

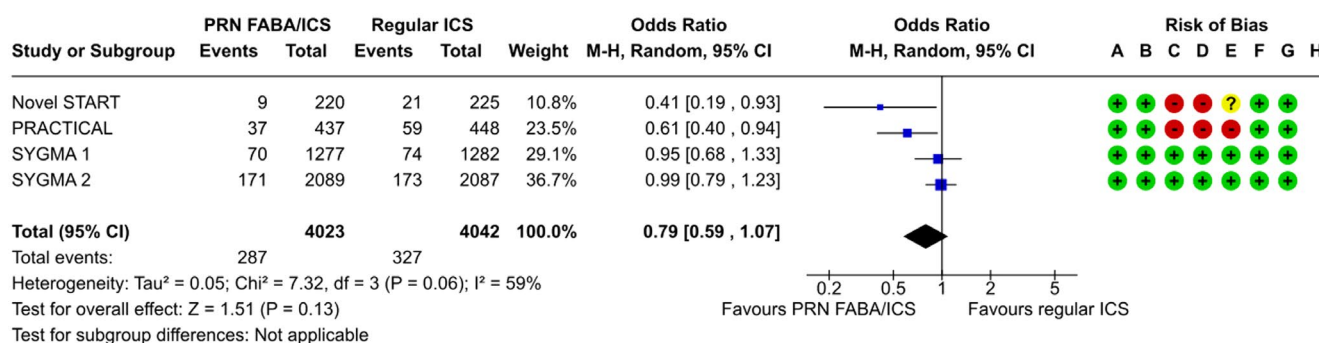
Allergy in India—a call for submissions

This month we launch a call for submissions for a special collection on “Allergy in India,” overseen by guest editor Professor Mamidipudi Krishna. Close to a fifth of the world's population and a quarter of all children live in India. As highlighted in a separate editorial by Professor Krishna and colleagues in this issue, air quality and access to allergy care present significant challenges for people with allergic conditions in India. The volume of research published on allergic diseases in India is low compared with the burden of disease. We welcome submissions to *Clinical and Experimental Allergy* describing novel findings relating to allergy in India.

Prior to the COVID-19 pandemic, tuberculosis killed more people each year than any other infectious organism. One-quarter of human tuberculosis occurs in India, so it is appropriate that we address the issue of hypersensitivity reactions to anti-tuberculosis drugs in this issue. Bermingham et al review the range of hypersensitivity reactions caused by anti-tuberculosis medications and highlight the impact such reactions can have on disease course and drug resistance.¹ A key clinical message is that most such reactions are cutaneous and benign. Up to 60% of people with tuberculosis report an adverse drug reaction, but only a minority of these is a reproducible hypersensitivity reaction. Discriminating hypersensitivity reactions and potentially severe hypersensitivity reactions

can be difficult. Bermingham and colleagues suggest that rifampicin is the most common cause of genuine allergic reactions and present a common-sense approach to diagnosis and management, including, where necessary, desensitization to candidate trigger drugs.

The burden of asthma in India is substantial, exacerbated by high exposure to airborne particulate matter. Regional data from Bengaluru in 2018 suggest that childhood asthma may have increased in prevalence since the ISAAC surveys of the 1990s and early 2000s.² However, access to specialist care and affordable anti-inflammatory treatments is variable. In this issue, we include a Cochrane Corner summarizing the evidence for the recent shift in asthma management in some high-income countries to using combination reliever inhalers without a daily steroid inhaler for mild asthma. The authors evaluated the effectiveness of combination beta-2 agonist/ steroid inhalers used as needed for preventing severe asthma exacerbations or hospital admissions in people with mild asthma. They found combination inhalers to be more effective than beta-2 agonists alone and similar to a regular inhaled steroid (Figure 1) for preventing exacerbations requiring steroids. This suggests that patients with mild asthma may no longer need to take a daily steroid inhaler for their intermittent symptoms.



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding (performance bias and detection bias)
- (D) Blinding of participants and personnel (performance bias)
- (E) Blinding of outcome assessment (detection bias)
- (F) Incomplete outcome data (attrition bias)
- (G) Selective reporting (reporting bias)
- (H) Other bias

FIGURE 1 Forest plot from the Cochrane Review ‘Combination fixed-dose beta-agonist and steroid inhaler as required for adults or children with mild asthma. The data show the effects of as needed combination beta-2 agonist/steroid inhaler (FABA/ICS) compared with regular daily inhaled steroid (ICS) on odds of severe asthma exacerbation requiring systemic steroids. There was little difference, but more work is needed to understand safety, long-term outcomes and effects in children

FIGURE 2 Interventions tested in published studies for managing symptoms of vocal cord dysfunction. From Mahoney et al³



A clinical issue that commonly leads to misdiagnosis or over-treatment of people with asthma is vocal cord dysfunction, sometimes termed “inducible laryngeal obstruction.” This common condition is an important differential diagnosis of asthma or anaphylaxis, and correct diagnosis can provide reassurance and reduce healthcare attendances. For patients whose symptoms persist despite a precise diagnosis, explanation and reassurance, management can be complex. In this month’s issue, Mahoney et al. highlight how little evidence there is to guide practice when symptoms of vocal cord dysfunction are persistent.³ A comprehensive systematic review found 17 published experimental studies evaluating interventions such as respiratory training, botulinum toxin and amitriptyline (Figure 2). All interventions were associated with reduced symptoms, but the risk of bias was high across all interventions, and not a single randomized controlled trial was identified. Much more work is to be done to strengthen the evidence base for interventions to treat this distressing condition.

