

Respiratory Research Review™

Making Education Easy

Issue 145 – 2018

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Abbreviations used in this issue

ACT = Asthma Control Test
ICS = inhaled corticosteroid
LABA = long-acting β -agonist
LOESS = locally weighted scatter plot smoother curve
MART = maintenance and reliever therapy
QOL = quality of life
RCT = randomised controlled trial

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Welcome to issue 145 of Respiratory Research Review.

"I have lost in every facet of my life. You know, my earning capacity, my self-esteem, my sense of achievement, my relationships. You name it, it's been there. And my asthma has been this severe all my life." This is the opening statement of a qualitative [article](#) based on in-depth, semistructured interviews of adults with severe asthma published by colleagues from the Woolcock Institute. It is accompanied by a very insightful [editorial](#) by Sally Wenzel, which she copublished with two patients with lifelong severe asthma, telling their story of biases from healthcare providers, media and trickledown biases of the general public. Our focus on adherence can be interpreted as being continuously 'blamed' for the severity of their asthma. Also, can anybody think of an inspiring story of a family struggling with asthma? Movies tend to depict asthma as a nuisance that can be fixed with the 'blue inhaler'. Movie characters with asthma tend to be weak or nerdy, and reach for the inhaler at any time of stress. Finally, the US and NZ share direct-to-consumer advertising, where the public, including friends and family, are barraged by messages that asthma is easily controlled, and that with the latest and greatest inhaler they can live a perfectly normal life.

The NZ child and adolescent asthma guidelines ([N Z Med J 2017;130\[1466\]:10–33](#)) may be addressing some of these issues by starting with the following ten tips for healthcare professionals when caring for people with asthma.

1. Build strong **relationships**.
2. Work towards **wellness**; do not accept sickness as the norm.
3. Ask about **smoke exposure** and refer to support services.
4. Ask about **housing** and unhealthy features.
5. **Income** – does the child qualify for a child disability allowance?
6. Assume little **health literacy**.
7. Ask about technique and **adherence** in a nonjudgmental way.
8. Develop an appropriate **asthma action plan**.
9. Identify any possible barriers to **accessing** healthcare.
10. Ensure the family knows when and how to call an **ambulance**.

The prescribing of correct medication is key to controlling asthma and reducing future risk. The guidelines remind us that Māori and Pacific children are more likely to have severe asthma symptoms and be hospitalised, and less likely to be prescribed ICSs, have an action plan or receive adequate education. As Richard Beasley and Bob Hancox point out in their accompanying [editorial](#), important aspects are: the diagnosis, which is not looking for a 'gold standard' investigation and instead based on characteristic patterns of symptoms and signs, the up- and down-titration of ICSs (inhaled corticosteroids), action plans and also the diagnostic label of preschool asthma. Preschool asthma should be considered in children with frequent preschool wheezing episodes and children should be offered an 8-week trial of steroids. If they respond they should be labelled preschool asthma; however, the parents can be reassured that this does NOT mean the child will go on to have asthma at school age or as an adult.

Here are two thoughts prior to the selection of articles. First, I greatly enjoyed two review articles I'd like to draw attention to. 'Does inhaled steroid therapy help emerging asthma in early childhood?' In this [personal view](#), the authors reassure us that ICSs improve symptoms, improve QOL and probably save lives; however, ICSs do not alter the natural course in children at risk of persistent asthma. Elliot Israel and Helen Reddel published an authoritative [review](#) on the management of 'severe and difficult-to-treat asthma in adults' in *N Engl J Med*. This leads to my second and final thought: we can be proud in NZ and Australia as some of the highest impact articles published over the last 6 months have been written by local researchers like Innes Asher, Helen Redell, Vanessa McDonald and Richard Beasley.

Let's apply this research to improve health outcomes for our patients. Thanks for your feedback, emails and engagement.

