

# Treating chronic childhood cough: Case Study

Chronic cough is a common problem in children that impairs quality of life, with a burden often unappreciated by health professionals. Protracted Bacterial Bronchitis (PBB) is the most common cause of chronic cough in children. Untreated, it leads to poor future lung health outcomes such as bronchiectasis. NHMRC-funded researchers at Queensland University of Technology (QUT) and Menzies School of Health Research (Menzies) first described PBB and have made substantial inroads into the understanding of its pathobiology and improving clinical outcomes in children with chronic cough. PBB is now recognised internationally and incorporated into all major international paediatric chronic cough guidelines.



## Origin

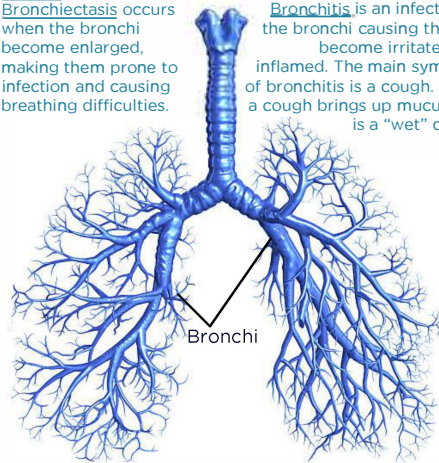
Cough is a common reason for patients presenting to doctors,<sup>1</sup> and some patients have chronic cough (>4-weeks duration).

In children, chronic cough impairs the quality of life (QoL) of both children and their parents<sup>2</sup> and causes a high healthcare burden.

Single,<sup>3,4</sup> and multi-centre<sup>2</sup> studies in Australia involving children with chronic cough presenting for the first time to respiratory specialists found that ~80% had seen >5 doctors for their cough, their QoL was as poor as those with cardiac disease and ~12% had a serious underlying illness (e.g. bronchiectasis).

However, the importance of chronic cough as indicating an underlying treatable disease has often been unrecognised by doctors, and until recently, the primary cause of chronic cough was unknown and required investigation by medical researchers.

**Bronchi** are the tubes that carry air into and out of the lungs. **Bronchiectasis** occurs when the bronchi become enlarged, making them prone to infection and causing breathing difficulties. **Bronchitis** is an infection of the bronchi causing them to become irritated and inflamed. The main symptom of bronchitis is a cough. When a cough brings up mucus, this is a "wet" cough.



Credit: iStock, DmitryDamichenko

## Grants and Investment

The need to improve the management of paediatric chronic cough was recognised by a team of researchers led by Anne Chang at QUT/Menzies and a group of collaborating researchers and clinicians located in a range of universities and hospitals, in Australia and internationally. NHMRC funded their research—including within the Cough and Airways Group (QUT)/Child Respiratory Group (Menzies) and other related collaborations—through a broad range of grants and fellowships.

Other funding sources include: Queensland (Qld) Children's Hospital Foundation (CHF), Perth CHF, Qld Children's Medical Research Institute (QCMRI), Qld Health, Western Australian (WA) Health, Royal College of Physicians, Rebecca L Cooper Foundation, Medical Research Future Fund (MRFF), Lung Foundation of Australia, Raine Medical Research and other NGOs.



Image: Lesley Versteegh—an Aboriginal research nurse in Chang's Darwin group—providing education to a mother using a digitalised version of the resources produced by the team.

Credit: Menzies School of Health Research

## Research and Collaboration

As a consequence of a comprehensive evaluation of children with chronic cough, the team were the first to recognise and describe PBB. They then undertook the first randomised controlled trial (RCT) on using antibiotics for children with chronic wet cough, and later synthesised the evidence in a Cochrane Review.

Concurrently, Chang was invited by the American College of Chest Physicians to write the world's first guidelines on the management of paediatric chronic cough.

Prior to these works, it was recommended that children with chronic cough be treated like adults, which is now understood to be associated with adverse events.

The team undertook studies focused on improving the management of paediatric chronic cough. These included development of 'cough pointers' and RCTs evaluating a chronic cough algorithm involving children presenting to specialists and primary care.

Microbiological studies to understand PBB's pathobiology during lower airway infection led to the first descriptions of biofilms in PBB and diagnostic criteria for infection.

