracted the attention of the nation and progressed to the development and introduction of the population-wide AEDC.

With the Australian Government providing \$21.9 million for implementation, its roll-out across the country in 2009 was fuelled by the understanding that the growth of young brains is shaped not only by genes and nutrition, but also experiences and opportunities provided in early childhood.

Keeping track of how every child has developed by the time they start their first year of full-time school, the AEDC measures five key areas: physical health and wellbeing; social competence; emotional maturity; language and cognitive skills; communication skills and general knowledge.

Through this, the AEDC has shone the light on how vitally important the early years are. It revealed that children who are developmentally vulnerable on the language and cognitive domain, or on the communication and general knowledge domain, have lower NAPLAN numeracy and reading test scores in Year 3 and do not catch up.

Also, it highlighted that where children live can impact on their development. Of children living in major cities, 21 per cent were developmentally vulnerable on one or more domains, compared to 47 per cent of children in very remote areas.

And the AEDC - conducted every three years - continues to keep watch. The third collection of AEDC data, undertaken just last year, has enabled communities, governments, early childhood professionals and researchers to compare AEDC data across time and, for the first time, to start tracking emerging trends.

The 2015 results show that around one in five children were developmentally vulnerable on one or more domains, which is in line with results

The AEDC story

1999

Early Development Index (EDI) developed in Canada

2002

EDI adapted for use in Australia by Sally Brinkman and Bret Hart

2003

EDI piloted in Perth with 4300 teachers of pre-primary students

2004 - 2008

Telethon Kids and the Centre for Community Child Health surveyed over 80,000 children in 60 communities across Australia as part of the Australian Early Development Index (AEDI)



2004 - 2008

AEDI adapted for use in Indigenous communities

2008

Council of Australian Governments endorsed the AEDI as a national progress measure of early childhood development

2009

AEDI completed nationwide for the first time

2012

Second round of AEDI data collection

2014

Programme name changed to Australian Early Development Census

2015

Third collection of AEDC data

from 2012, and an improvement on 2009. However, differences in developmental vulnerability across the domains and among children from different demographic profiles, suggests there is more work to be done.

Telethon Kids Institute lead researcher Dr Sally Brinkman said it was exciting to see the results from the third round.

“The AEDC is a proven and reliable measure of children’s development and the results help communities understand what’s working well and what needs to be improved so that everyone in the community can better support the development of young kids before they start school,” Dr Brinkman said.

“It has been very rewarding to see how our early work in piloting the EDI in Perth more than 10 years ago has progressed to a national measure of child development.”

“In our pilot study back in 2003, we surveyed the teachers of more than 4300 pre-primary students,” Dr Brinkman said. “In 2015, the AEDC collected information on more than 300,000 children.”

Population data like the AEDC, provides the evidence required to support resource allocation decisions.

“It is a measure – across five domains - of the things that children need to be able to do well by the time they enter school,” said Institute researcher Dr Yasmin Harman-Smith.

“They are not aspirations - measures of what we would love children to be able to do. These are the basic things. If these things are lacking, then children are going to struggle.

“And they are indicators of what has gone well, or not so well, in children’s lives before they start school.”

The Institute continues to play a central role in supporting AEDC stakeholders to use the data. It has developed resources in easy-to-understand

Already the AEDC has acted as a major catalyst for change.

For example, in WA, it was influential in the development of;

- 21 Child and Parent Centres set up by the State Government in areas where higher levels of developmental vulnerability was shown. The centres, operated by non-government organisations in collaboration with local schools and other child service providers, focus on the coordination and delivery of programs and services.
- Enhanced Transition to School project, which will see the development of playgroups on school sites. This is a partnership between the Department of Education, Playgroup WA, the Department of Local Government and Communities and non-government school sectors.
- Connecting Community for Kids, a collective partnership approach in Cockburn and Kwinana that has secured funding from Woodside Development Fund.



Dr Yasmin Harman-Smith, Matt Williams MP, Dr Sally Brinkman & Alex Gordon at the 2015 AEDC National Conference

formats, including infographics, case studies and videos. Also it supports states and territories, early childhood educators, researchers and community groups to think about the data and to integrate it into their planning and monitoring processes.

The focus now is on aiding big policy decisions.

“We are helping stakeholders understand population data, and understand how they can use it for informing policy and practice,” said Dr Harman-Smith. “We supply strategic advice and support and training.

“And we have taken the approach of broadening people’s horizons about how the data can be used.

“While communities around Australia have taken up the AEDC, there is a focus now on supporting its use with stakeholders in government, local councils and schools.”

And the AEDC continues to teach Australia important lessons, including the need for a balanced approach between the provision of universal programs and targeted supports.

“There is a strong relationship between socio-economic disadvantage and developmental vulnerability,” said Dr Harman-Smith. “In communities with fewer socio-economic resources, larger proportions of children show developmental vulnerabilities.

“What generally happens is people like to target services then to those communities. But many more children live in the centre of the socio economic spectrum.

“So when you look at the number of children who are vulnerable in communities, rather than the per cent alone, you can see that there are many more vulnerable children in suburbs that would not normally be targeted with services and support.

“In order to ensure that all children and families receive the level of support they need, we need a strong universal service base with targeted supports for families facing additional challenges.”

Other valuable insights have been revealed in gender and jurisdictional differences, the impact of the neighbourhood built environment, impact of low birth weight and smoking, academic outcome predictors, mental health and bilingual student issues and teacher and parent views.

The AEDC programme involves a partnership with the Australian Government, State and Territory Governments, the Social Research Centre, the Centre for Community Child Health, the Royal Children’s Hospital Melbourne and the Murdoch Childrens Research Institute.



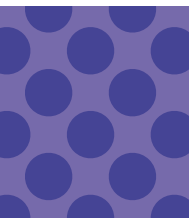
What's next?

- ▶ Using the 2015 census data to examine consistent trends.

Working on a low-cost measurement tool that can be used in developing countries to collect baseline data to monitor the success of early childhood reform programs financed by the World Bank.

Compare outcomes from around the globe and gauge the impact of such differing polices as maternity leave.





STARTING AND STAYING ON TRACK

Great gains have been recorded in the Pilbara where the nurturing of local children has been made a community-wide priority.

A decade of hard work, guided by the Telethon Kids Institute, has resulted in measurable improvements in the emotional, intellectual, physical and social development of Aboriginal children at the start of school.

And a significant positive shift has been detected in the number now showing multiple ready-for-school strengths. These strengths include self-regulation, high pro-social and communication skills and respectful behaviour towards peers, teachers and property, and curiosity about the world.

Revealed by a fine-tuning and re-focusing of early childhood development data to show strengths along with vulnerabilities, it has brought good news and renewed determination to Aboriginal communities

The gains in both town and remote communities, recorded between 2007 and 2012, have increased local confidence in the ability to “make a difference” and confirmed the “critical importance” of research and industry partnerships, said lead researcher Associate Professor Roz Walker of the Telethon Kids Institute.

The significant progress in improving early years outcomes was aided by BHP Billiton funding the 2007 ‘Staying on Track’ project and the 2010 joint partnership between the Telethon Kids Institute, BHP Billiton and World Vision Australia to make early investments to improve maternal and child health and increase opportunities and experiences for children in East Pilbara communities.

The ability to measure these changes over time and to measure strengths within the developmental domains has taken much effort

from Institute researchers, with implementation and translation led by Associate Professor Walker and data moderation and analysis led by Dr Sally Brinkman’s team at the Fraser Mustard Centre in Adelaide.

It has involved reviewing and comparing earlier regional research - Starting on Track which involved implementing the Australian Early Development Index (AEDI) survey across the Pilbara in 2007 and the Indigenous Adaptation of the AEDI in 2008 – and developing reliable mechanisms to allow comparison with the ongoing national census – the Australian Early Development Census (AEDC).

As early as 2002, the Telethon Kids Institute played a crucial role in validating the AEDI and then later making it culturally relevant to the needs of Aboriginal children and their influences on development.

To then enable a focus on strengths, the Institute went on to establish the Multiple Strength Index. This index is based on 39 ready-for-school strengths identified from among the 100 measures on the existing AEDC data collection checklist. The checklist is used to map areas where children may or may not be meeting ready-for-school requirements in physical health and wellbeing; social competence; emotional maturity; language and cognitive skills; communication skills and general knowledge.

For East Pilbara Aboriginal children, an analysis of results then revealed the good news that in 2012, 58 per cent of those starting school had a high level of strengths, compared to only 27 per cent in 2007. Also there had been statistically significant improvements across all developmental domains.



“These strengths were there, but they were not being highlighted,” said Associate Professor Walker.

“Now we are more aware of them, we can build on them with the parents and the schools.