Kind regards

Professor Lutz Beckert

lutzbeckert@researchreview.co.nz

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"I have lost in every facet of my life": the hidden burden of severe asthma

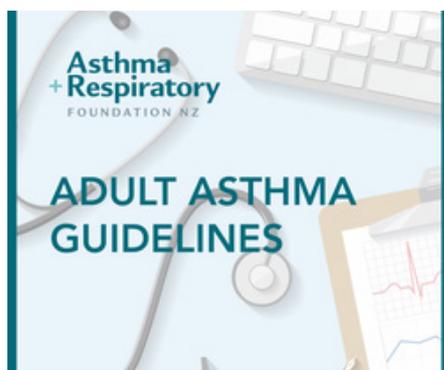
Authors: Foster JM et al.

Summary: Twenty-five telephone interviews were conducted with adults with severe asthma to survey their lesser known life experiences associated with their condition. Four themes emerged from the responses. Severe asthma was reported to place broad limits on life from daily chores to career, relationships and family life, resulting in emotional distress. While participants mostly accepted that they required treatment, they were concerned about the side effects of oral corticosteroids. Interviewees also often felt misunderstood and alone in their experience of breathlessness and frightening exacerbations. They felt there was often a lack of practical and emotional support, and those who reported little support also reported experiencing augmentation of emotional distress. Respondents also reported use of positive strategies and less positive strategies in order to adjust to living with severe asthma.

Comment: You can hear the patients' voices in this qualitative article published by our Australian colleagues. Information collected from 25 in-depth interviews was analysed using descriptive coding and inductive pattern coding to group data into themes. The theme headlines are: i) the body as a hindrance; ii) burden of treatment; iii) alone with asthma; and iv) striving to adapt. Quotes on the impact on ability to look after their own children, career choices, medical experiences and partnerships are sobering. This article is supported by an excellent [editorial](#) by Sally Wenzel. **Bottom line: severe asthma is a horrible and life-changing illness.**

Reference: *Eur Respir J* 2017;50:1700765

[Abstract](#)



Perceptions of asthma control in the United Kingdom: a cross-sectional study comparing patient and healthcare professionals' perceptions of asthma control with validated ACT scores

Authors: Menzies-Gow A & Chiu G

Summary: Data on actual versus perceived asthma control were collected from adults attending routine asthma reviews in UK primary, secondary and tertiary settings in this cross-sectional survey. Online questionnaires were used to gather the perception data from patients and their healthcare professionals, and the patients also completed the validated ACT (Asthma Control Test) for comparison. The patients were stratified according to the BTS/SIGN (British Thoracic Society/Scottish Intercollegiate Guidelines Network) 2014 treatment guidelines, with 33, 52, 50, 49 and 50 eligible participants in steps 1–5, respectively; women made up 70% of the participants, 47.4% were aged 45–64 years and 70% were classified as nonsmokers by the healthcare professionals. A perception of asthma was reported by 84.2% and 73.9% of patients and their healthcare professionals, respectively, but asthma control according to an ACT score ≥ 20 was identified in only 54.7% of patients, with 67.9% agreement between the ACT assessment and patient, and 68.8% between the ACT assessment and healthcare professional. Uncontrolled asthma was greatest and agreement worst for patients in steps 4 and 5 from the BTS/SIGN recommendations.

Comment: This study from the UK explored the perception of asthma control assessed by the patients, doctors and the ACT. Patients enrolled at general practitioner practices were identified and stratified according to severity, and following a doctor consultation, a researcher contacted patients asking 'in the last 4 weeks, did you feel that your asthma has been controlled or uncontrolled'. The answer was compared with the result achieved by the ACT. About 85% of patients thought their asthma was controlled, doctors felt the asthma was controlled in 75% of patients and the ACT judged asthma to be controlled in about 55%. **Bottom line: patients and doctors overestimate the control of asthma.**

Reference: *NPJ Prim Care Respir Med* 2017;27:48

[Abstract](#)

Electronic monitoring of adherence to inhaled corticosteroids: an essential tool in identifying severe asthma in children

Authors: Jochmann A et al.

