

Annual Report 2017

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Message from the Co-Directors

2017 has been a big year for the Centre of Excellence in Severe Asthma. At the half-way point of our funding, our programmes are well underway. We are excited to share some of our activities and outputs with you.

We are pleased to welcome new postdoctoral fellows and PhD scholars, who are now actively involved in generating new knowledge on severe asthma.



Co-Directors Profs. Peter Gibson and Vanessa McDonald

It is an exciting time in severe asthma research and clinical management. Our understanding of the mechanisms underlying disease are providing new treatment options. Multidisciplinary and multidimensional management approaches hold promise in reducing the burden of disease. The Centre of Excellence has been actively contributing to this new knowledge through research publications, expert commentaries, hosting expert forums and promoting international collaboration.

A major focus has been translating this new knowledge into evidence-based practice. We have developed clinical resources, hosted presentations and delivered workshops to guide clinical practice and provide training for the healthcare workforce. A major project undertaken in 2017 was the Severe Asthma Toolkit, which we officially launched March 2018. The Toolkit website provides evidence-based educational content and practical clinical resources to support healthcare professionals in the management of severe asthma.

About the Centre of Excellence in Severe Asthma

The Centre of Excellence in Severe Asthma supports training, research, collaboration and translation of findings for the management of severe asthma. It is funded by the Australian National Health and Medical Research Council (NHMRC) Centres of Research Excellence programme from 2014-2019. The Centre brings together researchers from universities and hospitals in Australia and internationally. Our Chief Investigators are located in Newcastle, Sydney, Melbourne, Brisbane and Perth. Leading researchers, clinicians and healthcare providers are teaming up with stakeholders, people with asthma and their significant others to improve the diagnosis, management and treatment of severe asthma.

Why Study Severe Asthma?

Asthma is a common disease, which directly affects approximately 10% of Australians. Not all asthma is the same, and approximately 3-10% of people with asthma have severe asthma. People with severe asthma have persistent symptoms that remain uncontrolled with standard treatment. People with severe asthma experience frequent asthma attacks, hospitalisations, major psychological and financial burden and reduced ability to work. Severe asthma negatively impacts on health and quality of life and is a major healthcare cost to society.

New approaches to the management of severe asthma are needed to improve outcomes for patients and the health care system. Directed approaches to manage severe asthma can improve patient outcomes. Further, multidimensional assessment and intervention and new targeted therapies can reduce symptom severity. Dedicated resources are required to support the implementation of these strategies into clinical practice.

Our Mission

The mission of the Centre is to *develop innovative solutions for severe asthma*. We are developing innovative approaches to understand why severe asthma occurs, to improve disease diagnosis and management and to inform the use of new therapies.

The specific objectives of the Centre are to:

- **Generate new knowledge** on the prevalence and burden of severe asthma in Australia
- **Design and validate tools and programmes** to more effectively manage severe asthma in the clinic
- Test new management strategies that combine **multidisciplinary team** management with **personalised diagnostic testing**
- Inform **uptake and access** to new targeted therapies for severe asthma
- Translate these initiatives into practice through policy development and collaboration

People

Chief Investigators:



Prof. Peter GibsonUniversity of Newcastle
Hunter Medical Research Institute
John Hunter Hospital

Prof. Vanessa McDonaldUniversity of Newcastle
Hunter Medical Research Institute
John Hunter Hospital

Prof. Greg King
University of Sydney
Woolcock Institute of Medical Research
Royal North Shore Hospital

Clin. Prof. Helen Reddel University of Sydney Woolcock Institute of Medical Research

A/Prof. Lorraine Smith University of Sydney

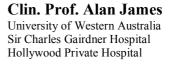


Prof. Guy Marks
University of New South Wales
Woolcock Institute of Medical Research
Liverpool Hospital
South Western Sydney Clinical School

Prof. Peter WarkUniversity of Newcastle
Hunter Medical Research Institute
John Hunter Hospital

Prof. Bruce ThompsonMonash University
Alfred Hospital

Prof. John Upham University of Queensland Princess Alexandra Hospital





Prof. Ian Yang
Prof. Sinthia Bosnic-Anticevich
A/Prof. Kerry Inder
Prof. Frank Thien

Prof. Paul Reynolds Prof. Christopher Doran A/Prof. Celeste Porsbjerg

PhD Scholars:

Prof. Nicholas Zwar Prof. Sandra Hodge A/Prof. Anne Vertigan

Post-Doctoral Researchers:

Dr. Michael Fricker (University of Newcastle)
Dr. Vanessa Clark (University of Newcastle)
Dr. Tong Gong (University of Sydney)
Dr. Farid Sanai (Woolcock Institute)

Affiliated Researchers:

Laura Cordova Rivera (University of Newcastle)
Dr. Katrina Tonga (Woolcock Institute)
Catherine Farrow (Woolcock Institute)
Dr. Sarah Hiles (University of Newcastle)
Dr. Michael Ramsahai (University of Newcastle)
Heather Powell (University of Newcastle)
Michelle Guilhermino (University of Newcastle)
Dr. Erin Harvey (University of Newcastle)

Dr. Ling Qin (University of Newcastle)
Dr. Kim Jones (University of Newcastle)
Blake Handley (Woolcock Institute)

Daniela Eassey (University of Sydney)
Bilal Malik (University of Newcastle)
Natalie Niessen (University of Newcastle)
Sai Praneeth Narla (University of Queensland)
Michelle Stubbs (University of Newcastle)
Natasha Winter (University of Newcastle)
Dr. Jeeva Sanjeevan (Monash University)
Eleanor Majellano (University of Newcastle)

Support Staff:

Dr. Steven Maltby (University of Newcastle)

BUILDING COLLABORATION:

The development of new knowledge, patient management strategies and effective implementation requires effective teamwork and collaboration. Our Centre's investigators have a long track record of collaborative research, integrating research findings and developing strategies for future research.