“We are now able to show the benefits of using this information, collected at the local level, to work with groups as a catalyst for change.”

Significant progress to date was due to the whole community coming together and combining efforts, says Associate Professor Walker.

“We can’t say it was one particular program and we can’t say it was one particular school or strategy,” she said.

“What it was, I believe, is that we were able to harness community-wide mobilisation and an increased understanding of the importance of the early years.

“This has resulted in a real focus on ‘mums and bubs’ groups, developed by World Vision Australia and the YMCA, going out to remote places like Jigalong and working with the local mums and teachers and getting play equipment out to where there has never been play equipment before.

“It is hard for many people to understand how a \$5,000 grant for play equipment or a food bank program can significantly change young children’s lives; let alone begin to measure their long term benefits”.

What’s next?

- ▶ “We are taking the information back to the early years groups in the Pilbara and we are able to affirm that the work they are doing, and the incredible focus of a lot of government and non-governmental organisations and industry partners, is making a positive change,” said Associate Professor Walker.
- ▶ “It gives them an extra sense of excitement and enthusiasm that they are on the right track, as well as providing an important evidence base of the critical factors required to improve early years outcomes and an ability to evaluate these initiatives in the future.”



Associate Professor Roz Walker



BOOSTING LITERACY IN ABORIGINAL KIDS

Books are an important vehicle for children to learn new things, expand their understanding of the world and develop the skills to communicate and participate in society. That is why it is essential that Aboriginal kids have access to books that reflect their own experience.

And thanks to our partnership with the Warburton Breakfast Ladies and Men, we had the opportunity to launch a series of books at the Telethon Kids Institute that do just that.

The 23 books, were put together by community groups at Warburton, Warakurna and Wanarn, and some had been translated into Ngaanyatjarra language.

“I was most impressed about these books from Warburton – there are so few books in language and also they related to everyday aspects of life for people in that region,” said Telethon Kids Institute Founding Director Professor Fiona Stanley who helped launch the books.

“As well, they provided useful advice about a range of important issues to help the community improve outcomes for their children and youth, as well as the whole community,” Professor Stanley said.

The Telethon Kids Institute’s partnership with the Warburton Breakfast Ladies and Men started back in 2008, following the release of our ground-breaking WA Aboriginal Child Health Survey, which found very low academic outcomes and attendance in the region.

Researchers were granted a National Health and Medical Research Council seeding grant to help develop a program to strengthen the capacity of families and community to improve school outcomes.

One of the outcomes of that program was *The Breakfast Story Book*, a classroom literacy resource for Aboriginal children written by the Warburton Breakfast Ladies and Men with the help of Associate Professor Ernie Stringer and Associate Professor Roz Walker from the Telethon Kids Institute.

“The breakfast story book was hugely popular and gave the Warburton Breakfast Ladies and Men the confidence and inspiration to do more,” said Associate Professor Roz Walker.

“Eight years down the track, they have written another twenty five books which provide readers with an insight into the many cultural activities and events that are part of everyday life in an Aboriginal community. The young people are proud of their culture and highlight what it really means to be connected to country.”

Examples of titles include *Ngirrikiku-latju Yanu*, which translated to English means ‘*We went out bush for bardi grubs*’ and *Purtikutu-ya Yanu Yirliltuku*, which translated to English means ‘*Hunting for honey ants*’.

Groups that contributed to the books include Home and Community Care, Healthy Lifestyles, the Warburton Playgroup, Kunkga Girls Group, Environmental Health, Warburton and other schools in the Lands, and the local Police.

Professor Stanley said it was vital that the Telethon Kids Institute supported these empowering cultural actions.



Professor Fiona Stanley with senior Warburton women, representing the groups who produced the books

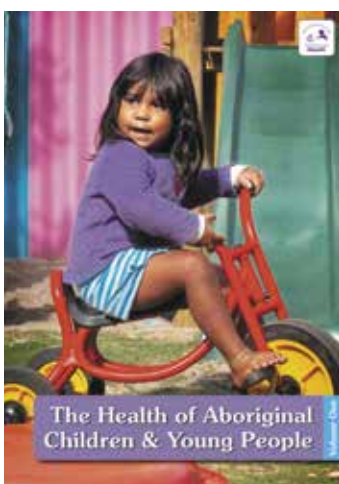
“The self-esteem from this kind of activity can permeate the whole group and in Canada and other places it has been shown to improve mental health and reduce suicides,” Professor Stanley said.

“The evidence is clear that if children are literate in their own language and learn English as a second language they have better development and manage school processes better. These books mean that they can use their own language and become proficient in that before taking on other languages.”

About Western Australian Aboriginal Child Health Survey

The Western Australian Aboriginal Child Health Survey (WAACHS) was the most comprehensive survey ever undertaken looking at the health, wellbeing and development of Western Australian Aboriginal and Torres Strait Islander children.

More than 5,300 kids from Perth to the most remote communities in WA were involved.



PARADIGM SHIFT



A NEW APPROACH FOR RESEARCH WITH ABORIGINAL COMMUNITIES

Winning the support of a remote Aboriginal community paved the way for a pioneering genetics study.

With Type 2 diabetes identified as a big health challenge for Indigenous people, this world-first genome-wide association study in an Australian Aboriginal population examined genetic variations that influence body mass index (BMI) and Type 2 diabetes.

Genome-wide association studies are used to identify genes associated with complex diseases and provide insight into risk factors.

In this study of a Western Desert community, genetic variations that influence a high BMI and Type 2 diabetes were found to be similar to those in non-Aboriginal populations.

Professor Jenefer Blackwell, head of Genetics and Health at the Telethon Kids Institute, said understanding the molecular basis to obesity and Type 2 diabetes in Aboriginal communities would assist in the development of better health management strategies.

She said it had been vital to overcome community concerns about the nature of genetic research and ensure culturally appropriate methods were employed.

“Overall, there was a huge mountain to climb initially to persuade Aboriginal researchers, Aboriginal communities, and Aboriginal ethics committees of the potential benefits of health-based genetic research,” she said.

“The first step for us was to gain the confidence and support of Aboriginal researchers at Telethon Kids Institute. The second step was to establish a rapport with a specific Aboriginal community, to learn from them what they perceived as major health issues where genetics might play a role, and to explain

to them what a study of genetic risk factors might tell us about disease pathways in their population.”

Working with the local Aboriginal Health Service and a remote-area school, they extracted DNA from saliva samples collected from about 400 people with Martu ancestry, including 89 with Type 2 diabetes.

“Studies in other communities worldwide had indicated that there was a heritable component of susceptibility to obesity and Type 2 diabetes but no one had looked at this using genome-wide analysis,” Professor Blackwell said.

The top association was between BMI and *NTRK2*, a gene which belonged to a pathway of genes that had already been shown to be genetic risks factors in other populations.

“*NTRK2* and the other genes in this pathway are providing signals in our brain that control our energy balance by regulating what we eat,” Professor Blackwell said.

“The more we understand about the pathogenesis of Type 2 diabetes, and how this relates to increasing obesity in the population, the better the advice that can be given. We aren’t necessarily at the stage of a magic bullet – a pill that will just cure everyone – but our work indicates that regulating our eating patterns will certainly help in prevention of Type 2 diabetes.”

Professor Blackwell said community participation in the project was essential. “We engaged with community to provide information and feedback in culturally-appropriate formats, including an art-based educational project for



Professor Jenefer Blackwell

feedback of scientific results,” she said.

Using storytelling and painting, local children worked with an animator to create a YouTube video called *The Story of the Goanna and the Gene*, which relates a story about four animals – the kangaroo, emu, goanna and eagle - and the effects of fast food and sugary drinks on the body.

Professor Blackwell said study team members also complemented the clinical care received by the community by undertaking additional specialist clinics. “All the data from these specialist visits has been recorded in Aboriginal Health Service records for local clinical use, and contributed to clinical phenotypes for genetic analysis,” she said.

“The genetic information we collected has also been applied in relation to other extreme clinical conditions in this population, including severe otitis media (ear infections) in children, and end-stage renal disease in adults.

“The data from our exome sequencing study has also provided the first Aboriginal reference panel for health-based research in Aboriginal populations. This data is already being used in the clinic as a reference panel to underpin diagnosis of rare diseases in Aboriginal Australians.”



What's next?

- ▶ Professor Blackwell said it was hoped that other researchers would take up the challenge to replicate the study in other Aboriginal populations. “That would provide stronger motivation for functional studies of these biochemical pathways to determine whether they provide targets for therapeutic interventions. We hope that much larger studies will be possible in the future so that they will be sufficiently well-powered statistically to obtain unequivocal results.”

What is BMI?