Summary: Children with asthma (n=93) had their persistence of ICS adherence prospectively assessed using electronic monitoring devices for a median of 92 days in this research. Median monitored adherence was 74%. The following four adherence groups emerged: i) likely previous poor adherence, in which good adherence was seen with improved control (24%); ii) severe therapy-resistant asthma, in which adherence was good but control was poor (18%); iii) likely overtreated, in which adherence was poor but control was good (26%) and iv) poor adherence with poor control (32%). These four groups could not be differentiated by any premonitoring clinical parameter.

Comment: We currently estimate that half of the children attending a severe asthma clinic don't pick up their prescriptions. This group from the Brompton explores the NZ device 'Adherium' to enhance patient adherence in a severe asthma clinic. In 93 children with severe asthma, they identified four groups of roughly a quarter each: i) monitoring improves adherence and asthma control; ii) good adherence with poor control, suggesting the need to escalate treatment; iii) poor adherence with good control, suggesting overtreatment; and, the largest group, iv) poor adherence and poor asthma control. **Bottom line: electronic monitoring is becoming essential in a severe asthma clinic.**

Reference: *Eur Respir J* 2017;50:1700910

[Abstract](#)

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A randomised clinical trial of feedback on inhaler adherence and technique in patients with severe uncontrolled asthma

Authors: Sulaiman I et al.

Summary: Patients with severe uncontrolled asthma were stratified by site and received intensive education involving repeated training in inhaler use adherence and disease management with or without enhancement by (bio)feedback in this randomised trial. Compared with participants who received the intensive education alone, those who received (bio)feedback enhancement had a higher mean adherence rate during month 3 (73% vs. 63% [$p=0.02$]). At study end, asthma was stable or improved in 38% of participants, uncontrolled with poor adherence in 35% and uncontrolled with good adherence in 27%.

Comment: In the previous study, the recording device was superior to tallying prescriptions filled. This Irish study added an INCA (Inhaler Compliance Assessment) attachment to the inhaler, which makes an audio recording each time the inhaler is used and provides biofeedback data on the adherence time, habit and technique. Randomising a group of severe asthmatics to intensive education and the INCA biofeedback device, the authors report a significant increase in adherence to medications. Asthma control was improved in both groups, although both groups were also still plagued by nonadherence. **Bottom line: the INCA device is a new tool to improve adherence and inhaler technique.**

Reference: *Eur Respir J* 2018;51:1701126

[Abstract](#)

Effect of the School-Based Telemedicine Enhanced Asthma Management (SB-TEAM) program on asthma morbidity

Authors: Halterman JS et al.

Summary: Children aged 3–10 years with persistent asthma ($n=400$) were stratified by baseline preventer therapy and randomised to: i) a programme that builds on school-based supervised therapy programmes for asthma management (SB-TEAM [School-Based Telemedicine Enhanced Asthma Management]) by incorporating telemedicine at school to overcome barriers; or ii) supervised administration of preventive asthma medication (enhanced usual care). Each trial arm lasted for a single school year. Nearly all (98%) of the children enrolled in the SB-TEAM arm participated in ≥ 1 telemedicine visit and 82.5% received supervised therapy through school. Compared with the usual care group, SB-TEAM participants had more symptom-free days after the intervention (11.6 vs. 10.97 per fortnight [$p=0.01$]), with the greatest difference seen at final follow-up, and a lower likelihood of requiring an emergency department visit or hospitalisation for asthma (7% vs. 15%; odds ratio 0.52 [95% CI 0.32, 0.84]).

Comment: We will probably need both programmes focusing on structured health plans supported by the state based on education, training and funding community providers, and improvements in technology. These American authors report on the success of a school-based telemedicine-enhanced asthma management programme to reduce asthma morbidity in children with persistent asthma. In partnership with the schools and without additional resources for the school nurse, the authors developed a telemedicine-enhanced programme to enhance usual care. **Bottom line: a telemedicine-enhanced school-based programme was acceptable to children and parents and led to significantly improved asthma control with more symptom-free days and fewer emergency department visits.**

Reference: *JAMA Pediatr*; Published online Jan 8, 2018

[Abstract](#)

Independent commentary by Professor Lutz Beckert.

Professor Lutz Beckert is the Head of Department of Medicine of the University of Otago, Christchurch. He is also a Respiratory Physician at Canterbury District Health Board.