Highlighted Collaboration: Cyclopharm Limited

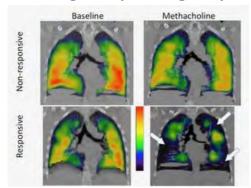
Cyclopharm Limited is an Australia-based radiopharmaceutical company. They develop nuclear medicine products for tissue imaging. Their product Technegas is inhaled as an ultra-fine mist of radioactive carbon, which acts as a marker of ventilation within the



lungs. Imaging with single photon emission computed tomography (SPECT) camera provides 3-dimensional images of ventilation and when combined with 99mTc-MAA (macroaggregated albumin), imaging also provides 3-dimensional information on perfusion. This technology is currently in routine clinical use for the diagnosis of pulmonary emboli in Australia, Asia and Europe.

Cyclopharm is pursuing the use of this technology to inform the diagnosis and treatment of other lung conditions. That's where the Centre of Excellence in Severe Asthma comes in. Prof. Greg King (Woolcock Institute of Medical Research) and Prof. Vanessa McDonald (University of Newcastle) are leading studies to look at the use of Technegas in severe asthma populations.

Measuring Airway Heterogeneity in Severe Asthma



Prof. King is leading a study on the use of SPECT imaging to identify changes in the airways of people with severe asthma. The study will focus on the differences in people with severe asthma and following treatment. The hope is that SPECT imaging will provide a better description of airway behaviour in asthma, when added to standard lung function assessments. Asthma is a highly complex disease and the necessity to address this complexity has been increasingly recognised in recent years. The study is being conducted in collaboration with The Woolcock Institute of Medical Research, the University of Sydney and the Northern Sydney

Local Health District.

We currently need tests that will provide information on the differences in the way that the lungs function in asthma. Just relying a brief clinical assessment and occasional use of spirometry, may suffice in mild and simple disease, it is clear that we need more information in complex disease e.g. severe and troublesome asthma. This is where new technologies, such as imaging will have future roles.

Press Release: https://smallcaps.com.au/cyclopharm-fight-against-asthma-via-technegas/

Imaging Treatable Traits

Prof. McDonald is leading a study to determine whether SPECT imaging can be used to identify treatable traits in obstructive airway disease, including COPD and severe asthma. Current disease metrics are subjective, not specific for small airways disease or insensitive to treatment. In contrast, SPECT imaging is an objective test of lung ventilation and structure. Ventilation and perfusion imaging will be performed to identify ventilation changes in people with lung disease. Measurements will also be taken following treatment with targeted therapies to look for factors that predict treatment response. This study is a collaboration between the University of Newcastle, Hunter New England Health and the Hunter Medical Research Institute

Press Release: https://hmri.org.au/news-article/nuclear-imaging-clear-airway-diagnosis

Highlighted Publications

We are pleased to feature several research publications, which highlight some of the important work being conducted within the Centre of Excellence in Severe Asthma.

"This illness diminishes me. What it does is like theft": A qualitative metasynthesis of people's experiences of living with asthma. Pickles K, Eassey D,

Reddel HK, Locock L, Kirkpatrick S, Smith L. *Health Expectations*

Studies assessing the effects of asthma on the individual mainly focus on medical aspects of disease (e.g. symptoms and lung function). This is the first systematic review of the qualitative literature focussed on people's views and experiences of living with asthma.

In data from 26 qualitative studies, there was only limited literature on the physical burden of asthma symptoms and the importance of social support. A recurring theme was the



concept that living with asthma is "work" and an intensely emotional experience. The study highlights aspects of asthma management which should be considered to support patient-centred care.

Effect of Azithromycin on Asthma Exacerbations and Quality of Life in Adults with Persistent Uncontrolled Asthma (AMAZES): A Randomised, Double-Blind, Placebo-Controlled Trial. Gibson PG, Yang IA, Upham JW, Reynolds PN, Hodge S, James AL, Jenkins C, Peters MJ, Marks GB, Baraket M, Powell H, Taylor SL, Leong LEX, Rogers GB, Simpson JL. *The Lancet*



Macrolide antibiotics have antibacterial effects, as well as anti-viral and anti-inflammatory effects. Previous studies reported benefits of macrolide treatment on asthma symptoms. However, insufficient data existed to demonstrate whether treatment with the macrolide antibiotic azithromycin improved other endpoints, including asthma attacks / exacerbations.

In a randomized, double-blind, placebo-controlled study of patients with uncontrolled persistent asthma, 48 weeks of azithromycin treatment reduced

asthma attacks. Treatment also improved quality of life. Treatment was well-tolerated, with a small increase in diarrhea noted in the treatment group. Thus, azithromycin may be a useful add-on therapy in persistent asthma.

