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EDITORIAL

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Asthma management and impact on COVID-19 outcomes

This month we focus on the two most burdensome allergic conditions—asthma and eczema. We continue our new Cochrane Corner series with a summary of a recent Cochrane network meta-analysis of systemic treatments for eczema (Figure 1). We include several interesting eczema reports about nomenclature, life-course trajectories and the increased mortality associated with eczema and asthma. However, our free-to-read Editor's Choice articles for this month are three novel reports related to asthma management.

The mainstay of asthma management is fast becoming combination inhaled corticosteroid (ICS) and long-acting beta-2 agonist (LABA) therapy as both maintenance and reliever, at least in adolescents and adults. Therefore, it is very timely that Karimi et al. report an analysis of genetic determinants of ICS/LABA response in this issue of *Clinical and Experimental Allergy*. Individual response to ICS/LABA therapy varies, often due to issues with treatment concordance and effectiveness of the inhaler device and technique used to deliver ICS/LABA to the airway mucosa. However, even in people with asthma who use their combination inhaler regularly and appropriately, treatment responses vary between individuals. Targeted asthma treatments based on inflammatory phenotype are part of mainstream clinical practice.[1] One area of intense current research interest in asthma is pharmacogenomics, that is evaluating genetic variants that might explain the response to treatment and lead to targeted asthma treatments based on genotype.[2] Karimi et al. previously reported in this journal that a genetic variant in the low-affinity IgE receptor may influence airway inflammation as measured by exhaled nitric oxide.[3] In this issue, the same group report work from the multiethnic Pharmacogenomics in Childhood Asthma (PiCA) consortium of 10 separate studies.[4] They built on previous reports that a glycine to arginine single nucleotide polymorphism in the beta-2 adrenergic receptor (Arg16) may be associated with increased risk for asthma exacerbations in asthmatic children treated with LABA. This new study found an association between Arg16 and increased odds of asthma exacerbation in children and young people treated with ICS/LABA. The association was remarkably consistent across the ten studies included in the PiCA consortium and did not appear to relate to a linked polymorphism (Gln27). This supports the potential value of genotype-guided asthma treatment algorithms, which the authors are currently testing in relation to the Arg16 polymorphism in their PUFFIN trial. In PUFFIN, children with poor asthma control are directed to use ICS/LABA if they do not have the Arg16 polymorphism, but high-dose ICS without LABA if they have the Arg16 polymorphism.

Asthma is a long-term health condition. As with other long-term health conditions, many sufferers prefer to look for natural approaches to improve the condition or mitigate its effects rather than entirely relying on pharmacological approaches.[5,6] Diets high in fruits and vegetables are thought to be health-promoting for a number of reasons—for people with asthma, there is a hypothesis that the anti-oxidants in these foods might counter the increased oxidative stress seen in asthmatic airways. There is some support for that hypothesis from a previous trial in adults undertaken in Newcastle, Australia. In this month's issue of *Clinical and Experimental Allergy*, Professor Wood's Newcastle team reports the first randomized, controlled trial of increased fruit and vegetable intake in children with asthma.[7] In a small but well-conducted trial, they showed that their intervention more than doubled reported fruit and vegetable intake in asthmatic children. The objective evaluation of plasma carotenoids confirmed good adherence to the dietary intervention. The intervention consisted of home delivery of fruit and vegetables, supplemented by telephone dietetic counselling. The control group received home delivery of bread, rice, pasta and cereal without dietetic counselling. Unfortunately, there was no clear change in asthma exacerbation rates during the 6-month intervention period. Still, confidence intervals were wide in this preliminary study, and the group has shown this approach to be feasible enough to test in a larger, definitive trial. In the meantime, it is worth noting that intake of fruit and (especially) vegetables is below recommendations in many children and adults, so encouraging increased fruit and vegetable intake should be considered for general health reasons, if not yet specifically for helping prevent asthma exacerbations.