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Effectiveness of fluticasone furoate plus vilanterol on asthma control in clinical practice

Authors: Woodcock A et al., on behalf of the Salford Lung Study Investigators

Summary: This open-label trial enrolled 4233 adults with symptomatic asthma on maintenance inhaler therapy from 74 UK general practice clinics. The participants were randomised to initiate treatment with a once-daily inhaled combination of fluticasone furoate either 100 μ g or 200 μ g with vilanterol 25 μ g ($n=2114$) or to receive optimised usual care ($n=2119$); follow-up was 12 months. An intent-to-treat analysis revealed that patients who initiated treatment with fluticasone furoate and vilanterol were significantly more likely than those receiving usual care to be classified as responders (i.e. those with a baseline ACT score of <20 who achieved a score of ≥ 20 points or an increase from baseline of ≥ 3 points at 24 weeks; 71% vs. 56%; odds ratio 2.00 [95% CI 1.70, 2.34]). At week 24, the adjusted mean ACT score was increased from baseline by 4.4 points with fluticasone furoate and vilanterol, compared with 2.8 points with usual care ($p<0.0001$); this outcome remained unchanged at 12 months. Pneumonia was uncommon, with no between-group difference in rates. Similarly, other serious adverse events did not differ significantly between the groups.

Comment: Peter Gibson crystallised the novelty and importance of this paper in his accompanying [editorial](#) 'Effectiveness trials in asthma: time to SaLSA?'. RCTs give us the best evidence; however, on average only 4% of patients we see in our clinic would fit the inclusion criteria for an asthma RCT. The exciting new methodology in this trial is that it is embedded within usual primary care. Based on electronic health records, patients with symptomatic asthma were identified, consented and offered either standard therapy or fluticasone furoate/vilanterol combination. **Bottom line: in routine clinical care settings the once-daily fluticasone furoate/vilanterol combination improves asthma control.**

Reference: *Lancet* 2017;390:2247–55

[Abstract](#)

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Budesonide/formoterol maintenance and reliever therapy in adolescent patients with asthma

Authors: Jorup C et al.

Summary: The efficacy and safety of budesonide/formoterol MART (maintenance and reliever therapy) for persistent asthma was assessed for adolescent participants (n=1847) from six randomised, double-blind trials in this *post hoc* analysis. Compared with trial comparators, budesonide/formoterol MART was similar or more effective across each of the studies for reducing first severe exacerbation risk (pooled hazard ratio 0.49 [95% CI 0.34, 0.70]), which was comparable with adult participants (n=12,197); similar benefits with budesonide/formoterol MART were seen for the secondary endpoints of number of severe exacerbations, asthma-related symptoms, night-time awakenings, morning peak expiratory flow, FEV₁ (forced expiratory volume in 1 second), as-needed medication use and 5-item Asthma Control Questionnaire score. As-needed budesonide/formoterol use was lower in the adolescent participants compared with adults. The tolerability of treatment was good.

Comment: Asthma can be particularly difficult to manage in adolescents and they continue to carry an unacceptably high asthma burden. I recommend the BMJ Open [article](#): 'What do adolescents with asthma really think about adherence to inhalers? Insights from a qualitative analysis of a UK online forum'. These Danish/Swedish authors present a meta-analysis of adolescent patients included in RCTs comparing MART with standard care. In their [editorial](#) on where to go from here, Richard Beasley and colleagues from the Medical Research Institute of New Zealand give us **the bottom line: the MART regimen about halves the risk of a first severe asthma exacerbation in adolescents.**

Reference: *Eur Respir J* 2018;51:1701688

[Abstract](#)

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

Authors: Reddel HK et al.