Body mass index is calculated by dividing your weight in kilograms by your height in metres squared. The result is used to determine whether you are in a healthy weight range for your height - between 18.5–25. This measure does, however, have its limitations, including not distinguishing between fat or muscle. For Aboriginals, a BMI over 22 is considered a risk factor for Type 2 diabetes.



YOUNG MINDS REALLY DO MATTER

The Telethon Kids Institute is playing a crucial role in showing how mental health services should be overhauled to ensure they are tailor-made to meet the pressing needs of a new generation of kids.

Kids who live with their smart phone in their pocket are constantly connected to the internet and surrounded by concerns about climate change and global unrest.

A surprising unexpected shifting emphasis was detected in the landmark 2nd Australian Child and Adolescent Survey of Mental Health and Wellbeing recently conducted for the Australian Government by the Institute, in partnership with Roy Morgan Research and the University of WA.

The biggest and most comprehensive ever, analysis of the results from 6300 households across the country revealed that while the overall prevalence of mental health problems in those aged 4 to 17 had remained stable at 14 per cent over that past 15 years, what had changed was the “mix” of disorders. The types and the gender and age at which young people were most commonly experiencing them were now different.

And for the first time, this recent Young Minds Matter survey managed to capture the voice of Australia’s youth, inviting them to answer, in private via a tablet computer device, questions on their own needs and how they seek help.

Around 90 per cent of those aged 11 to 17 took up this opportunity. And based on the information young people themselves supplied, the prevalence of major depressive disorder was nearly double that indicated in parent-reported information.

High rates of self-harm and suicidal behaviour in adolescent girls were also revealed.

“What we are hoping is that these results from this 2013-14 survey will now be used to continue to reform the mental health delivery for children and families across Australia, to ensure the development and targeting of services to those who need it most,” said the study’s chief investigator, Associate Professor David Lawrence from the Telethon Kids Institute.

“It certainly is an issue that needs to be taken very seriously. A significant number of young people are obviously experiencing a level of distress in their life that is having an impact on their functioning and impacting on their families as well.”

Joint chief investigator Professor Stephen Zubrick said the Institute had been surprised by the mix of disorders changing and what was driving this now needed to be explored.

“That is why it is very important to do this type of work,” he said. “We had no particular theory that would suggest it would change.”

“And now we need to tailor our clinical, school and community services to make sure we have the skills in our teachers, in our clinicians and with young people themselves to address those kind of mental health problems.”

Telethon Kids Institute involvement began 18 years ago, when Australia became the first country in the world to undertake a national survey of child and adolescent mental health and a plan was established for future snapshots. Embarking on this new area of research required the Institute to further



Associate Professor David Lawrence
and Professor Stephen Zubrick

develop effective measurement techniques to allow reliable exposure of emerging issues.

That initial 1998 survey exposed significant unmet needs, which then triggered substantial growth in mental health services specifically designed for children and adolescents. This included the establishment of headspace, Kids Helpline, KidsMatter and school social and mental wellbeing policies. Medicare's Better Access program for psychological and psychiatric support and counselling was also rolled out.

"When the first survey was conducted in 1998, we found only one of four kids who had a significant mental health problem had received any form of help in the six months prior to the survey, so that was instrumental in triggering a range of changes," said Associate Professor Lawrence.

"Those new services have certainly come through for kids. What we found in the recent survey is that a higher proportion of kids with a mental health problem are now receiving help.

"But there is still a substantial number of families that don't receive help or don't receive the help that they need at the time they need it, so there is still room for further improvement."

Professor Zubrick said insights on needs provided by the two surveys were invaluable.

"We can't really rely on clinic data, because there is only a subset of kids reaching clinical services," he said. "The value of Young Minds Matter is that it is a random sample of households and it's a community-based sample. It's what is actually out there in the suburbs, in the rural areas, what parents are faced with and what they are doing about it.

"And what we have gained is the voice of young people on what it is like to be growing up now.

"It's just staggering to see the changes. Twenty years ago, nobody had a mobile phone in their pocket. We did not have things like climate change on the agenda. We did not have the kind of global disruption that kids are watching and asking 'What kind of world am I going to be living in?'

"The other thing is that they know things about their mental health that we cannot know about by simply observing them.

"If a young person is deeply anxious or seriously depressed, we might not know as a parent simply by looking at their behaviour.

"They may be very skilful at concealing it and sometimes kids do not even know that they are suffering from conditions like that."

The Institute could now say with confidence that the prevalence of mental health disorders was about 14 per cent in Australia's child and adolescent population, said Professor Zubrick.

"That appears to be a pretty consistent proportion that we as a society are going to have to work with over time," he said.

Professor Zubrick said the first survey had created an understanding of what the need was and had resulted in a great number of services and quite a major pipeline of funding being put in place.

"This recent survey has allowed us to find out how that pipeline is being used and what has been the impact on young people," he said.

"And the survey found children and adolescents are certainly using the services that have been created specifically for them.

"Now, I think it is completely fair to ask, now that they are finding their way to youth-based services, 'Do we have the most effective services and are we delivering what we need to deliver?'"



What's next?

- Promote the results of the Young Minds Matter survey to researchers, families and service providers to use via the Australian Data Archive.
- Work to expand the survey to cover the mental health of Indigenous youth.



Key Results of the 2nd Survey

Fewer now have ADHD and conduct disorder but there has been an increase in the number of adolescents with major depressive disorder.

Adolescent girls had high levels of distress. One in five aged 16-17 years met diagnostic criteria for major depressive disorder, one in six had self-harmed in the past 12 months and one in 20 had attempted suicide in that time frame.

More than 50 per cent of young people with a mental health condition were receiving some kind of help and almost 90 per cent of those with serious disorders were getting help.

Schools play a key role in identification and management, with a school staff member among those to suggest that some help for emotional or behavioural problems was needed in 40 per cent of cases.



ON A QUEST FOR KIDS WITH CYSTIC FIBROSIS

A new way of measuring early lung disease in young kids with cystic fibrosis is changing the way we detect and treat CF, creating a more targeted and personalised approach.

Lung damage is the big killer of people with cystic fibrosis (CF). Once damage to the lung has occurred, it's irreversible resulting in many people with CF requiring a lung transplant to survive.

Detecting lung disease early is vital for intervention and therapy to give kids the best possible outcome. But accurately detecting disease in very young kids has not been possible with no standardised outcome measures currently available for children younger than 6 years.

This effectively excludes babies and young children from clinical trials, in an era where new, potentially disease-modifying drugs are becoming available.

This drove Institute researcher Tim Rosenow to search for a solution.

He started by looking at the current gold standard approach for detecting cystic fibrosis airway disease, chest CT (computed tomography). A chest CT scan provides a detailed 3D image of the organs of the chest cavity, right down to the airways and lung tissues.

A chest CT is the most sensitive measure of CF-related lung disease, and can detect the earliest signs of lung abnormalities even before the onset of symptoms or infection.

Researchers then look at these scans and score patients based on the amount of overall disease in each lobe of the lung - no damage gets a score of 0, less than 50 per cent damage gets a

score of 1, and more than 50 per cent damage gets a score of 2. This score, known as a CF-CT score, quantifies the extent of disease. But this categorical system was designed for use in adults with more severe disease and it is not sensitive enough to detect the mild disease seen in young children.

"We found that using the CF-CT score in young kids pretty much gave us the same result for every child," explains Tim. "The majority of kids would get a score of 1 as they had less than 50 per cent lung damage, which is what we would expect in the early days when CF lung disease is quite mild."

"Each year when the kids were re-tested, they would get a score of 1 again. It didn't give us any insight into whether their lung disease had changed by a little or a lot or what types of disease were affecting their lungs."

"We needed something better, to give us a more accurate picture of the lung health of these young kids with CF."

Tim had an idea.

Building on the gold standard chest CT, Tim had the idea of overlaying a grid in a way similar to stereology being used to count cells in tissues.

PRAGMA-CF was born. It was developed in collaboration with our research partners in Rotterdam with PRAGMA an acronym for Perth-Rotterdam Annotated Grid Morphometric Analysis.

"PRAGMA involves overlaying a grid on the CT images of a child's lung, and allocating each

grid square a colour based on the presence of various lung abnormalities,” explains Tim. “From this, the extent of lung disease, as a percentage of total lung volume, is calculated.”

There are three main types of lung disease researchers are looking for when they use PRAGMA to annotate the CT scans. Bronchiectasis, the most important lung abnormality in CF, which will be coloured red on the grid; bronchial wall thickening which will be coloured orange on the grid; and mucous plugging (when the airways are completely filled with mucous) which is coloured yellow on the grid. Normal lung tissue is coloured green.

