



CENTRE OF EXCELLENCE IN  
**SEVERE ASTHMA**

*Innovative solutions for severe asthma*

**Centre of Excellence in Severe Asthma Newsletter**  
**(Volume 3 – July 2017)**

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Welcome to the third Centre of Excellence in Severe Asthma newsletter. Our newsletters provide updates on activities, personnel, upcoming events and developments relevant to severe asthma.

Newsletter Vol. 1 (August 2016): [click here](#) / Newsletter Vol. 2 (December 2016): [click here](#)  
Annual Report (2015 / 2016): [click here](#)

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**TSANZ 2017 Annual Conference**



The [TSANZ Annual Scientific Meeting](#) was recently hosted in Canberra from the 24<sup>th</sup> to 28<sup>th</sup> of March 2017.

This well-attended event provided an excellent update on research findings relevant to respiratory health and clinical management.

The Centre of Excellence in Severe Asthma was well-represented, with investigators hosting and contributing to workshops, symposia and numerous oral and poster presentations.

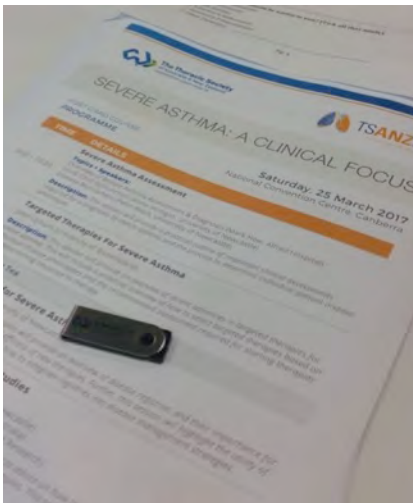
The annual conference was an excellent event, sparking interesting discussions and providing insights into cutting-edge research results.

**The Centre of Excellence in Severe Asthma  
Annual Report 2015 / 2016 is Available – [Click Here](#)**

# TSANZ 2017 Highlights!



The Annual TSANZ Scientific Meeting in Canberra showcased the latest Australian and international research. A number of areas relevant to severe asthma were highlighted.



## Post-Graduate Workshop on Severe Asthma

This year, TSANZ introduced Post-Graduate workshops to the Annual Symposium schedule.

We hosted a workshop entitled “**Severe Asthma: A Clinical Focus**”.

Approximately 100 attendees enrolled in the workshop, which featured presentations on:

**Severe Asthma and Assessment** - Mark Hew

**Vocal Cord Dysfunction** - Anne Vertigan

**Disease Biomarkers** - Peter Wark

**Targeted Therapies** - John Upham

**Registries** - Erin Harvey

**Case Studies** - Vanessa McDonald, Alan James and Greg King

**Prof. Peter Gibson (out-going TSANZ President) opens the proceedings.**



## Themed Symposium - New insights from the pathology of severe asthma



International expert **Sally Wenzel** presented on **biopsy data for severe asthma**, emphasising the heterogeneity of tissue inflammation in asthma.

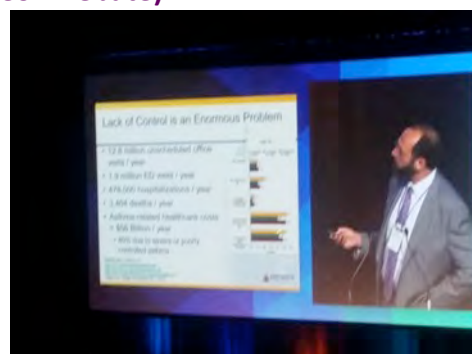
**Alan James** presented **autopsy findings**. While inflammation was present across all cases, heterogeneity in smooth muscle thickening was observed between different airway sizes.

**Gerard Kaiko** provided an overview of **mouse models** and their relevance to the assessment of severe asthma. He highlighted mechanisms governing steroid-resistance and “reverse translation”, where changes identified in patients can be assessed in mice, to determine the functional effects on disease mechanisms.

**Lauren Troy** provided an update on **cryobiopsy**, whereby tissue samples are collected using a freezing probe. This allows collection of larger specimens, but comes with additional risk.