Summary: A web-based survey was used to determine differences in asthma management and asthma-related outcomes between NZ and Australia. The respondents included 537 randomly selected individuals aged ≥ 16 years with asthma from NZ and 2686 from Australia. Compared with the Australian respondents, more New Zealanders reported use of ICS-containing medications (68.8% vs. 60.9% [$p=0.006$]), but fewer reported use of ICS/LABA combinations (44.4% vs. 81.5% [$p<0.0001$]). Adherence rates were significantly greater among the New Zealanders than the Australians, and also among ICS/LABA users than ICS-only users ($p<0.0001$ for both). There was no significant difference between the countries for ACT scores, with symptoms well controlled in 58.6% and 54.4% of respondents from NZ and Australia, respectively. Respondents from NZ had a higher rate of nonurgent asthma reviews than their Australian counterparts (56.6% vs. 50.4% [$p=0.009$]), whereas the proportions requiring urgent asthma visits did not differ significantly (27.9% vs. 28.6% [$p=0.75$]).

Comment: Our prescribing in NZ is regulated by PHARMAC, and its restrictions on our prescribing behaviour are auditable. This study on asthma control performed in 2012–2013 demonstrated a similar level of (poor) asthma control in both populations. The use of any ICS was similar; however, in Australia almost twice the ICSs were taken as part of a combination product. At the time of the survey, PHARMAC was restricting their use, which reduced the cost; however, it didn't impact asthma control. **Bottom line: we need technology, medications, funded healthcare systems and good relationships with our patients to treat asthma.**

Reference: *Respirology* 2017;22:1570–8

[Abstract](#)

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Trends in international asthma mortality

Authors: Ebmeier S et al.

Summary: This analysis collated age-standardised country-specific asthma mortality rates in the 5- to 34-year age group from the online WHO Mortality Database for 46 countries worldwide (36 high-income countries and 10 middle-income countries). A LOESS (locally weighted scatter plot smoother curve), weighted by the individual country population in the 5- to 34-year age group, was used to illustrate the global trends in asthma mortality rates with time. The LOESS estimate of the global asthma mortality rate was 0.44 deaths per 100,000 people in 1993 and 0.19 deaths per 100,000 people in 2006. The researchers found evidence for further reductions in some countries and regions of the world, but no appreciable change in global asthma mortality rates from 2006 through to 2012, with a LOESS estimate of 0.19 deaths per 100,000 people.

Comment: This article is written by Richard Beasley and colleagues from the Medical Research Institute of New Zealand, and the accompanying [editorial](#) is written by Christine Jenkins from the George Institute for Global Health. It is likely that asthma mortality reduced in the 1990s as we stopped doing harm by overprescribing short-acting β_2 agonists. It is possible that some countries have made good progress, mainly by facilitating access to ICSs, while others, like the US, have made little progress. **Bottom line: half of all asthma deaths are preventable with current treatment; the stalling mortality rates are a call for action and novel strategies.**

Reference: *Lancet* 2017;390:935–45

[Abstract](#)

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES)

Authors: Gibson PG et al.

Summary: Adults with symptomatic asthma despite current ICS and long-acting bronchodilator treatment were randomised to receive azithromycin 500mg (n=213) or placebo (n=207) three times each week for 48 weeks. Compared with placebo, azithromycin was associated with: i) a significant reduction in moderate or severe asthma exacerbations over 48 weeks (primary endpoint; 1.07 vs. 1.86 per patient-year; incidence rate ratio 0.59 [95% CI 0.47, 0.74]); ii) a lower proportion of participants experiencing ≥ 1 exacerbation (44% vs. 61% [$p<0.0001$]); and iii) a significant improvement in asthma-related QOL ($p=0.001$). Regarding adverse events, a significantly greater proportion of azithromycin recipients experienced diarrhoea compared with placebo recipients (34% vs. 19% [$p=0.001$]).

Comment: The final article in this review is from our colleagues in Australia who performed an investigator-initiated, randomised, placebo controlled trial on the use of azithromycin to reduce asthma exacerbations in patients aged greater than 18 years. Macrolide antibiotics have antibacterial, antiviral and anti-inflammatory properties. Azithromycin was well tolerated, with diarrhoea in only four people. Azithromycin was also associated with more resistant organisms at the end of the study; however, the study was not designed to explore the effect on the community. **Bottom line: azithromycin in addition to standard therapy reduced exacerbations and improved asthma-related QOL.**

Reference: *Lancet* 2017;390:659–68

[Abstract](#)



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