Tim says this gives researchers the ability to detect lung disease extents as low as less than one per cent of the lung. It also allows them to accurately track the progression of CF lung disease from year-to-year with PRAGMA being able to show if disease has increased a little or a lot.

“We have demonstrated that lung disease progression from age one to three is related to levels of inflammation in the lung, and that children with higher PRAGMA-CF scores at baseline have more rapid deterioration in lung structure.”



Tim Rosenow

The results have been published in the “Blue Journal,” the world’s highest-rated respiratory medical journal. PRAGMA is attracting international attention and builds upon broader CF research at Telethon Kids which is changing the way we think about the disease.

A fellow respiratory researcher says PRAGMA *“... can give true insight into early changes and effects of treatment. It will also create a more targeted approach toward personalized medicine. Therefore, we should adopt these imaging methods into future clinical trials to continue the quest to offer sufferers of this devastating disease access to new treatments and a possible cure and, ultimately, an outlook on life that is similar to that of their healthy peers.”*

PRAGMA is currently being used as an outcome measure in a number of clinical trials - the COMBAT-CF trial of azithromycin and the new SHIP-CT study of hypertonic saline in pre-schoolers. PRAGMA-CF has also been submitted to the European Medicines Agency, the organisation responsible for approving clinical trial outcome measures in Europe. Some pharma trials are also underway.

Tim hopes that PRAGMA-CF will become a standard measurement tool for CF lung disease in all young patients.

“Infants and young children stand to benefit the most from the many new medications and therapies becoming available, with the aim to prevent (rather than reverse) structural lung disease,” he says.

“Without a reliable outcome measure, clinical trials in this age group have not been possible. We have shown that PRAGMA-CF is a reliable and sensitive outcome measure in children below six years: the first of its kind in the world.”

“My hope is that my research will help bring new therapies to babies and young kids with CF so we can prevent lung disease early. Prevention really is better than cure.”

What is cystic fibrosis?

Cystic fibrosis affects the lungs and digestive system because of a malfunction in the exocrine system, responsible for producing saliva, sweat, tears and mucus. There is no cure.

People with cystic fibrosis develop an abnormal amount of thick and sticky mucus within the lungs, airways and digestive system. This mucus traps bacteria in the lungs resulting in recurrent infections. Lung failure is the major cause of death.

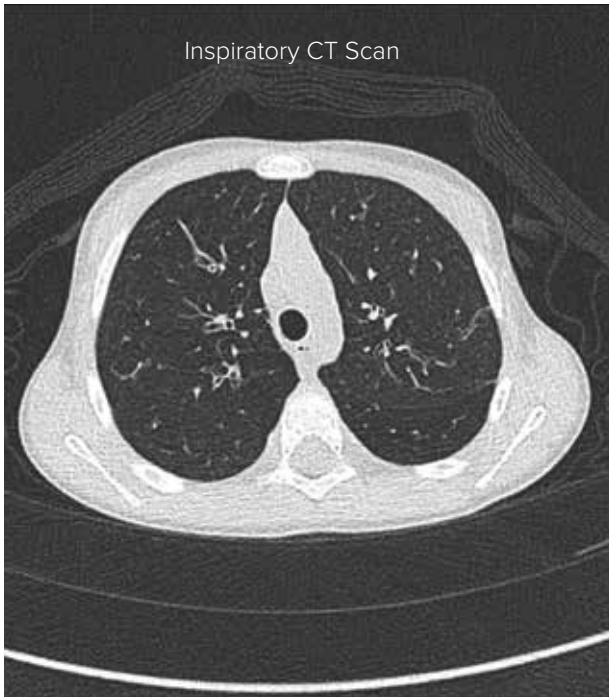
Cystic fibrosis affects one in every 2500 babies born in Australia.

The CF gene must be inherited from both parents - and it is carried by one in 25 people.

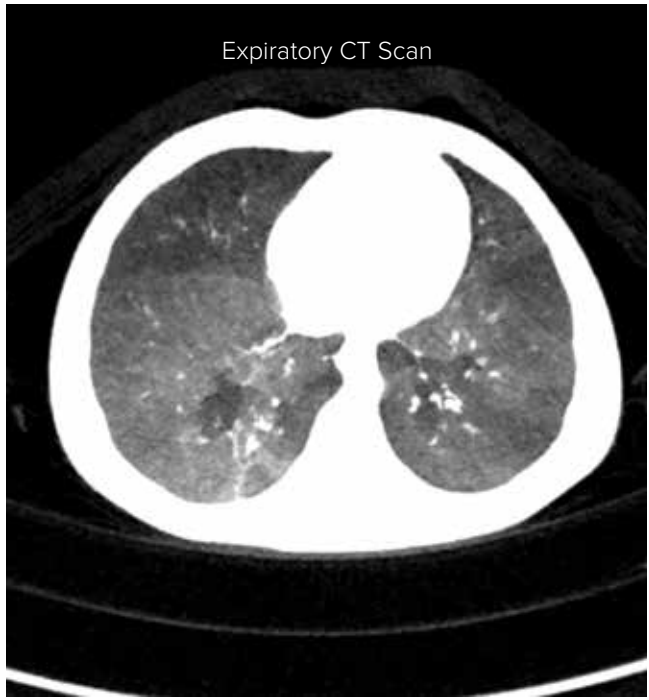


What's next?

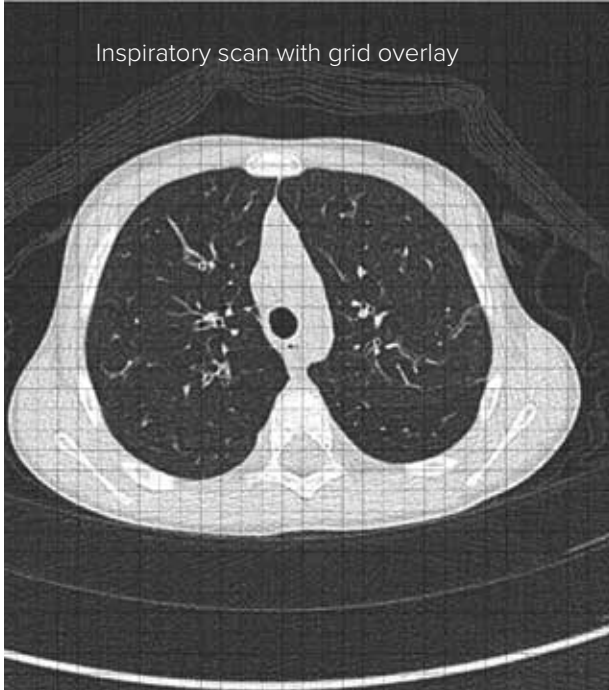
- ▶ PRAGMA-CF will become automated. In a similar way to fingerprint technology, Tim is working on training a computer to do all the work currently being done manually. The computer will be ‘trained’ by feeding in the CT images already collected and annotated using PRAGMA, then using computer learning to teach the computer to detect the different types of lung damage and colour them in. Once trained, new CT images will be fed into the computer which will then colour in the grid automatically.
- ▶ PRAGMA is also being used in other diseases like premature lung disease, asthma and Primary ciliary dyskinesia (PCD).