A more topical question in asthma management is the interaction between asthma genes, airway inflammation and COVID-19.[8] In a timely and important paper on long-COVID in this month's issue, Professor Daniel Munblit and colleagues from the StopCOVID research team report the relationship between asthma and longer-term outcomes in adults hospitalized for COVID-19 in Moscow, Russia.[9] They evaluated over 2500 adults admitted to hospital with acute SARS-CoV-2 during the first wave

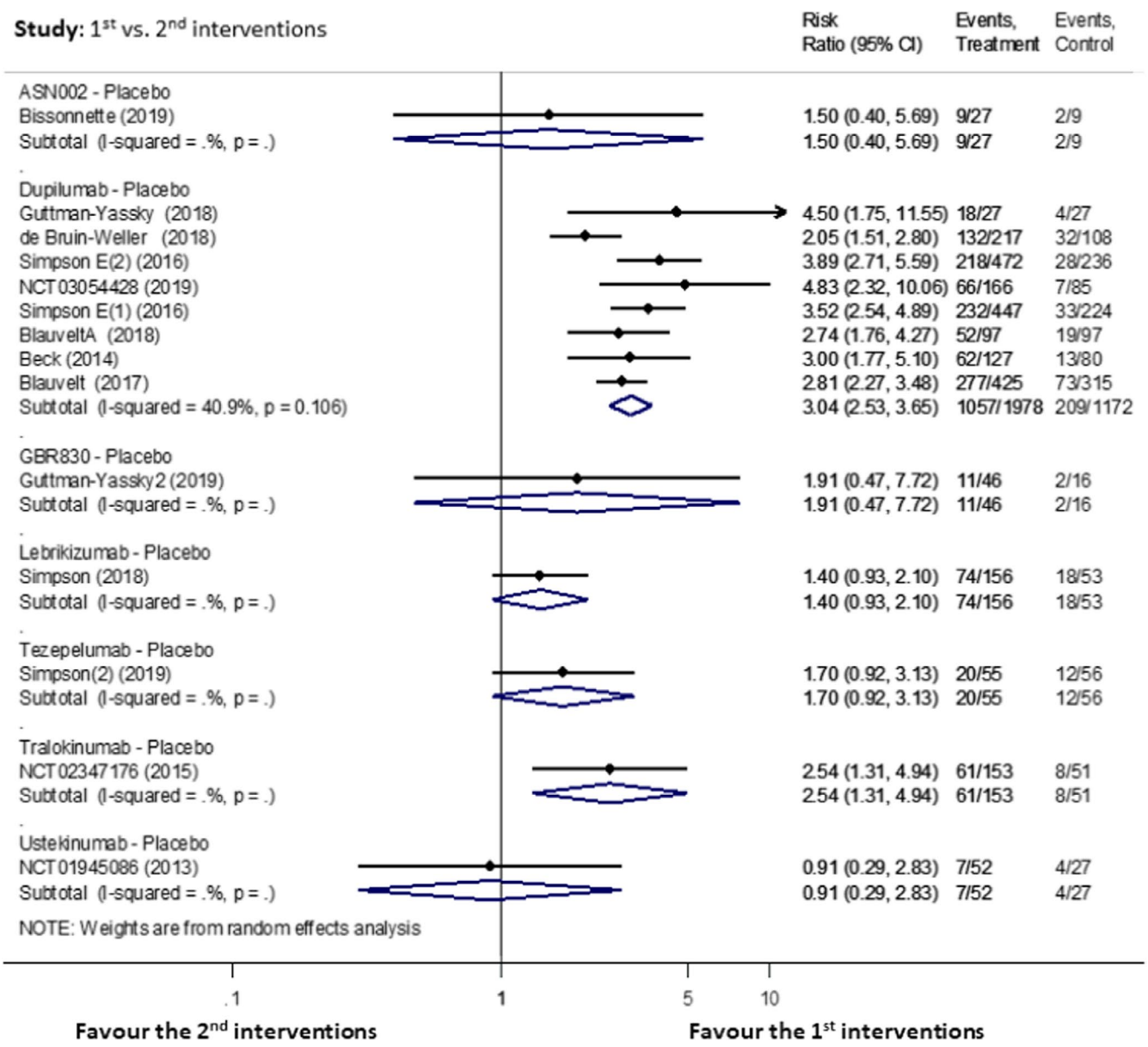

FIGURE 1 Forest plot from the Cochrane Review 'Systemic treatments for eczema: a network meta-analysis'. The data show the effects of biological therapies on the objective assessment of eczema severity, measured as ≥75% improvement in EASI score during short-term (2–16 week) follow-up. Dupilumab was the most effective biologic for short-term improvement in eczema symptoms and signs. Longer-term data regarding the effectiveness and safety of biologics were limited, and there was insufficient information to compare biologics with older systemic treatments such as ciclosporin