An RCT involving First Nations children hospitalised for acute respiratory infection led to the discovery of an association between the presence of chronic cough and future bronchiectasis. Along with research on various aspects of bronchiectasis in children—including two international multi-centre RCTs—this provided evidence of the paradigm linking PBB to bronchiectasis, proposed in 2008 and now internationally accepted.

Subsequent research described the enablers and barriers to the timely detection of, and optimal management of children with, chronic cough in First Nations communities in the Kimberley, Western Australia.

## Results and Translation

The discovery of PBB changed international approaches to paediatric chronic cough management and these changes have been incorporated into the European Respiratory Society (ERS) curriculum and all current major chronic cough guidelines.

In June 2022, PBB was recognised as a disease by the World Health Organisation (WHO).

Other on-going work has shown that using an evidenced-based chronic cough algorithm improves parents' and children's QoL and enhances accurate diagnosis. These are now standard practice in point-of-care manuals (e.g. in Up-To-Date—an online resource for physicians).

Utilisation of the concept of wet cough and 'cough pointers' is now a standard differentiating feature used in patient education resources internationally. In response to community requests, the team developed First Nations-specific flip-charts and software based around these tools.

Discovery of the association between the presence of chronic cough and future bronchiectasis in First Nations children hospitalised for a respiratory infection led to changes in policy/practice to ensure they are followed-up in the community and—when chronic cough is present—are treated for PBB. These are now recommendations in First Nations oriented point-of-care manuals and guidelines.

With the Lung Foundation of Australia, podcast and modules for training of health practitioners were produced. The knowledge translation approach in partnership with local champions has led to doctors recognising and treating PBB earlier in First Nations communities in the Kimberley.

A medical algorithm is a decision-making support tool designed to assist clinicians to provide the most appropriate health-care treatment.

## Health Outcomes and Impact

As a direct consequence of the NHMRC-funded research undertaken by Chang and her colleagues there has been a change in global clinical practice in the treatment of children with chronic cough that has led to improved QoL and clinical outcomes in both urban and First Nation settings.

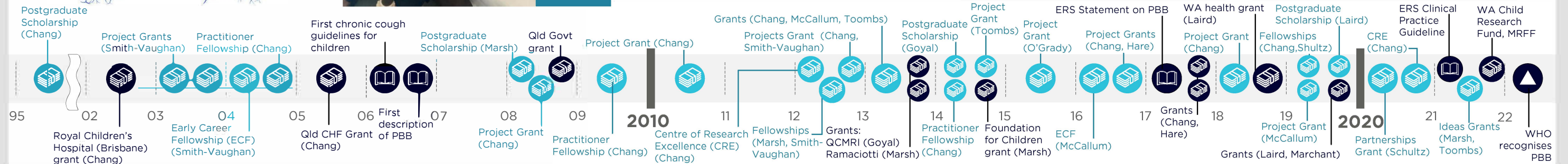
Improvements include: resolution of chronic cough, prevention and reversal of bronchiectasis, improved lung function, and reduced use of unnecessary medications. In Australia, these changes are expected to lead to a reduction in costs of \$161 million over the period 2012 to 2041.<sup>5</sup>

In Australia, there has also been a change in policy and practice involving the follow-up of First Nations children hospitalised with respiratory infections. Prior to the team's work, chronic cough among First Nations children—and the poor lung health that resulted from it—were often seen as being 'normal' among carers.

Better recognition and detection of chronic wet cough (PBB and bronchiectasis)—including in remote First Nations communities—has led to improved management and clinical outcomes, including: using the right antibiotics for the right child for the right indication, earlier recognition and detection of bronchiectasis, prevention of severe bronchiectasis, reduced hospitalisations and improvements to patients' lung function.

The team's research work has also resulted in capacity-building of 11 trainees—including 8 First Nations trainees—in the context of higher degrees by research, undergraduate degrees, vocational education and training and translation activities.

All research and other activities involving First Nations Australians (both in Darwin and Brisbane) are discussed with and informed by the Child Health First Nations Advisory Board at Menzies. Other research activities (since 2019) are informed by a Parent Advisory Group.



Note: NHMRC grants are dated by their start year. This timeline is abridged. Refer HTML version of case study for complete timeline.

### Prof Anne Chang AM

Anne Chang graduated in medicine from The University of Melbourne. She is now a paediatric respiratory physician who is Head of the Child Health Division at Menzies and the Cough and Airways Research Group at QUT. In 2019 she was made a Member of the Order of Australia.