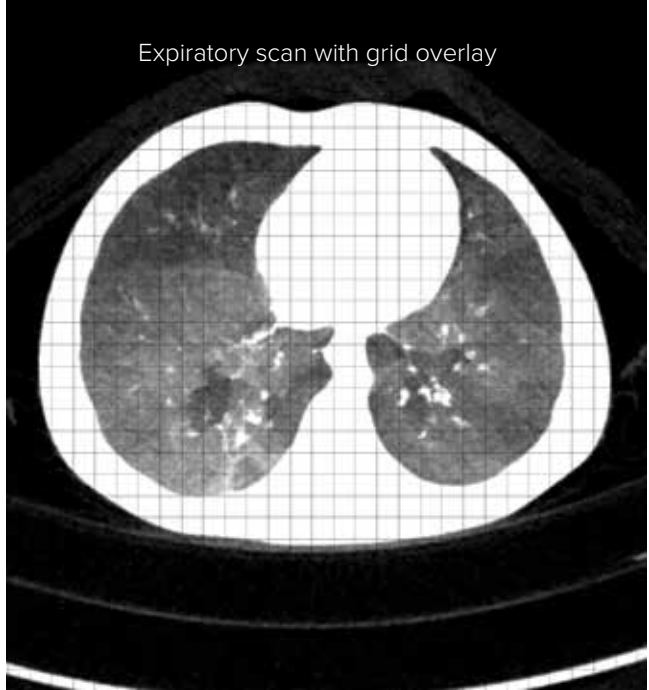
Inspiratory CT Scan



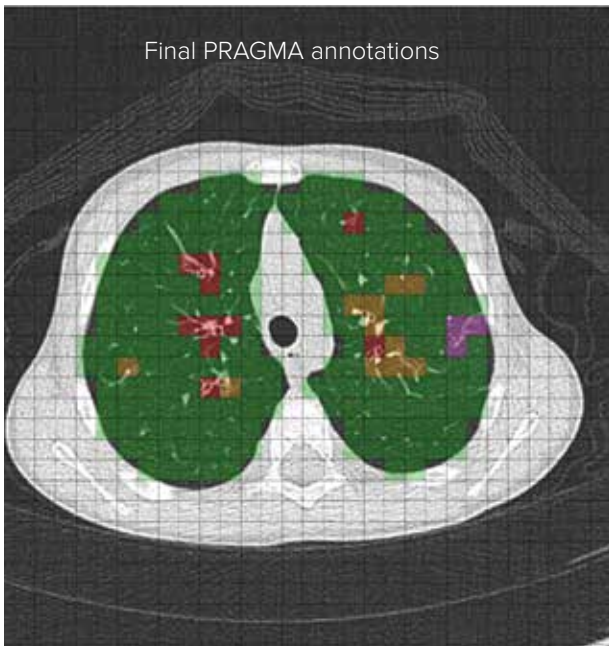
Expiratory CT Scan



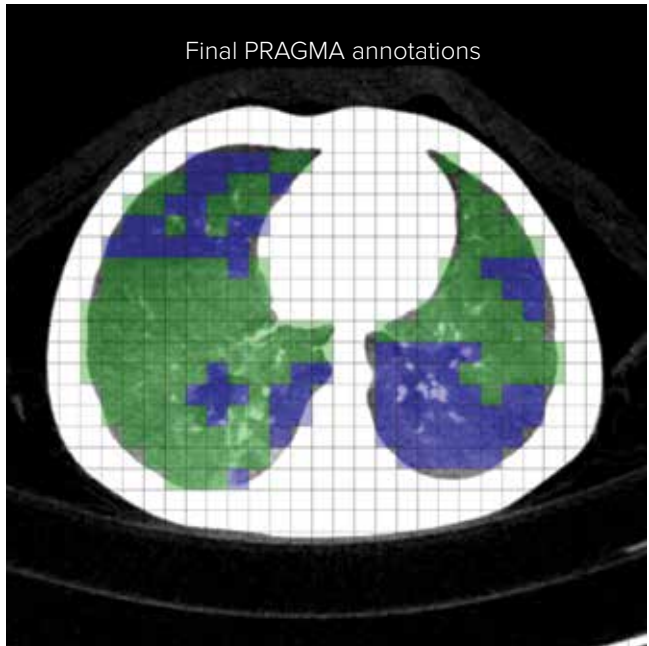
Inspiratory scan with grid overlay



Expiratory scan with grid overlay



Final PRAGMA annotations



Final PRAGMA annotations



MAKING FASD HISTORY IN THE FITZROY VALLEY

Long before the Fitzroy Valley region of remote north-western Australia was shown to have one of the highest rates of Fetal Alcohol Spectrum Disorders in the world, it was the local grandmothers who were the first to notice that the young children they were raising were responding and behaving differently to past generations.

Operating on a diagnostic hunch that excessive alcohol consumption in pregnancy may be to blame, and worried both about the extent of harm and threat to the intergenerational transfer of Aboriginal language and culture, they set alarm bells ringing.

Banding together in an historic show of strength, headed by June Oscar of the Marninwarntikura Women's Resource Centre, Emily Carter and Maureen Carter of the Nindilingarri Cultural Health Services, they successfully fought for local alcohol restrictions in 2007. Then they became the driving force behind the comprehensive community-led *Make FASD History* campaign.

Guided by both elders and the evidence-based Marulu FASD Strategy, drawn up in consultation with research partners the Telethon Kids Institute, the University of Sydney and the George Institute, a three-pronged attack was launched.

It focused on prevention, diagnosis and providing therapy support to affected individuals and families coping with life-long physical and mental health problems. Also, a team of 20 local Aboriginal community researchers were trained and enlisted to run the programs.

Results just now emerging from this partnership are exceeding all expectations. Midwife-collected data has revealed a dramatic fall off of drinking in pregnancy in the Fitzroy Valley

to below the rate of the general community in Australia. Whereas before, 65 per cent of pregnant mothers drank, now it's only 18 per cent.

And in all three areas of prevention, diagnosis and therapy, huge inroads have been made.

"This community is incredibly courageous because they put their hands up and they said 'Right, we have got a problem with alcohol' and they put themselves under the microscope," said Dr James Fitzpatrick from the Telethon Kids Institute.

"They reached out to research partners to confirm their concerns and, very importantly, we were able to do that.

"And what is really remarkable about this story is that over the last eight years really – particularly the last five years – we have worked with them on their solution to the problems and we have been able to document that the prevention efforts around Fetal Alcohol Spectrum Disorders (FASD) have been successful."

The gains are wide-reaching.

"There's nobody in the community now that does not know that alcohol use in pregnancy can harm the baby," said Dr Fitzpatrick. "And almost nobody who believes it's OK to drink in pregnancy.

"We have documented that very accurately, through interviewing 400 people towards the



Dr James Fitzpatrick

end of last year to gauge their knowledge, attitudes and practice.

“And we have also documented, through midwife data, that where previously 65 per cent of women used to drink and drink heavily in pregnancy, now only 18 per cent of women drink in pregnancy and the risk levels are much lower. It is actually less than rates in the general community in Australia.

“In prevention and diagnosis and therapy, we have made huge inroads in each.

“So now we have got really solid data measuring the success of this community’s own campaign to ‘Make FASD History.’”

Such significant changes in mindset and behaviour are expected to pay off in the next generation of Fitzroy Valley children, by improving their health, quality of life and social and economic potential. Also, they have highlighted successful practical strategies to reduce and eliminate FASD that can now be implemented elsewhere in Aboriginal and non-Aboriginal communities.

“It really is the kind of campaign where you needed to have hundreds upon hundreds of individual conversations about this issue and show people evidence of the link between alcohol use and pregnancy and lifelong brain damage,” said Dr Fitzpatrick.

“We did it by getting into four-wheel-drives and taking the message to the end of the dirt roads, to the most remote communities”.

The Fitzroy Valley is located approximately 400km east of Broome in the remote Kimberley region of WA. It is home to 3500 predominantly Aboriginal people belonging to four language groups and living in more than 45 remote communities.

Marulu – the name of the FASD strategy - is a local Bunuba word meaning “precious, worth nurturing”.

“In the Fitzroy Valley, there were a lot of heavy drinkers who were reliant on alcohol and were fairly closed to the idea that excessive alcohol supply and use in the community might have been a cause of concern for their young people,” said Dr Fitzpatrick.

“In each community we went to, we would have a bbq and a movie night and a discussion about FASD and alcohol.

“So it was a matter of actually sitting in people’s front yards and in schools or in the local community store and just having the same conversation over and over. Also, engaging and employing local Aboriginal people as community researchers to have similar conversations and they become champions for this issue.”

Fitzroy Valley Aboriginal woman and community researcher Sue Cherel said it was vital that locals were involved in researching their own issues because they brought understanding and gained knowledge. And she stressed there was no shame in being involved in programs that helped your child.

“Also it’s really important that the Telethon Kids Institute decided to stay the long haul,” said Dr Fitzpatrick. “We have kept people up there and worked on the solutions as part of a high quality research program in response to the worrying statistics that we found.”


An initial important component of the Marulu strategy had been for the community to invite researchers to conduct Australia’s first population-based study into the prevalence of FASD, called the Lirilwan Project. Carried out in conjunction with the George Institute and the University of Sydney, the results were reported in the *Journal of Paediatrics and Child Health*.

“Because it was a community question that we helped to answer - and to be honest that is the only way research should be done - our FASD prevalence study had a 95 per cent participation rate,” said Dr Fitzpatrick.

“This was even though women knew we would sit with them for an hour and ask them all about themselves and all about their behaviours and their drinking before the pregnancy.”

But work is far from over.