of the COVID-19 pandemic in Moscow, using the standardized ISARIC long-term follow-up questionnaire. The group found that about half of the evaluated COVID-19 survivors reported persistent symptoms 6–8 months after discharge, with chronic fatigue, shortness of breath and forgetfulness the most common symptoms reported (Figure 2). Consistent with a parallel ISARIC publication from a smaller, UK cohort, women reported more persistent symptoms than men. In this Moscow cohort, pre-existing asthma and chronic pulmonary disease were not associated with changes in the overall prevalence of persistent symptoms. There was, however, an association between self-reported diagnosis of asthma and some specific neurological and psychological symptoms, suggesting that asthma may be a risk factor for some long-COVID subtypes. Overall, the picture with regard to asthma and COVID-19 is reassuring for allergists, pulmonologists and their patients. As reported in this journal last year[10] and summarized again in a World Health Organization scientific brief on 19 April 2021, there is little evidence to suggest asthma is a risk factor for short-term adverse outcomes from COVID-19 infection. However, these new data raise concerns about the possibility that people with asthma admitted to hospital with SARS-CoV-2 may have increased long-term neurological and psychological symptoms. These new

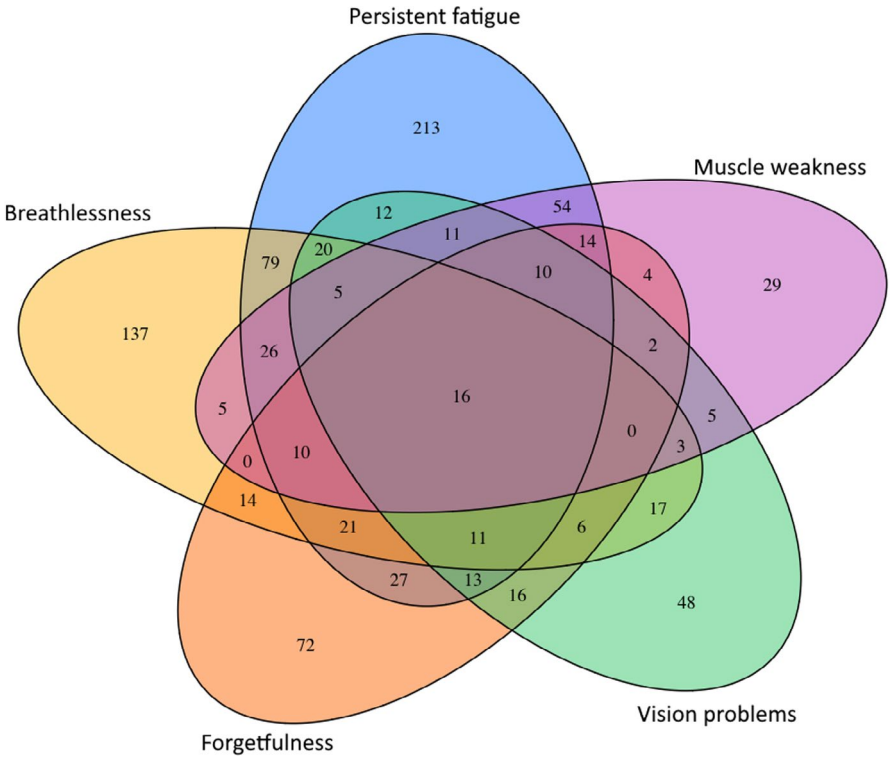

FIGURE 2 Long-COVID symptoms reported in the Moscow StopCOVID cohort of adult patients, who were evaluated 6–8 months after hospitalization for SARS-CoV-2 during the first wave of the COVID-19 pandemic

data support the case for proactively addressing vaccine hesitancy and social distancing when consulting with people who have asthma and their carers.

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