### Prof Maree Toombs

Maree Toombs is the Associate Dean Indigenous Engagement in the Faculty of Medicine at The University of Queensland. She is also the past-Chair of Carbal Aboriginal Medical Services and was appointed a Professorial Fellow at Menzies in 2021.

### Prof Keith Grimwood

Keith Grimwood is Deputy Head (Research) of the School of Medicine and Dentistry at Griffith University. Grimwood is a paediatric infectious diseases physician with a joint appointment as Professor of Infectious Diseases with Gold Coast Hospital and Health Services.

### A/Prof Julie Marchant

Julie Marchant is an Associate Professor within the School of Public Health & Social Work at QUT. She is a Paediatric Respiratory Physician at the Queensland Children's Hospital and a senior research fellow at the Centre for Children's Health Research, Brisbane.

### A/Prof André Schultz

André Schultz is the Program Head of Respiratory Health and Head of the BREATH Team at Telethon Kids Institute. He is also a paediatric respiratory physician and Director of Cystic Fibrosis at Perth Children's Hospital, and co-founder and Chair of the multinational chILDranZ Peer Support Team.

### A/Prof Stephanie Yerkovich

Stephanie Yerkovich is a scientist and biostatistician at Menzies and QUT. She studies both immune development and the association between altered immunity and paediatric and adult respiratory disease, especially in relation to the microbiome and infectious burden.

### A/Prof Heidi Smith-Vaughan

Heidi Smith-Vaughan is a Principal Research Fellow and Associate Director for Research (HDR and ethics) at Menzies. She leads HealthLAB (for health education implementation) and co-leads the Menzies Ramaciotti Regional and Remote Health Science Training Centre.

### Dr Robyn Marsh

Robyn Marsh is a Senior Research Fellow at Menzies who leads the Menzies (Darwin) Child Health Division's Respiratory Microbiome Program and co-leads the Ramaciotti Regional and Remote Health Science Training Centre. She is a 2020 AI & Val Rosenstraus Fellowship recipient.

### Dr Pamela Laird

Pamela Laird is a senior respiratory physiotherapist at Perth Children's Hospital and the Kimberley/Pilbara specialist respiratory service. Laird is a Raine Fellow and has worked in partnership with Aboriginal communities and other collaborators to develop lung health literacy tools.

### Dr Gabrielle McCallum

Gabrielle McCallum is a Senior Research Fellow, Clinical Nurse, and Program Leader of Menzies' Child Health Respiratory team in Darwin. McCallum's work includes multi-centre RCTs and other observational studies extending to New Zealand, Alaska and Malaysia.

### Dr Vikas Goyal

Vikas Goyal trained as a Paediatric Respiratory and Sleep Medicine Physician, is based at the Queensland Children's Hospital and works within the Cough and Airways Research QUT group. His PhD focused on bronchiectasis in children and included two international RCTs.

### Other researchers

A/Prof Kerry-Ann O'Grady, QUT  
Dr Kim Hare, Menzies  
Professor Peter Morris, Menzies  
Dr Katie Baines, University of Newcastle  
Professor John Upham, University of Queensland  
Professor Sandra Hodge, University of Adelaide



## References

This case study was developed with input from Professor Anne Chang and team members and in partnership with Queensland University of Technology and the Menzies School of Health Research.

The information and images from which impact case studies are produced may be obtained from a number of sources including our case study partner, NHMRC's internal records and publicly available materials.

The following sources were consulted for this case study:

- 1 Britt H, Miller GC, Bayram C, et al. A decade of Australian general practice activity 2006-07 to 2015-16. Sydney University Press 2016; General practice series no. 41.
- 2 Chang AB, Robertson CF, van Asperen PP, et al. A multi-centre study on chronic cough in children: burden and etiologies based on a standardized management pathway. Chest 2012; 142: 943-50.
- 3 Marchant JM, Newcombe PA, Juniper EF, Sheffield JK, Stathis SL, Chang AB. What is the burden of chronic cough for families? Chest 2008; 134: 303-09.
- 4 Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. Chest 2006; 129: 1132-41
- 5 Deloitte Access Economics. The social and economic contribution of the Menzies School of Health Research. February 2022. Deloitte.

## Partner/s