## TSANZ Plenary – Bronchial Thermoplasty in Asthma (Pro / Con Debate)

David Feller-Kopman, Sally Wenzel and Alvin Ing presented an informative and informal update and debate on bronchial thermoplasty. While positive outcome data exists, they emphasised the need for further research on who will respond to treatment, associated risks and the need for long-term efficacy and safety follow-up. A detailed summary is available in [The Limbic](#)



## Special Session: Thunderstorm Asthma

In a dedicated session, **Guy Marks** provided an overview of thunderstorm asthma and **Frank Thien** provided an update on the Melbourne thunderstorm asthma that occurred in November 2016, and the subsequent response.



## TSANZ Plenary – Biological Therapies for Severe Asthma

**Sally Wenzel** provided an overview of monoclonal antibodies available, and in the development pipeline, for severe asthma.

**Steve Bozinovski** provided insight from the COPD perspective, highlighting mechanisms in COPD that may be relevant for future severe asthma therapies.

**Vanessa McDonald** concluded with an overview of how to cope with **Asthma-COPD overlap**. She highlighted the fact that limited clinical trials data are available to inform treatment in this patient population.

## Prizes for Severe Asthma Presentations

- **The debilitating burdens of living with severe asthma** Juliet Foster (Primary Care Special Interest Group – supported by Boehringer Ingelheim) presented results from semi-structured interviews. Most participants experienced daily asthma symptoms and significant disease burden across various aspects of their life. This burden exceeded the impact of milder disease.
- **Omalizumab treatment response in a severe allergic asthma population with overlapping COPD** Steven Maltby (COPD Special Interest Group – supported by Boehringer Ingelheim) presented an assessment of the effect of omalizumab treatment in individuals with asthma-COPD overlap from the Australian Xolair Registry (AXR). Omalizumab treatment improved asthma control and quality of life to a similar degree for individuals with asthma alone and overlap.

## Additional Presentations Relating to Severe Asthma ([link to Oral Presentation Abstracts](#)):

- **Azithromycin Reduces Exacerbations in Adults with Persistent Symptomatic Eosinophilic Asthma** Peter Gibson presented the AMAZES trial, which assessed the effects of azithromycin (a macrolide antibiotic) on acute exacerbations in a population with symptomatic eosinophilic asthma. Azithromycin treatment (for 48 weeks) significantly reduced severe asthma exacerbations. The complete findings from this trial were recently published in the *Lancet* ([link](#)).
- **“I’m a person with asthma” not the asthma first? – Personal experiences in severe asthma: A review** Daniela Eassey presented a review of the qualitative literature, relating to the personal experience of living with severe asthma. She found that living with severe asthma challenges personal autonomy and individuals with severe asthma make efforts to re-claim control. The study also highlighted the scarcity of studies assessing personal experiences in this population.
- **Multidimensional assessment and targeted therapy of severe persistent asthma: A randomised controlled trial** Vanessa McDonald provided evidence that multidimensional assessment and intervention significantly improves outcomes in a population with severe asthma, compared to standard care. In particular, intervention improved asthma control and health-status.

### Additional Presentations Relating to Severe Asthma ([link to Poster Presentation Abstracts](#)):

- **Suitability of Australian electronic medical records to guide the design of the NOVELTY study** Helen Reddel provided insight into utility of medical records in the NOVELTY study (a NOVEL observational longiTudinal studY on patients with asthma and/or COPD). The assessment indicated that Australian patients may be eligible for this international study based on medical records, but highlighted that many study variables are missing in the current data collection.
- **Bronchial thermoplasty response in asthma is influenced by number of radiofrequency activations** Joy Sha presented follow-up data on 20 patients receiving bronchial thermoplasty as treatment for severe asthma. Patients exhibited significant improvements in asthma control after 6-months, which were significantly correlated with the number of activations performed during the thermoplasty procedure. The data indicated that to induce a ACQ-5 improvement of 0.5 units or greater, 116 activations are required.
- **High fat diet-induced obesity promotes steroid-resistant asthma through an NLRP3 inflammasome-dependent mechanism** Jay Horvat presented findings from a novel mouse model where high-fat diet combined with allergic sensitisation and challenge results in steroid-resistant disease. They identified a key role for inflammasome components (including NLRP3) in the development of disease, and propose this pathway as a therapeutic target for clinical intervention.

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## International Visitor – Dr. Robert Niven (University of Manchester)



In March 2017, we were delighted to host Dr. Robert Niven for a research visit to Australia. Dr. Niven is an acknowledged international expert in severe asthma and this was his first trip down-under.

Upon arrival in Australia, Dr. Niven took part in the 2<sup>nd</sup> Severe Asthma Expert's Forum, presenting insights on **Bronchial Thermoplasty**, from a UK perspective. He then visited Sydney, Newcastle, Brisbane, Melbourne and Perth for research discussions, presentations and to develop new collaborations.