Peripheral Ventilation Heterogeneity Determines the Extent of Bronchoconstriction in Asthma. Farrow CE, Salome CM, Harris BE, Bailey DL, Berend N, King GG. <u>Journal of Applied Physiology</u>

Tightening of the airways (bronchoconstriction) is a key feature in asthma, leading to difficulty breathing and shortness of breath. The pattern of bronchoconstriction that occurs throughout the lungs in asthma is poorly understood.

Using a three-dimensional ventilation imaging technique (SPECT), this study demonstrated the development of areas of low air ventilation in the lung, in people with asthma. The pattern of changes was determined by the function of the small airways within the very peripheral region of the lungs (the 'acinar' airway



zone). These lung zones may be difficult to reach using puffers and may be increasingly important in severe asthma and therefore, more work needs to be done using such ventilation imaging techniques combined with small airway tests.

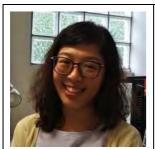
Training

Training the next generation

The Centre of Excellence supports PhD students and post-doctoral fellows, as well as affiliated trainees. Learn more about our researchers on our <u>website</u>.

We have implemented an innovative and engaging training programme, with the goal of building the next generation of severe asthma clinical researchers. Our scholars are supported through seed and travel grants. Seed grants help generate pilot data that serve as the basis for national and international project grant applications. Travel grants provide an opportunity to present research at conferences and to support networking and collaboration. Scholars are actively involved with the severe asthma research community, through our Annual Scientific Meeting, educational activities and within the mentor programme. To support our scholars' research training and career development, we have developed a number of programmes, including career development sessions and a severe asthma webinar series. Further, we have developed a trainee-mentoring programme, where trainees are connected with a chief investigator and encouraged to discuss their research progress, career development and future directions.

Meet Some of Our Researchers!



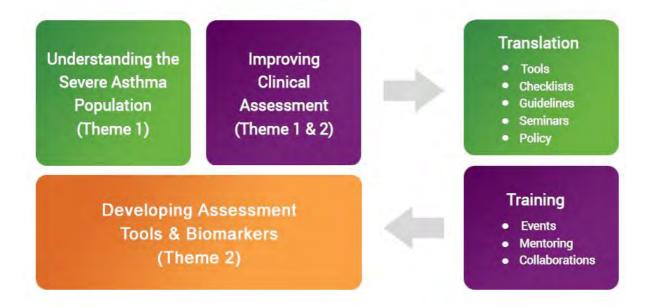
Tong Gong completed a master program of Public Health Sciences and a PhD education in epidemiology from Karolinska Institute. Her major research interest is on genetic and environmental risk factors for asthma and neurodevelopmental disorders. She is currently working as a postdoctoral researcher on the development of national indicators for severe asthma with colleagues at the Australian Centre for Asthma Monitoring (ACAM).



Sai Praneeth Narla graduated with a Masters in Immunology and Allergy with the Developing Solutions Masters Scholarship from The University of Nottingham, UK. Sai is currently a PhD scholar under the supervision of Prof. John Upham and Prof. Peter Wark. His research project focuses on anti-viral immunity and the regulation of macrophages and dendritic cells, in relation to severe asthma.

Research

A primary focus of the Centre of Excellence is to generate new knowledge through research and translate new findings into clinical practice. Research outcomes inform translation and training activities, which in turn improve disease management.



THEME 1: Monitoring the Burden of Severe Asthma in Australia

To better understand the impact of severe asthma, we are using disease registers to determine disease prevalence and impact, performing data linkage analysis to assess patient outcomes and using qualitative methods to better understand the experience of patients with severe asthma and improve management approaches.

Research Programs Underway:

- Developing National Indicators for Severe Asthma
- Phenotypic Heterogeneity and Illness Burden in Severe Asthma
- Concordance and Goal Setting in Severe Asthma Care
- Managing New Therapies in Severe Asthma

Outputs:

- Australian Xolair Registry (AXR) & Australian Mepolizumab Registry (AMR):
 Disease therapy registries provide real-world observational data on patient outcomes
 to identify the effects of treatment and which patient populations respond to therapy.
 These registries provide insight into the effects of the targeted monoclonal antibody
 therapies omalizumab (Xolair; anti-IgE) and mepolizumab (Nucala; anti-IL-5) on
 severe asthma. Details on each registry and research outputs to-date are available on
 our website, for the <u>Australian Xolair Registry</u> and <u>Australian Mepolizumab Registry</u>.
- Example Publication:
 - "This illness diminishes me. What it does is like theft": A qualitative metasynthesis of people's experiences of living with asthma. Pickles K, Eassey D, Reddel HK, Locock L, Kirkpatrick S, Smith L. <u>Health Expectations</u>

THEME 2: Initiatives to Aid Management of Severe Asthma

Severe asthma requires a different management approach to mild or moderate asthma. Personalised treatment approaches using new, targeted therapies provide better patient outcomes. We are assessing the utility of new diagnostic tests and techniques to better inform patient phenotyping and management.