Over the next two years, all 250 school-aged children in the Fitzroy Valley are to be involved in a behavioural management Alert program to optimise student functioning. It is part of a randomised controlled trial and is based on the analogy of the body being like a car engine to teach self-regulation and improve executive functioning. Children are taught five ways to change their level of alertness through listening, moving, touching, looking or putting something

 <p>The FASD story</p>	<p>1980 - current</p> <p>Collection of data on the prevalence of FASD</p>	<p>1995 - 1997</p> <p>Survey of WA women about alcohol use in pregnancy</p>	<p>2002 - 2004</p> <p>Survey of WA health professionals’ knowledge, attitudes and practice in relation to alcohol use in pregnancy and FASD</p>	<p>2006 - 2008</p> <p>Resources for health professionals developed and evaluated</p>	<p>2009</p> <p>Submission to NHMRC on Australian Guidelines to Reduce Health Risks from Drinking Alcohol, Guideline 4 Pregnancy and Breastfeeding</p>	<p>2009 - 2016</p> <p>Studies looking at outcomes of children of mothers with alcohol-related diagnoses – health, education, birth defects, intellectual disabilities, cerebral palsy, perinatal infant mortality</p>	<p>Collaboration with WA Drug and Alcohol Office on prevention messages for Aboriginal and non-Aboriginal populations</p>	<p>Lirilwan Project in the Fitzroy Valley, with results showing among the world’s highest rates of FASD</p>
--	--	--	--	---	--	--	---	---

in their mouth. The program also supports families, school staff and carers.

“That is part of the therapy intervention,” said Dr Fitzpatrick. “We wanted to make sure that we did not just measure the size of the problem in the Fitzroy Valley, but came as part of the solution.

“We also have a regular outreach team visit six times a year to the Fitzroy Valley to run diagnostic clinics. What that then does is it accurately documents the impairments that young people might have and it triggers eligibility to support funding - either education funding through the schools or disability services funding.

“And we have employed a local Aboriginal person from the community who is a therapist and a local-based speech pathologist. They are the on-the-ground therapy team.”

What is FASD ?

An umbrella term used to describe a range of physical and central nervous system abnormalities that are caused by prenatal exposure to alcohol. FASD leads to difficulties with executive functioning skills (ability to plan, organise, attend, inhibit responses and self-regulate emotion and behaviour) and impacts on education and work opportunities. Early diagnosis and intervention reduces the likelihood of these secondary disabilities.

The Marulu FASD Strategy includes:

- The establishment of the Marulu Unit at Marninwarrtikura Fitzroy Women’s Resource Centre to provide resources and support to families affected by FASD
- An NHMRC-funded Alert Program.
- Australia’s first comprehensive FASD Prevention strategy (funded by the WA Health Department, Department of Aboriginal Affairs and Drug and Alcohol Office, and McCusker Charitable Foundation)
- An innovative child health service, Patches Paediatrics, working with WA Country Health Services.
- A Kimberley FASD Education network developed within the region’s schools.



What's next?

- Scaling up the successful model and translating lessons learned to other sites.
- Working through the whole of the Pilbara on large projects on FASD prevention, diagnosis and therapy.
- Working with Derby to support its FASD program and research on prevalence.

2010 - 2012

Collaboration with the WA Department of Health on the development of the WA FASD Model of Care

2010 - 2016

Development and implementation of a FASD diagnostic instrument for Australia

2010 - current

Marulu FASD Prevention Strategy in the Kimberley

FASD Prevention Strategy in the Pilbara

2011 - 2013

Evaluation of FASD information and services for parents and carers

2013 - 2015

Study on knowledge, attitudes and practice of midwives and development of resources and training

2014 - current

FASD knowledge, attitudes and practice in the WA justice system, development of FASD resources for justice professionals, diagnosis of juveniles in detention and justice workforce development

2015 - 2016

Study looking at knowledge of breastfeeding and alcohol guidelines by health professionals and mothers

IN THE PIPELINE



TAKING ON A COMMON RESPIRATORY INFECTION IN KIDS

Mapping when a common childhood respiratory infection reaches its seasonal peak will assist how future vaccination programs are carried out.

Epidemiologist Dr Hannah Moore, a senior research fellow with the Telethon Kids Institute's Wesfarmers Centre of Vaccines and Infectious Diseases, has been focusing on Respiratory Syncytial Virus (RSV) - the most commonly identified respiratory infection in children under the age of two.

"It affects more children and is estimated to cost the health system more money for young kids than influenza," she said. "RSV is something that I am really passionate about because there are so many kids who are affected by it. It's one of the most common reasons young children end up in hospital."

With different vaccines undergoing trials around the world, Dr Moore hopes the mathematical modelling undertaken by her team, in collaboration with Australian National University in Canberra, will lead to greater understanding about the transmission of RSV and seasonal factors that influence its spread.

Dr Moore said the data linkage and modelling team had been able to harness a variety of hospital and birth-cohort records available in WA, which carries out routine laboratory testing of any child hospitalised with respiratory infection.

It is the first group in Australia to have developed a dynamic transmission model for RSV, which mimics the biennial pattern of its seasonal epidemics, with an alternating peak in the winter months.

"In temperate Perth, the peak is always in the middle of July," Dr Moore said. "But we have found that the northern region of the State, which experiences more of a tropical climate, doesn't have this annual peak in July. The seasonality is a

bit all over the place.

"If we can develop a model that accurately links what we see in the actual data, then we can start modelling different interventions. So when we do have a vaccine available, we can see what time of the year would be the best time to vaccinate and what difference would that make in terms of preventing infection.

"WA is a really interesting place to do all of this because not only do we have data for the whole population but we have different climate zones.

"If we can say that some aspect of climate, whether it's rainfall or humidity or temperature, if that is driving the transmission, then we can have greater predictiveness to say when are we going to have a really high season and when are we going to have lots of children affected."

Dr Moore said this would enhance community health management, including knowing when hospital beds would be needed. "If we can predict the timing and peak of future epidemics of RSV, we'll be able to forecast when the burden on the health system is going to be the highest."

Preventing RSV in young children would also have a long-lasting benefit, she said. "Some of the other research I've done shows that kids who are infected with RSV in their first year often end up having later respiratory problems as well, like asthma."

Research is also being undertaken into whether a drug called *Palivizumab*, an RSV-specific monoclonal antibody, is a cost-efficient and effective prophylactic treatment. It is recommended for young children at highest



Dr Hannah Moore

risk, such as premature babies and those with chronic lung disease or congenital heart disease. “Currently it’s the only available tool to prevent RSV but it is expensive - about \$8750 per infant per season course - and requires monthly injections for five months,” Dr Moore said.

What is Respiratory Syncytial Virus?

It is a virus that causes infection of the lungs and breathing passages. A common illness for children under three, it usually manifests as bronchiolitis and in some cases can cause pneumonia. It is spread via tiny droplets that enter the air when a person coughs or sneezes.



What’s next?

- ▶ Working out what effect climatic variations have: “We’ve used our dataset from Perth to produce a model that accurately mimics what we see. Now we are trying to extend that model to link to the seasonality we see in non-temperate areas.”
- ▶ Ensuring a vaccination program is based on accurate data.



A NEW JOB FOR A SPECIALISED DRUG

WA researchers may have uncovered a new treatment for the recurrent ear infection known as glue ear. A clinical trial is investigating whether a cystic fibrosis medication may be the answer to dissolving the glue in glue ear, reducing the need for antibiotics and surgery.

A preschooler ignores her mother's instruction to pack away her toys and instead turns up the volume on her favourite TV show. A three-year-old, irritable after a bout of sleepless nights, throws a huge tantrum at the supermarket. And another young boy brings home a note from school reporting that he isn't interacting well with his classmates.

But instead of having behavioural issues, it turns out these children have a middle ear infection known as otitis media or 'glue ear' – which can cause hearing and speech difficulties and ear aches.

Dr Ruth Thornton, of the Telethon Kids Institute's Vaccine Trials Group, has been part of a University of WA team examining the role of bacterial biofilm in otitis media and believes this new finding has the potential to lead to the first major change in treatment of ear infections in two decades.

“Ear infections are the main reason kids will get taken to their GP and be prescribed antibiotics,” she said. “It is also the second most common reason children will need surgery.

“The main complication associated with middle ear infections is hearing loss, this occurs at a time when children are developing language and can have major effects on language acquisition, behaviour, education and subsequent life course.

“The current treatments have limited efficacy and we need to better understand this disease

so we can improve these and ultimately prevent disease.”

Children with acute otitis media often require antibiotics or surgery. About 3,800 operations are carried out in WA each year, where tiny tubes, or grommets, are inserted into the eardrum to drain fluid and ventilate the middle ear.

The clinical trial involving 60 children under five years of age has applied Dornase alfa – a drug that breaks up thick secretions in the lungs of cystic fibrosis patients - in one ear at the time of grommet insertion. Each child has been followed up over two years, with hearing checks every three months. Dr Thornton said this follow-up stage was almost complete, which should let them know how well the Dornase alfa treatment has worked.

This trial follows on from the UWA team's discovery that the recurrence of otitis media is due to the presence of bacteria in slimy biofilm.