Dr. Niven leads one of 4 centres developing the Severe Asthma National Database Programme in the UK. His recent research has focused on new treatments and new technologies to assess and treat respiratory disease, dysfunctional breathing and psychological factors and their interaction with disease.

### Dr. Niven presented seminars on:

**Clinical Trial Endpoints for Severe Asthma** (HMRI, Newcastle)

**UK Approach to Severe Asthma** (Princess Alexandra Hospital, Brisbane)

**Bronchial Thermoplasty** (Princess Alexandra Hospital, Brisbane)

**Severe Asthma Phenotyping** (The Alfred Hospital, Melbourne)

**Dysfunctional Breathing** (The Alfred Hospital, Melbourne)

**Experience with Allergic Asthma and Xolair in the UK** (Lung Club, Perth)

**Bronchial Thermoplasty – Early Clinical Experience in the UK and Europe** (Perth)



Recorded Newcastle Webinar: Clinical Trial Endpoints for Severe Asthma

<http://www.severeasthma.org.au/tools-resources/past-webinars/>

## Webinar Series



Our most recent webinar on 04 May 2017 was presented by Prof. Charles Irvin, Director of the Vermont Lung Center and Professor of Medicine at the University of Vermont

### **Physiological Phenotyping of Airways Responsiveness in Asthma – Implications for Personal Medicine**

Prof. Irvin's scientific career has focused on understanding the mechanisms of airways dysfunction of the patient with asthma.

Refreshments and Prof. Irvin's travel were supported by funding from AstraZeneca.

#### **Other recent webinars:**

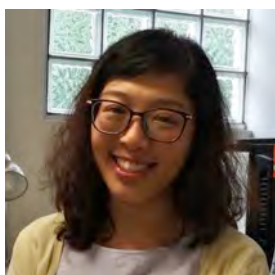
Seminars are recorded and made available on our [past webinars](#) site.

- A/Prof. Celeste Porsbjerg – Non-Eosinophilic Asthma – Common But Poorly Understood

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## Meet Our Researchers

We have welcomed new scholars, including post-doctoral fellows and PhD scholars. Find out more about our trainees and investigators [here](#)



**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).



**Bilal Malik** completed a Masters and M.Phil in Biochemistry and Molecular Biology from Quaid-i-Azam University Islamabad, Pakistan. He subsequently worked as a research associate at Shaukat Khanum Memorial Cancer Hospital and Research Center and in the Department of Biophysics, Center for Molecular Biomedicine in Jena, Germany. Bilal is currently a PhD candidate under the supervision of Profs. Peter Wark and John Upham. His research project focuses on viral infection, anti-viral immunity and the regulation of innate lymphoid type-2 cells, in relation to severe asthma.



**Natalie Niessen** completed a Masters in Molecular Biosciences at Goethe University Frankfurt, Germany. Natalie is currently a PhD candidate under the supervision of Dr. Michael Fricker and Prof. Peter Gibson. Her research project focuses on understanding aberrant inflammatory signaling in asthma.

## Severe Asthma News



**Thunderstorm Asthma:** There have been a number of updates in response to the tragic thunderstorm asthma episode of 21<sup>st</sup> Nov. 2016, in Melbourne. This terrible event resulted in 9 deaths and directly affected thousands of individuals. A summary of events was published in The Age ([link](#)).

The Epidemic Thunderstorm Asthma Symposium was hosted on 17 March in Melbourne by the Department of Health and Human Services Victoria to assess responses and identify areas for improvement in future events.

**A government report is now available in response to this episode:**

- [Inspector General Review of Response](#)

**You may be interested in the following publications relating to this event:**

- [The Melbourne thunderstorm asthma event: can we avert another strike?](#) Mark Hew, Michael Sutherland, Francis Thien & Robyn O’Hehir *Internal Medicine Journal*
- [Hospitals overwhelmed with patients after “thunderstorm asthma” hits Melbourne](#) Michael Woodhead *The British Medical Journal*
- [Thunderstorm asthma: potential danger but a unique opportunity](#) Francis Thien *Asia Pacific Allergy*

A recording of our **Special Seminar on Thunderstorm Asthma**, by Guy Marks is also available on our website for more information:

<http://www.severeasthma.org.au/tools-resources/past-webinars/>



**PBS Approval of Mepolizumab:** Nucala/mepolizumab was recently PBS-approved as an add-on therapy for people with severe refractory eosinophilic asthma,  $\geq 12$  years of age. Mepolizumab is monoclonal antibody that blocks interleukin-5 (IL-5) function and reduces the production and survival of eosinophils.