Research Programs Underway:

- Multidimensional Management of Severe Asthma
- Accessible Severe Asthma Biomarkers
- Developing a Severe Asthma Treatment Algorithm
- Exacerbation Risk in Severe Asthma
- Small Airway Physiology in Severe Asthma

Outputs:

- **Severe Asthma Expert Forum #2:** Clinical experts in severe asthma discussed new models of care and medications for severe asthma, focussed on how they treat patients and what evidence is required to inform management.
- **Expert Reviews & Clinical Perspectives:** These publications provide up-to-date insights into best practices for patient treatment and management in the severe asthmaclinic.
 - Selected Publications:
 - Management of Severe Asthma: Targeting the Airways, Comorbidities and Risk Factors. Gibson P, McDonald VM. <u>Internal Medicine Journal</u>
 - Multidimensional Assessment of Severe Asthma: A Systematic Review and Meta-Analysis. Clark V, Gibson P, Genn G, Hiles S, Pavord I, McDonald VM. <u>Respirology</u>
 - Can Biomarkers Help Us Hit Targets in Difficult-to-Treat Asthma? Fricker M, Heaney L, Upham
 J. <u>Respirology</u>
 - Outcomes. Cordova-Rivera L, Gibson P, Gardiner PA, McDonald VM. *IACI In Practice*

NHMRC Funding Success

We are delighted to report NHMRC grant success by Centre of Excellence chief investigators. These projects build on work funded through trainee fellowships and seed grants.



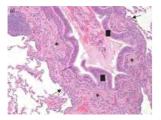
NHMRC Project grant 2018-2020 (\$697,273)

Understanding how azithromycin prevents exacerbations in severe asthma

CI team: John Upham, Jodie Simpson, Katie Baines, Kim-Anh Le Cao

The MOSAIC study (Multi-Omic Signatures in Asthma to improve Inflammation Control) will examine predictors of asthma exacerbations in the AMAZES trial and identify global mRNA and

protein signatures that explain or predict azithromycin treatment responses. This will be a major step towards understanding the mechanisms by which azithromycin reduces asthma exacerbations.



NHMRC Project grant 2018-2020 (\$623,078)

Heterogeneity of airway smooth muscle remodelling in asthma

CI team: Alan James, Peter Noble, David Sampson, Graham Donovan, Annette McWilliams, John Elliot, Li Ping Chung

Building on seed grant-supported findings that heterogeneity exists in smooth muscle remodelling in severe asthma. The findings will aid in the assessment and management of severe asthma by identifying a

potential biomarker to target treatment approaches.

TRANSLATION

Our translation activities are focused on implementing evidenced-based recommendations into practice.

Translation activities:

Seeking Innovative Solutions in Severe Asthma: A review series edited by Centre of Excellence investigators in *Respirology,* featuring reviews of topics relevant to severe asthma. The full series of review articles is freely available on the *Respirology* website

- Example Publications:
 - o Severe Asthma in Children. Bush A, Fleming L, Saglani S.
 - <u>Co-Morbidities in Severe Asthma: Clinical Impact and Management.</u> Porsbjerg C, Menzies-Gow A.
 - o <u>Mouse Models of Severe Asthma: Understanding the Mechanisms of Steroid Resistance, Tissue Remodelling and Disease Exacerbation.</u> Maltby S, Tay H, Yang M, Foster P.
- **Post-Graduate Workshops:** We hosted clinical workshops for healthcare professionals to translate recent research evidence and increase workforce capacity to manage severe asthma. For more information on our workshops at the TSANZ & APSR Annual Scientific meetings, see Events below (pg. 13).

Translation Highlight: The Severe Asthma Toolkit

Providing clinicians from a range of disciplines with resources to implement new treatment for severe asthma into practice is a priority. The Severe Asthma Toolkit was developed to address this need.



We officially launched the Severe Asthma Toolkit on 26 March 2018 at the TSANZ Annual Scientific Meeting in Adelaide

This dedicated online severe asthma resource has been developed to for clinicians caring for people with severe asthma. A reference group consisting of peak and consumer bodies and experts was convened to provide advice and feedback. A multidisciplinary team of international experts was engaged to develop content.

The Severe Asthma Toolkit is a comprehensive, accessible and independent resource developed by leading severe asthma experts to improve clinician knowledge and skill in severe asthma management.

Modules:

- What is Severe Asthma?
- Diagnosis & Assessment
- Management
- Medications
- Co-Morbidities
- Living with Severe Asthma
- Establishing a Clinic
- Paediatrics
- Resources



Learn more about the Severe Asthma Toolkit: toolkit.severeasthma.org.au/about

Online Content:

The Centre of Excellence in Severe Asthma website launched April 2016. Since that time, we have expanded our website, to include resources and educational content relevant for severe asthma.

www.severeasthma.org.au

Our website provides useful resources for severe asthma management, which have been developed for a range of audiences. If you are interested in hearing more about our activities, please sign up for our newsletter, at the bottom of our homepage.

Topics Include:

- News
- Events
- Funded Projects
- Recorded Seminars
- Tools & Resources
- Educational Materials
- Publications
- Contact Details



Website Metrics (to 05 January 2018)

Mailing List Subscribers	Total Website Visitors	Total Page Visits
120	5,119	17,465

You can also follow us on Twitter <a>@SevereAsthmaCRE

Clinical Resources

We are developing clinical resources and algorithms to help with severe asthma diagnosis, management and treatment, which will be made available on our website (http://www.severeasthma.org.au/tools-resources/toolkits/) and through the new Severe Asthma Toolkit (toolkit.severasthma.org.au).