Dr Thornton said laboratory research found that middle ear fluid was sticky because of the DNA that came from the children's immune response to the bacteria causing the infection. “Instead of killing the bugs, this immune response was hijacked by the bacteria to help provide them with a home in the middle ear from which they could keep re-infecting the children's ears,” she said.

“When the bugs are in this slime, they are up to 1000 times more resistant to antibiotics. This



Dr Ruth Thornton

means that the infection is never completely resolved, the children get chronic or recurrent infections and they usually end up needing surgery for grommets to be placed in their eardrums. While this is great short term and allows the children to hear, up to a third of children having grommets will need to go back for repeat operations.”

Dr Thornton said a search for enzymes that could cut up DNA resulted in them identifying Dornase alfa as a possible agent. “When we put this into some middle ear fluid in a tube in the lab, we saw that it dissolved the DNA in the fluid which got us really excited and made us think that we might be able to dissolve the glue in these kids’ middle ears,” she said.

This research also offers hope to those aiming to prevent hearing loss in Aboriginal communities.

“We know that Aboriginal children experience unacceptably high burdens of middle ear infections and that in some communities it affects nearly every single child,” Dr Thornton said.

“These children are affected for longer than non-

Aboriginal children on a whole and experience much more severe disease which makes them at much higher risk for the lifelong consequences, particularly in relation to health, education and learning.”



What's next?

- ▶ “The next phase will be to implement the use of Dornase alfa in ear washes for those children with chronic suppurative otitis media (chronically runny ears), which is the most severe form of middle ear infection,” Dr Thornton said. “We will also hopefully do a larger-scale, multi-centre trial with different treatment regimens.”



NEW APP HELPS TEENS THINK TWICE

Few fields of study are evolving with the speed of Professor Donna Cross' innovative research, which aims to protect children from the harmful effects of online bullying.

"The advantage of our research is that we have a reference group of young people who constantly update me as new social networking sites and other sites appear online," she said.

"We've conducted many studies with more than 30,000 children and as we've looked at the ways young people are treating each other, we've had to evolve. When it comes to bullying, the most humiliation and harm to the target comes from posting negative images or footage of them. This behaviour has become quite common since mobile phones included cameras."

The most recent cyber bullying intervention research conducted by Professor Cross' team is the Cyber Savvy project, which focuses on reducing harm from "sexting" or the posting of sexually explicit content using a mobile phone.

"Clearly children are putting themselves at great risk by sending nude or semi-nude photographs of themselves, but there's enormous peer pressure to do so," Professor Cross said.

"We've previously worked with schools and families to educate young people about how to use their phone safely but we've also seen the need for an in the moment intervention for children when they are in the process of sending an image of themselves, but are not thinking about the consequences."

With the assistance of 70 teenagers who participated in a two-day summit, the team developed the *Image Up* app for mobile

phones. The app stores a photo for 10 seconds while humorous and educative messages are delivered, encouraging the young person to reconsider sending explicit or illegal images.

The media provided on the app can also be quickly downloaded and sent as instant alternatives to the photo, helping the child to save face when responding to a request for a "nude."

"More than 30 messages cycle through the app so the children see different content developed by young people and momentarily pause to reflect on their actions each time they send an image," Professor Cross said.

Professor Donna Cross





“The young people in our reference group told us these messages have to be funny, relevant and available in the moment on the phone to positively influence young people’s decision making. The media content also includes reminders that it’s illegal to possess, transmit or store nude photos of a person aged under 16.”

The Cyber Savvy program, Image Up app and educational resources are being tested in approximately 20 schools in the Perth metropolitan area targeting 12 and 13 year old students.

“We want to empower children to prevent a harmful activity rather than only helping them to deal with it once it’s happened,” Professor Cross says. “It’s devastating to see a girl drop out of school because everybody’s seen her nude photo. Our years of research have given us reason to believe these interventions can help change the online behaviour of young people.”



What's next?

- ▶ By the end of this year Professor Cross’ team will have data to determine teachers’ and students’ use of and satisfaction with the school intervention program and the “Image Up” app on mobile phones. These comprehensive pilot data will inform a full three-year randomised control trial to determine the longer-term impact of this intervention.

COLLABORATING
FOR IMPACT



GLOBAL WAR ON BRAIN CANCER

Two Telethon Kids researchers are the driving force behind an innovative, global action group on child brain cancer, which has been described by their peers as the “pinnacle of collaboration and cooperation.”

Paediatric Oncologist Dr Nick Gottardo and researcher Dr Raelene Endersby, who first met during their post-doctoral training in the United States, brought internationally renowned scientists and clinicians together, in a bid to save the lives of children with medulloblastoma brain tumours.

Working with a unity and passion that is unprecedented in the field, the International Medulloblastoma Working Group now shares resources needed for medical research into the rare tumour, which mainly affects children aged between five and eight.

“We are all focused on the most urgent things which are needed to help find new treatments for kids with this type of brain tumour – genetics, experimental models, drug screening and better diagnosis,” said Dr Endersby.

“Working together prevents duplication of our research across the world and should lead to quicker results.”

The group of more than 50 clinicians and scientists first united in Perth and now maintain regular contact. They are based in the United States, Canada, England, France, Germany, Italy, New Zealand and every major cancer research centre in Australia.

“All of us just want what’s best for the patient,” Dr Gottardo said. “We share data, technology and other resources. There’s a lot of generosity and goodwill.”

The collaborative cancer research project started

after Dr Gottardo helped in the treatment of young medulloblastoma patient Elliot Parish at Princess Margaret Hospital six years ago.

It was apparent that medical progress in improving the survival of children using conventional therapies had stalled. Patients needed large doses of radiation and survivors had a reduced quality of life due to treatment-related side effects.

Elliot’s parents Rick and Emily were passionate about supporting brain tumour research and started major fundraising campaigns to help Elliot and other children with brain tumours.

Thanks to the family’s efforts, high-tech equipment was purchased and Dr Endersby was brought to the Telethon Kids Institute from St Jude Children’s Research Hospital in the United States, where she set up the research team in Perth with her old colleague, Dr Gottardo.

When the then Director, Professor Fiona Stanley suggested bringing all the finest minds in the world into one room to look at the best way to tackle medulloblastoma, the Parish family raised money to hold the inaugural global meeting at Bunker Bay, south of Perth.

Dr Gottardo and Dr Endersby brought the international experts together.

“The Bunker Bay meeting wasn’t like other scientific conferences,” Dr Endersby said. “I’ve never been to a meeting like that before and very few fields in medical research would have had one like it.”



Dr Raelene Endersby and Dr Nick Gottardo

- Medulloblastoma is the most common malignant brain tumour of childhood.
- The disease affects one in five children who have a brain tumour.
- Medulloblastoma is curable in approximately 70% of patients.

“We set the agenda to look for the strategic ways to move towards finding better treatments for medulloblastoma. We talked about where we wanted to be and how to get there. Rick and Emily Parish were there for the whole two-day meeting which helped all the scientists and clinicians to maintain a focus on finding better outcomes for the patient.”

Dr Endersby said that the field of paediatric brain tumour research was very collaborative because the cancers were rare and the children became very sick.

“No single centre can run a trial without collaborating with other centres because it would take decades,” she explained. “We only have about five medulloblastoma patients in WA each year and you need large numbers to conduct a trial into a new drug, so you find hospitals and people are willing to work together.”

Treatment of medulloblastoma has also been difficult because research over many years has revealed the cancer is not a single disease entity, but instead consists of at least four distinct molecular subgroups: WNT/Wingless, Sonic Hedgehog/SHH, Group 3, and Group 4. All respond differently to the existing treatments.

A German group who are renowned as the world leaders in the genetic fingerprinting of all types of paediatric cancers, help diagnose samples of brain tumours sent over by Telethon Kids free of charge.

A group in the United States taught the Perth team better processes when running their high-throughput screening, which the researchers use to quickly conduct a large number of drug tests.

“If drug screening is not done properly you end up chasing false leads,” Dr Gottardo explained. “Our US collaborators taught us how to do very tight quality control and then after they helped

us to set up we started to do some of our own experiments and found some very promising drugs which we hope can help cure more children.”

Dr Gottardo said that currently, 20 to 30 per cent of children with some of the more aggressive sub-groups of the disease could not be cured despite aggressive treatment. This was unfortunately the case with Elliot Parish, who passed away in 2011, aged four.

“That’s why we need new drugs and we want to test them in the clinic and make a difference,” Dr Gottardo said. “This research will really affect people’s lives.”



What's next?

- ▶ The Perth team is now negotiating to start a clinical trial of a new class of drugs, which were developed for adult cancer and have never been tested in children.

“The hope is that we’ll find some more treatments which will maximise the effects of the chemotherapy so we can reduce the radiation which has more damaging side-effects on the patient in the long term,” Dr Gottardo said.