We developed **clinical recommendation** documents for mepolizumab and omalizumab that cover treatment, eligibility, enrolment, precautions and administration procedures, which you may find useful. **Clinic recommendations are available on our [Toolkits](#) page.**

**Australian Mepolizumab Registry (AMR):** The AMR collects and reports data from people who receive mepolizumab. This registry provides a mechanism to better understand the use, efficacy and safety of mepolizumab treatment in the Australian population. For further information and to enrol patients, please contact Dr. Erin Harvey [erin.harvey@newcastle.edu.au](mailto:erin.harvey@newcastle.edu.au)

## Highlighted Recent Severe Asthma Publications

### Publications Presented in the Severe Asthma Journal Club ([link](#)):

- [The Level of Diagnostic Assessment in Severe Asthma: A Nationwide Real-Life Study](#) *Respiratory Medicine* A retrospective analysis of assessments performed in specialist respiratory clinics in Denmark. This study revealed relatively low rates of objective assessment to confirm a diagnosis of asthma.
- [The Asthma-Anxiety Connection](#) *Respiratory Medicine* A significant association between anxiety and asthma is recognised, but the nature of this association is unclear. A significant association and a bidirectional relationship between anxiety and asthma development was observed.
- [T-Helper Cell Type 2 \(Th2\) and Non-Th2 Molecular Phenotypes of Asthma Using Sputum Transcriptomics in U-BIOPRED](#) Sputum gene expression in moderate-to-severe asthma patients revealed 3 patient clusters. In addition to the well-characterised Th2 pathway, individuals with non-Th2 disease had gene signatures suggestive of innate immune activation or alterations in metabolic and mitochondrial function.

### AMAZES Clinical Trial:

- [Effects of Azithromycin on Asthma Exacerbations and Quality of Life in Adults with Persistent Uncontrolled Asthma \(AMAZES\): A Randomised, Double-blind Placebo-Controlled Trial](#) Azithromycin treatment (for 48 weeks) significantly reduced exacerbations by 40% and improved quality of life. This trial also received a comment in *The Lancet* ([link](#)) and was featured by ABC news ([link](#)).

### “Seeking Innovative Solutions in Severe Asthma” series for *Respirology*:

- [Severe Asthma: Can We Fix It? Prologue to Seeking Innovative Solutions for Severe Asthma](#) Vanessa McDonald, Steven Maltby and Peter Gibson
- [Severe Asthma: Current Management, Targeted Therapies and Future Directions – A Roundtable Report](#). Vanessa McDonald, Steven Maltby, Helen Reddel, Greg King, Peter Wark, Lorraine Smith, John Upham, Alan James, Guy Marks and Peter Gibson
- [Severe Asthma in Children](#). Andrew Bush, Louise Fleming and Sejal Saglani
- [Co-Morbidities in Severe Asthma: Clinical Impact and Management](#). Celeste Porsbjerg and Andrew Menzies-Gow
- [Can Biomarkers Help Us Hit Targets in Difficult-to-Treat Asthma?](#) Michael Fricker, Liam Heaney and John Upham
- [Mouse Models of Severe Asthma: Understanding the Mechanisms of Steroid Resistance, Tissue Remodelling and Disease Exacerbation](#). Steven Maltby, Hock Tay, Ming Yang and Paul Foster

### Clinical Perspectives:

- [Management of Severe Asthma: Targeting the Airways, Comorbidities and Risk Factors](#). Peter Gibson and Vanessa McDonald *Internal Medicine Journal*

### Recent Commentaries by CRE Members:

- [No need to wait for European consensus on severe eosinophilic asthma](#): Expert Commentary from Peter Wark *The Limbic*
- [ACOS not a useful disease concept](#): Expert Commentary from Vanessa McDonald and Peter Gibson *The Limbic*

For a complete list of publications by CRE investigators, please see our website ([link](#)).

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### Explore Our Website And Follow Us On Twitter!

Our website (<http://www.severeasthma.org.au>) is the best source of information on the Centre of Excellence in Severe Asthma. If you would like to receive updates on events, resources and research join our mailing list on our homepage and follow us on Twitter [@SevereAsthmaCRE](#).