Resources Available Include:

- Clinical Recommendations For The Use Of Omalizumab In Severe Asthma
- Clinical Recommendations For The Use Of Mepolizumab In Severe Asthma
- Severe Asthma Assessment Checklist
- Newcastle Laryngeal Hypersensitivity Questionnaire
- Vocal Hygiene Information Sheet
- Chronic Cough Information Sheet
- Chronic Cough A Tutorial for Speech-Language Pathologists
- Protocol for the AustralAsian Severe Asthma Network (ASAN) Severe Asthma Registry (SAWD) & Research Register

Webinar Presentations

The Centre regularly hosts national and international experts for seminars on topics related to severe asthma. Whenever possible, these seminars are recorded and made available on our website (www.severeasthma.org.au/tools-resources/past-webinars/).

Highlighted Recorded Webinars Available:



Defective Innate Immunity in Airway Disease

Prof. Louise Donnelly. This presentation focuses on the cellular profile of inflammatory lung diseases, including asthma and COPD. In particular, it reports on how innate inflammatory cell function is altered in inflammatory lung disease.



Early-Life Factors and Asthma Development

Prof. Urs Frey. There is increasing recognition that early-life lung development has long-term effects on the development of asthma. Factors that affect early life lung development include tobacco smoke exposure, pollution, birth weight, breastfeeding and early-life airway remodelling. There is no single mechanism leading to impaired lung function growth. Rather, many small effects in early life combine to determine long-term outcomes.



Physiological Phenotyping of Airways Responsiveness in Asthma – Implications for Personalised Medicine

Prof. Charles Irvin. Assessments of patient lung function provide evidence of broad variability between individuals. Prof. Irvin highlights the contribution of airways closing versus narrowing to decreased lung function. Further, in clinical trials, distinct lung function phenotypes exist that do not respond to treatment.



Clinical Trial Endpoints for Severe Asthma

Dr. Robert Niven. A range of endpoint measures are used in clinical trials assessing novel therapies for asthma. The relative benefits and drawbacks of assessments for severe asthma are discussed. Careful selection of endpoint measures is critical, with consideration of the treatment approach and relevance to patient outcomes.



Non-Eosinophic Asthma - Common but Poorly Understood

A/Prof. Celeste Porsbjerg. The recognition that individuals with different phenotypes of severe asthma have differing response to therapy is now well-recognised. While significant progress has been made in our understanding of "eosinophilic" asthma, noneosinophilic asthma remains poorly understood. Non-eosinophilic asthma is common, although disease mechanisms are poorly understood. Alternate approaches may be required for this population and an improved understanding of the mechanisms of inhaled corticosteroids in this population is required.

Webinar Metrics (to 05 January 2018)

Total Recordings	Total Number of Views	Total Watch-Time (Minutes)
15	1,044	14,984

Events

Events and seminars are regularly hosted, form an integral part of our training programme and promote collaboration. We post regular updates about upcoming events, including faceto-face meetings and seminars, and live webinars on our website (www.severeasthma.org.au).



Dr. Robert Niven (University of Manchester) - March 2017

Dr. Niven leads one of 4 centres developing the Severe Asthma National Database Programme in the UK. We hosted his international visit, which included presentations on a range of topics including: bronchial thermoplasty, the UK approach to severe asthma and severe asthma phenotyping in Sydney, Newcastle, Brisbane, Melbourne and Perth.

A recording of Dr. Niven's presentation on **Clinical Trials Endpoints for Severe Asthma** is available on our <u>website</u>.



TSANZ Annual Conference 2017 (25th March 2017, Canberra)

We hosted a symposium at the 2017 <u>TSANZ Annual Scientific Meeting</u> titled "**Pathophysiology of Severe Asthma**", featuring presentations on biopsy, autopsy findings, animal models and cryobiopsy techniques, in severe asthma.



We also hosted a post-graduate workshop before the 2017 TSANZ conference entitled "Severe Asthma: A Clinical Focus". The workshop provided practical insights into the assessment of severe asthma, vocal cord dysfunction, disease biomarkers, targeted therapies, disease registries and case studies.

Centre of Excellence Annual Scientific Meeting (25 October 2017)

We held our annual research meeting at the Hunter Medical Research Institute in Newcastle. The programme included an excellent opportunity for trainees and investigators to present updates on their research and strengthen collaborations



The meeting featured a keynote presentation by Prof. Urs Frey (University of Basel) on **Early-Life Factors and Asthma Development**. A recording is available on our website.

The meeting also featured an interactive career development workshop on **Effective Grant Writing** and **The Grant Panel Process** by Profs. Phil Hansbro (University of Newcastle) and Bruce Thompson (Monash University).



APSR Severe Asthma Workshop (23 November 2018)

We hosted a workshop at the annual Asian Pacific Society of Respirology meeting in Sydney, for a range of range of professionals including physicians and trainees, nurses, allied health professional and researchers. The workshop provided detailed and practical information about how to assess severe asthma, optimize treatment and options available for disease management.

Funded Projects & Travel Grants



As part of our research programme, the Centre of Excellence funds research seed grants and travel grants. The goal of these schemes is to provide pilot funding for research projects and to support trainees to present their research findings at national and international conferences.