In the March issue of *Clinical and Experimental Allergy* last year, we reported several studies concerned with eczema epidemiology or prevention.^{4–6} Among these, two systematic reviews evaluated the evidence that environmental factors might change infant skin physiology enough to promote or prevent eczema. Kelleher et al. found a lack of evidence that moisturizing baby skin changes the

development of eczema.⁷ In contrast, Jabbar-Lopez et al. did find a positive association between exposure to “hard” water, high in calcium carbonate and childhood eczema.⁸ This association may be mediated through the deposition of sodium lauryl sulphate, which is present in some wash products such as soaps. Randomized controlled trials of water softeners for people who already have eczema have not identified positive effects on symptoms. In this issue, Jabbar-Lopez and colleagues take the field of eczema prevention through skincare interventions one more step forward. They evaluated using water softeners from birth on the basis that hard water may trigger the development of eczema in early infancy. In a well-conducted and transparently reported feasibility trial, they found it possible to undertake a randomized controlled trial of water softener installation for eczema prevention.⁹ They randomized 80 pregnant women living in an area with hard water to have an ion-exchange water softener installed in their home, or “usual care,” and followed their children for a blinded assessment of eczema at age six months. For a significant minority of eligible families (28%), it was not feasible to install a water softener. For those families with space for a water softener, this intervention appears to be achievable and therefore worthy of a larger, definitive intervention trial. Indeed, in this small feasibility trial, less eczema was reported in children whose families had a water softener installed during pregnancy than the “usual

care" group, although these differences should be interpreted with caution given the size of the study. There is still a possibility of preventing eczema through novel skincare interventions in early life. Perhaps approaches such as water softeners, which aim to reduce skin damage, may prove more effective than trying to ameliorate skin barrier dysfunction through the application of moisturizers.

Robert J. Boyle¹
Mamidipudi T. Krishna²
Mohamed H. Shamji^{1,3}

¹National Heart and Lung Institute, Imperial College London,
London, UK

²University Hospitals Birmingham NHS Foundation Trust and
Institute of Immunology and Immunotherapy, University of
Birmingham, Birmingham, UK

³NIHR Imperial Biomedical Research Centre, London, UK

Correspondence

National Heart and Lung Institute, Wright Fleming Institute,
Imperial College London, London W2 1PG, UK.
Email: r.boyle@imperial.ac.uk

REFERENCES

1. Bermingham WH, Bhogal R, Audi Nagarajan S, et al. Practical management of suspected hypersensitivity reactions to anti-tuberculosis drugs. *Clin Exp Allergy*. 2021.
2. Parthasarathi A, Padukudru S, Rajgopal N, Holla AD, Krishna MT, Mahesh PA. Allergic disease prevalence in schoolchildren in Bengaluru, India: A cross-sectional survey. *Clin Exp Allergy*. 2021;51(7):955-958.
3. Mahoney J, Hew M, Vertigan A, Oates J. Treatment effectiveness for Vocal Cord Dysfunction in adults and adolescents: A systematic review. *Clin Exp Allergy*. 2021.
4. de Lusignan S, Alexander H, Broderick C, et al. Patterns and trends in eczema management in UK primary care (2009–2018): A population-based cohort study. *Clin Exp Allergy*. 2021;51(3):483-494.
5. de Lusignan S, Alexander H, Broderick C, et al. The epidemiology of eczema in children and adults in England: A population-based study using primary care data. *Clin Exp Allergy*. 2021;51(3):471-482.
6. Ridd MJ, Webb D, Roberts K, et al. Test-guided dietary management of eczema in children: A randomised controlled feasibility trial (TEST). *Clin Exp Allergy*. 2021;51(3):452-462.
7. Kelleher MM, Cro S, Van Vogt E, et al. Skincare interventions in infants for preventing eczema and food allergy: A Cochrane systematic review and individual participant data meta-analysis. *Clin Exp Allergy*. 2021;51(3):402-418.
8. Jabbar-Lopez ZK, Ung CY, Alexander H, et al. The effect of water hardness on atopic eczema, skin barrier function: A systematic review, meta-analysis. *Clin Exp Allergy*. 2021;51(3):430-451.
9. Jabbar-Lopez ZK, Ezzamouri B, Briley A, et al. Randomised controlled pilot trial with ion-exchange water softeners to prevent eczema (SOFTER trial). *Clin Exp Allergy*. 2021.