COLLABORATING TO PREVENT KILLER DISEASES IN PNG

For more than a decade, researchers from the Telethon Kids Institute and Papua New Guinea Institute of Medical Research (PNGIMR) have been working together in the fight against killer infectious diseases.

Papua New Guinea (PNG) has one of the highest child death rates in the Western Pacific Region - one in every 15 children won't reach their fifth birthday - and many will die from pneumonia. Meningitis is another of the top five killers and for those who do survive, the majority will have ongoing problems like blindness, hearing loss and brain damage.

While these illnesses are quite common in PNG, they aren't seen too often in Australia due to nationwide vaccination programs. However, immunisations are not yet commonplace in PNG and children still die from these vaccine-preventable infections.

That's where our collaboration with local researchers in PNG is trying to change things.

The Institute's Dr Chris Blyth, who is also an infectious disease paediatrician at Princess Margaret Hospital, has been leading a study in Goroka (in PNG's Eastern Highlands Province) looking at what bacteria and viruses are causing pneumonia. The bacteria *Streptococcus pneumoniae* and *Haemophilus influenzae type B (Hib)* are suspected of being the main causes of severe pneumonia and meningitis in kids.

Dr Blyth says the researcher team, which includes the Institute's Dr Peter Richmond, Dr Lea-Ann Kirkham and Associate Professor Deborah Lehmann as well as Dr Willie Pomat from PNGIMR, need to know which bacteria are causing disease before they can find ways of preventing and best treating them.

"Other studies done in the highlands of PNG

many years ago, identified *Streptococcus pneumoniae* and *Haemophilus influenzae type B* as playing important roles in causing disease," says Dr Blyth. "We also know that these two bacteria together are estimated to account for two-thirds of the world's pneumonia and meningitis deaths in children under five."

"But these local studies were done more than 20 years ago and in that time a lot has changed - new vaccines and treatments are available, lifestyle is different and there are now better techniques to find out which bacteria are causing disease."

"We also know that antibiotic resistance is increasing in PNG so there is an urgent need to monitor the circulating bacteria and re-assess vaccination programs."

In 2008, the PNG Government introduced a Hib vaccine and in 2014, a Prevenar13 vaccine program was implemented to protect kids against pneumococcal pneumonia and meningitis.

It was years of research led by the Institute's Associate Professor Deborah Lehmann which helped inform the government about the best pneumococcal vaccine to use.

Most recently the research team has looked at the safety and immune response of two different pneumococcal vaccines - the 10-valent Synflorix and 13-valent Prevenar vaccines.

"The field work for these pneumococcal conjugate vaccines has now been completed,"



Dr Chris Blyth and Associate Professor Deborah Lehmann (right)

says Associate Professor Lehmann, “with some more lab work to be done.”

“Our results so far show that both vaccines give a good immune response with some differences between the two. It’s important to know that both will work in PNG, just in case stocks of the vaccine chosen for PNG (Prevenar13) run out due to world demand.”

Dr Blyth’s study in the Goroka Hospital will keep monitoring pneumococcal and Hib bacteria in the study children allowing researchers to assess the impact of vaccination programs.

What's next?

- ▶ The Bill and Melinda Gates Foundation has now joined the fight, funding the next phase of the research – PneuCAPTIVE. This study will continue to find out the causes of moderate or severe pneumonia and meningitis as well as the level of vaccine coverage in the community needed to have a herd immunity effect, that is, the minimum level of pneumococcal vaccine uptake needed to protect people who themselves are not vaccinated. Papua New Guinea is one of three locations for the PneuCAPTIVE study along with Laos and Mongolia.



IMPROVING THE LIVES OF KIDS WITH TYPE 1 DIABETES

Diabetes research got a huge boost when the WA Children's Diabetes Research and Education Centre for Research Excellence opened late last year.

The centre, based at the Telethon Kids Institute, is the only paediatric unit of its kind in Australia and aims to improve the lives of children with Type 1 diabetes.

Centre co-directors Professor Tim Jones and Associate Professor Liz Davis said the centre enabled them to broaden their approach and embrace new partnerships.

"It was the impetus for us to grow the research program outside of what we traditionally have been doing into areas that are becoming increasingly important, such as working with consumers, educationalists, psychosocial teams and health economists," Associate Professor Davis said. "It has really broadened the perspective that we bring to each study and trial that we do."

It has also led to more collaborations - locally, nationally and internationally.

"The centre is a world leader in terms of the breadth of our work and the impact of our work," Professor Jones said. "Its focus is translation. Research may find better ways to treat patients but this is of no use unless what is found is put into practice in the clinic. The centre involves a range of people and collaborators that are needed to translate new knowledge into practice."

The centre is currently involved in the well-publicised international effort to develop revolutionary closed-loop technology. It first tested the system for overnight blood glucose control and is now leading an Australia-wide trial of these portable devices at home.

Also known as an artificial pancreas, the system comprises a continuous glucose monitoring sensor that sits under the skin and an insulin pump with a special algorithm to calculate the amount of insulin needed to keep blood glucose levels within normal range.

By automatically monitoring these levels and adjusting insulin doses, it alleviates the need for people with Type 1 diabetes to continually prick their fingers to test. It also stops insulin delivery during a hypoglycemic attack, when levels fall dangerously low.

This gives peace of mind not only to the diabetic but other family members as well, especially since these low episodes often occur at night when the person is asleep.

Professor Jones said the cost of parents waking at night worrying about their child needed to be taken into account when assessing the economic benefits of such a system.

He expected a closed-loop device would be available commercially within 12 months.

"Short-term studies have found they do control glucose levels better but we don't yet know what happens over a long time period such as six months, when it's used at home in the community," Professor Jones said. "Will it really improve control, will people find them easier, what does it do to the burden of living with diabetes?"

Early work suggests it will be well accepted as a therapy.

Maintaining controlled glucose levels can prevent long-term complications, such as



Professor Tim Jones

kidney failure, blindness and cardiovascular disease.

Associate Professor Davis said being involved in these trials meant Australians had the opportunity to familiarise themselves with the new technology before it came on to the market. “It actually changes the whole approach of the diabetes community to the use of a technology, once you have the experience, confidence and understanding of them,” she said.

Other studies at the WA Children’s Diabetes Research and Education Centre for Research Excellence revolve around exercise and food intake – two critical areas in the management of diabetes.

“We are seeking ways to help patients on a day-to-day basis reduce the impact of blood glucose variability in relation to exercise and food,” Associate Professor Davis said.

“We are involving the families in helping us know which areas are most challenging, so

we can then design studies which will result in guidelines or information that will be made available to health-care professionals and consumers.

“We are not only completing the gaps in the science but also how we translate or feed that information back so it does go back into the community where it is needed.”

One trial is evaluating whether interspersing short sprints into physical activities such as running or cycling can be used as a therapeutic measure to avoid lows since previous studies have shown that sprints raise blood glucose levels.

Another is investigating the effects of different food content.

“We understand carbs pretty well but we’re starting to look at the impact of high protein and high fat in meals and how this impacts on blood glucose levels and how we might improve our insulin dose for those meals,” Associate Professor Davis said.



Professor Tim Jones

She said research into the effects of exercise and food dove-tailed nicely into the closed-loop studies. “If we understand what’s needed with insulin adjustments and the way we give insulin around each of these things that challenge you every day, that is really important information to feed into development of technology,” she said.

Seeing minute-by-minute updates of blood glucose levels through sensors was giving a better window into what was happening, in all facets of a diabetic’s life.

Other areas of interest include developing programs to support people with Type 1 diabetes at school, sending a child’s readings direct to a parent’s smartphone, and the testing of an app to track emotional state to see how it relates to blood glucose levels.

“We want to see how emotional stress impacts on blood glucose levels,” Associate Professor Davis said. “We are being told that it does in clinics but there is not a lot of data.”

The centre relies heavily on community participation and is never short of volunteers to take part in research.

“Families are always keen to step up and do studies because it is all really important to them,” Associate Professor Davis said. “It reflects the impact that diabetes does have on families.”

What’s next?

- Better advice for families about eating and exercise to improve blood glucose control.
- Better understanding of the new technologies and how they work. “Teaching health-care professionals and families how to use this equipment properly and maximise what they get out of it is quite a challenge in itself,” Associate Professor Davis said.
- Reduced burden of diabetes care for young people and their families.



KIDS are at the 
of everything we do

To find out more about our research visit
telethonkids.org.au



100 Roberts Road, Subiaco Western Australia 6008
PO Box 855, West Perth Western Australia 6872
T | 08 9489 7777
E | contact@telethonkids.org.au
W | telethonkids.org.au

PRINCIPAL PARTNER



STRATEGIC PARTNER