Seed Grant Round 3 (commenced January 2017)

- **Marcus Ross Christensen:** Gene expression profiling a novel and efficient method for phenotyping severe asthma?
- **Vanessa Clark:** Targeting anxiety and depression in severe asthma: a pilot randomised controlled trial
- Michael Fricker: Macrophage dysfunction in severe asthma
- **Vanessa McDonald:** <u>Patient Reported Outcome Measure in Severe Asthma (PROMISe): a new tool that measures severe asthma's impact on quality of life</u>
- **Anne Vertigan:** Voice and upper airway symptoms in asthma

Travel Grants



Vanessa Clark: Multidimensional Assessment in Severe Asthma: A Systematic Review

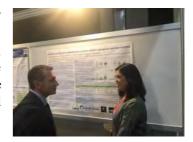
Vanessa attended the European Respiratory Society (ERS) congress in Milan. Vanessa highlighted the importance of her travel grant, which enabled her to "promote her research to an international audience" and be "exposed to cutting edge research in respiratory medicine from around the world". Attendance also allowed Vanessa to engage with world-leading researchers, including a visit to meet Prof. Janelle Yorke (University of Manchester).

Daniela Eassey: "I like to know and make my own choices". Personal Experiences of Severe Asthma: A Review

Daniela gave oral presentations at the TSANZ annual meeting and the International Conference on Communication in Healthcare (ICCH) in Baltimore. The conferences "provided a great opportunity to share ideas, discuss methodology and listen to ongoing work and experiences within both the medical and sociological research community." Discussions have "shaped the way she is currently analysing her preliminary data."

Laura Cordova Rivera: Physical Inactivity and Sedentary Behaviour in Severe Asthma: Prevalence and Associations

Laura attended the ERS congress, which was an "invaluable experience as a PhD candidate" and served as an opportunity to gain exposure to "the impressive amount of research being developed worldwide." Her attendance highlighted the limited number of studies "reporting on physical activity and sedentary time outcomes in severe asthma.



Catherine Farrow: Heterogenous Bronchoconstriction Measured by Ventilation Single Photon Emission Computed Tomography / Computed Tomography

Catherine presented her findings at an invited research talk at the Flow Volume Underworld Lung Physiology Meeting, Harvard University and presented a poster at the American Thoracic Society Annual Scientific Meeting in Washington, DC. Her talk resulted in discussions with the editor of the New England Journal, Dean of Boston University and lung imaging experts from Massachusetts General Hospital. The trip facilitated informal discussions with world-renowned lung physiology experts. Her presentation led to interesting discussions about the future directions of lung imaging in airway diseases.

Michael Fricker: Flow Cytometry-Based Profiling of Immune Cells in Asthmatic Sputum

Michael presented his findings at the Keystone Symposia – Asthma: From Pathway Biology to Precision Therapeutics, in Keystone, Colorado. The meeting largely "focussed on clinical studies but with a very strong discovery and basic science slant". It provided "excellent and encouraging feedback" on Michael's studies and allowed him to connect with and discuss sputum flow cytometry techniques with research from the University of California San Francisco, who are amongst the only researchers in the world currently using the same techniques. The talks also included a large number performing RNAseq analysis of clinical samples, which has directly informed the design of Michael's upcoming studies.



Katrina Tonga: Blood Neutrophils Relate to Lung Volume and DLCO in Older Asthmatics with Fixed Airflow Obstruction

Katrina presented her research findings at the TSANZ Annual Scientific Meeting, the ATS International Congress in Washington DC and the Flow Volume Underworld meeting in Boston. This allowed her to engage and network with experts, in particular experts in airway physiology. One of the tests that Katrina uses in her study (the oesophageal balloon test) is performed by few people in the world. This grant helped her to receive very helpful feedback from

clinician scientists with expertise with this complex test. The will lead to future collaborations and future research into the debilitating asthma phenotype with fixed airflow obstruction. Katrina also received an ATS – Assembly on Respiratory Structure and Function Abstract Scholarship.

Publications

Research published by Centre of Excellence in Severe Asthma investigators is highlighted below, focused on publications that are directly relevant to severe asthma. Chief Investigators are indicated in **bold**, funded trainees, staff and associate investigators are <u>underlined</u>.

2017

- 1. Woodruff PG, Van Den Berge M, Boucher RC, Brightling C, Burchard EG, Christenson SA, Han MK, Holtzman MJ, Kraft M, Lynch DA, Martinez FD, **Reddel HK,** Sin DD, Washko GR, Wenzel SE, Punturieri A, Freemer MM, Wise RA (2017) American thoracic society/national heart, lung, and blood institute asthma-chronic obstructive pulmonary disease overlap workshop report. American Journal of Respiratory and Critical Care Medicine 196: 375-381.
- 2. Wang L, Liang R, Zhou T, Zheng J, Liang BM, Zhang HP, Luo FM, **Gibson PG**, Wang G (2017) Identification and validation of asthma phenotypes in Chinese population using cluster analysis. Annals of Allergy, Asthma and Immunology 119: 324-332.
- 3. Wang G, Wang F, **Gibson PG**, Guo M, Zhang WJ, Gao P, Zhang HP, Harvey ES, Li H, Zhang J (2017) Severe and uncontrolled asthma in China: A cross-sectional survey from the Australasian Severe Asthma Network. Journal of Thoracic Disease 9: 1333-1344.
- 4. **Upham JW,** Xi Y (2017) Dendritic Cells in Human Lung Disease: Recent Advances. Chest 151: 668-673.
- 5. Scott HA, Wood LG, **Gibson PG** (2017) Role of Obesity in Asthma: Mechanisms and Management Strategies. Current Allergy and Asthma Reports 17.
- 6. Rosner SR, Pascoe CD, Blankman E, Jensen CC, Krishnan R, **James AL**, Elliot JG, Green FH, Liu JC, Seow CY, Park JA, Beckerle MC, Paré PD, Fredberg JJ, Smith MA (2017) The actin regulator zyxin reinforces airway smooth muscle and accumulates in airways of fatal asthmatics. PloS one 12: e0171728.

- 7. Robinson PD, **King GG**, Sears MR, Hong CY, Hancox RJ (2017) Determinants of peripheral airway function in adults with and without asthma. Respirology 22: 1110-1117.
- 8. **Reddel HK,** Valenti L, Easton KL, Gordon J, Bayram C, Miller GC (2017) Assessment and management of asthma and chronic obstructive pulmonary disease in Australian general practice. Australian Family Physician 46: 413-419.
- 9. **Reddel HK,** Busse WW, Pedersen S, Tan WC, Chen YZ, Jorup C, Lythgoe D, O'Byrne PM (2017) Should recommendations about starting inhaled corticosteroid treatment for mild asthma be based on symptom frequency: a post-hoc efficacy analysis of the START study. The Lancet 389: 157-166.
- 10. **Reddel HK,** Beckert L, Moran A, Ingham T, Ampon RD, Peters MJ, Sawyer SM (2017) Is higher population-level use of ICS/LABA combination associated with better asthma outcomes? Cross-sectional surveys of nationally representative populations in New Zealand and Australia. Respirology 22: 1570-1578.
- 11. **Reddel HK,** Ampon RD, Sawyer SM, Peters MJ (2017) Risks associated with managing asthma without a preventer: Urgent healthcare, poor asthma control and over-the-counter reliever use in a cross-sectional population survey. BMJ Open 7.
- 12. Pavord ID, Beasley R, Agusti A, Anderson GP, Bel E, Brusselle G, Cullinan P, Custovic A, Ducharme FM, Fahy JV, Frey U, **Gibson P**, Heaney LG, Holt PG, Humbert M, Lloyd CM, **Marks G**, Martinez FD, Sly PD, von Mutius E, Wenzel S, Zar HJ, Bush A (2017) After asthma: Redefining airways diseases. The Lancet.
- 13. Papi A, Brightling C, Pedersen SE, Reddel HK (2017) Asthma. The Lancet.
- 14. O'Byrne PM, FitzGerald JM, Zhong N, Bateman E, Barnes PJ, Keen C, Almqvist G, Pemberton K, Jorup C, Ivanov S, **Reddel HK** (2017) The SYGMA programme of phase 3 trials to evaluate the efficacy and safety of budesonide/formoterol given 'as needed' in mild asthma: Study protocols for two randomised controlled trials. Trials 18.
- 15. Murphy VE, Jensen ME, Powell H, **Gibson PG** (2017) Influence of Maternal Body Mass Index and Macrophage Activation on Asthma Exacerbations in Pregnancy. Journal of Allergy and Clinical Immunology: In Practice 5: 981-987.e981.
- 16. Murphy VE, Jensen ME, **Gibson PG** (2017) Asthma during Pregnancy: Exacerbations, Management, and Health Outcomes for Mother and Infant. Seminars in Respiratory and Critical Care Medicine 38: 160-173.
- 17. Jenkins CR, Eriksson G, Bateman ED, **Reddel HK**, Sears MR, Lindberg M, O'Byrne PM (2017) Efficacy of budesonide/formoterol maintenance and reliever therapy compared with higher-dose budesonide as step-up from low-dose inhaled corticosteroid treatment. BMC Pulmonary Medicine 17.
- 18. **James A** (2017) Airway remodeling in asthma: Is it fixed or variable? American Journal of Respiratory and Critical Care Medicine 195: 968-970.
- 19. Israel E, **Reddel HK** (2017) Severe and difficult-to-treat asthma in adults. New England Journal of Medicine 377: 965-976.
- 20. **Gibson PG**, <u>Yang IA</u>, **Upham JW**, <u>Reynolds PN</u>, <u>Hodge S</u>, **James AL**, Jenkins C, Peters MJ, **Marks GB**, Baraket M, Powell H, Taylor SL, Leong LEX, Rogers GB, Simpson JL (2017) Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial. The Lancet 390: 659-668.
- 21. <u>Fricker M.</u> **Gibson PG** (2017) Macrophage dysfunction in the pathogenesis and treatment of asthma. European Respiratory Journal 50.
- 22. Foster JM, **Reddel HK**, Usherwood T, Sawyer SM, **Smith L** (2017) Patient-perceived acceptability and behaviour change benefits of inhaler reminders and adherence feedback: A qualitative study. Respiratory Medicine 129: 39-45.
- 23. Foster JM, **McDonald VM**, Guo M, **Reddel HK** (2017) "I have lost in every facet of my life": The hidden burden of severe asthma. European Respiratory Journal 50.
- 24. Fingleton J, Hardy J, Baggott C, Pilcher J, Corin A, Hancox RJ, Harwood M, Holliday M, **Reddel HK**, Shirtcliffe P, Snively S, Weatherall M, Beasley R (2017) Description of the protocol for the PRACTICAL study: a randomised controlled trial of the efficacy and safety of ICS/LABA reliever therapy in asthma. BMJ Open Respir Res 4: e000217.

- 25. Farrow CE, Salome CM, Harris BE, Bailey DL, Berend N, **King GG** (2017) Peripheral ventilation heterogeneity determines the extent of bronchoconstriction in asthma. Journal of Applied Physiology 123: 1188-1194.
- 26. Ellwood P, Asher MI, Billo NE, Bissell K, Chiang CY, Ellwood EM, El-Sony A, García-Marcos L, Mallol J, **Marks GB**, Pearce NE, Strachan DP (2017) The Global Asthma Network rationale and methods for Phase I global surveillance: prevalence, severity, management and risk factors. European Respiratory Journal 49.
- 27. Basheti IA, Obeidat NM, **Reddel HK** (2017) Effect of novel inhaler technique reminder labels on the retention of inhaler technique skills in asthma: A single-blind randomized controlled trial. npj Primary Care Respiratory Medicine 27.
- 28. **McDonald VM**, **Gibson PG** (2017) "to define is to limit": Perspectives on asthma COPD overlap syndrome and personalised medicine. European Respiratory Journal 49.
- 29. Lau EMT, Roche NA, **Reddel HK** (2017) Therapeutic approaches to asthma-chronic obstructive pulmonary disease overlap. Expert Review of Clinical Immunology 13: 449-455.
- 30. Hosseini B, Berthon BS, **Wark P**, Wood LG (2017) Effects of fruit and vegetable consumption on risk of asthma, wheezing and immune responses: A systematic review and meta-analysis. Nutrients 9.
- 31. Halnes I, Baines KJ, Berthon BS, MacDonald-Wicks LK, **Gibson PG**, Wood LG (2017) Soluble fibre meal challenge reduces airway inflammation and expression of GPR43 and GPR41 in asthma. Nutrients 9.
- 32. **Gibson PG**, Peters MJ, Wainwright CE (2017) Targeted therapy for chronic respiratory disease: a new paradigm. The Medical journal of Australia 206: 136-140.
- 33. <u>Fricker M</u>, Heaney LG, **Upham JW** (2017) Can biomarkers help us hit targets in difficult-to-treat asthma? Respirology 22: 430-442.
- 34. Ferreira MAR, Jansen R, Willemsen G, Penninx B, Bain LM, Vicente CT, Revez JA, Matheson MC, Hui J, Tung JY, Baltic S, Le Souëf P, Montgomery GW, Martin NG, Robertson CF, **James A**, Thompson PJ, Boomsma DI, Hopper JL, Hinds DA, Werder RB, Phipps S (2017) Gene-based analysis of regulatory variants identifies 4 putative novel asthma risk genes related to nucleotide synthesis and signaling. Journal of Allergy and Clinical Immunology 139: 1148-1157.
- 35. Bowatte G, Lodge CJ, Knibbs LD, Lowe AJ, Erbas B, Dennekamp M, **Marks GB**, Giles G, Morrison S, **Thompson B**, Thomas PS, Hui J, Perret JL, Abramson MJ, Walters H, Matheson MC, Dharmage SC (2017) Traffic-related air pollution exposure is associated with allergic sensitization, asthma, and poor lung function in middle age. Journal of Allergy and Clinical Immunology 139: 122-129.e121.
- 36. Baines KJ, Fu JJ, **McDonald VM**, **Gibson PG** (2017) Airway gene expression of IL-1 pathway mediators predicts exacerbation risk in obstructive airway disease. International Journal of COPD 12: 541-550.
- 37. Arikkatt J, Ullah MA, Short KR, Zhang V, Gan WJ, Loh Z, Werder RB, Simpson J, Sly PD, Mazzone SB, Spann KM, Ferreira MAR, **Upham JW**, Sukkar MB, Phipps S (2017) RAGE deficiency predisposes mice to virus-induced paucigranulocytic asthma. eLife 6.
- 38. Murray LA, Grainge C, **Wark PA**, Knight DA (2017) Use of biologics to treat acute exacerbations and manage disease in asthma, COPD and IPF. Pharmacol Ther 169: 1-12.
- 39. McDonald VM, Maltby S, Reddel HK, King GG, Wark PA, Smith L, Upham JW, James AL, Marks GB, Gibson PG (2017) Severe asthma: Current management, targeted therapies and future directions-A roundtable report. Respirology 22: 53-60.
- 40. **McDonald VM**, <u>Maltby S</u>, **Gibson PG** (2017) Severe asthma: Can we fix it? Prologue to seeking innovative solutions for severe asthma. Respirology 22: 19-20.
- 41. <u>Maltby S</u>, **Gibson PG**, Powell H, **McDonald VM** (2017) Omalizumab treatment response in a population with severe allergic asthma and overlapping COPD. Chest 151: 78-89.

Contact Information

Would you like to get involved with the Centre of Excellence in Severe Asthma? We would be happy to speak with you. The best way to contact us is via email: please include a brief description of your enquiry and we will get back to you ASAP.

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Our website (http://www.severeasthma.org.au) is the best source of information on the Centre of Excellence in Severe Asthma and is regularly updated with news and upcoming events. If you would like to receive updates on events, useful resources and research please join our mailing list, at the bottom of our homepage, and follow us on Twitter @SevereAsthmaCRE.

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