Cochrane Corner in Paediatric Respiratory reviews

Interventions for autumn exacerbations of asthma in children

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Why was it important to do this Cochrane review?(1)

Asthma exacerbations in school-aged children peak in autumn (2). The peak follows shortly after the summer school holiday; occurring in September in the Northern Hemisphere (3) and February in the Southern Hemisphere (4). This likely reflects a combination of risk factors, including poor treatment adherence, increased allergen and viral exposure, and altered immune tolerance (5). Asthma admissions during the month when children return to school account for approaching a quarter of the annual total (6). Interventions targeting modifiable risk factors might reduce exacerbation-associated morbidity and strain upon health resources during the autumn.

There are practical difficulties associated with minimising viral or allergen exposure, but two main strategies remain which might reduce autumn asthma exacerbations. The first would be add on, or increased, asthma pharmacotherapy before autumn and the second improved treatment adherence and symptom control during and in anticipation of this period.

Current national and international guidelines offer no guidance on avoiding autumn asthma exacerbations. However, a recent trial of seasonal omalizumab treatment reported reduced exacerbations amongst children with severe or poorly controlled asthma (7). This treatment is costly, requires fortnightly or monthly subcutaneous injections, and in countries such as the United Kingdom is subject to strict severity-based prescribing criteria. It is important to identify whether cheaper, less invasive strategies exist which might be more widely generalisable.

What were the objectives of this review?

This review aimed to assess the effects of pharmacotherapy and behavioural interventions enacted in anticipation of school return in the autumn and designed to reduce asthma exacerbations in children during this period. The primary outcome was exacerbation, defined as need for oral corticosteroids or hospitalisation. Adverse events were considered as a secondary outcome.

What was the evidence base for this review?

Relevant trials were identified from the Cochrane Airways Group's Trials Register. We found five studies which randomised school-aged children with asthma to either an intervention designed to reduce autumn asthma exacerbations or to standard asthma care. A total of 14252 children were randomised, the majority to a single trial cluster randomised at general practice level (8). The remaining trials recruited 200-1200 children each, according to variable severity, atopic status or age criteria.

There were four randomised controlled trials of pharmacological interventions. This included the PROSE trial, in which participants sensitised to one or more perennial allergens were randomised to receive either omalizumab, doubling of their inhaled corticosteroid dose or placebo from 4-6 weeks before school return (7). Additionally, there were two blinded (9, 10) and one open (11) study of leukotriene receptor antagonist (LTRA) administration from school return.

One study tested a behavioural intervention (8). This study recruited 12179 participants to a cluster-randomised trial of sending a reminder letter at the end of July to parents/carers reminding them to pick up their children's asthma medication.

What were the findings of the review?

The risk of bias was generally low with the exception of a lack of blinding in the open study (11). Evidence for each type of intervention was based on single studies except from studies of montelukast (9, 10). Adverse events were only reported in the pharmacotherapy trials.

Two pharmacological studies reported a reduction in the proportion of participants experiencing asthma exacerbations associated with the intervention. Compared to placebo a 50% reduction (from 21.0% to 11.3%) was found in children receiving omalizumab in the 90 days following school return, OR 0.48 (95% CI, 0.25–0.92) (7). Subgroup analyses within this study demonstrated reduced exacerbation risk in those receiving treatment for severe asthma and those with a recent exacerbation. In one montelukast trial a 70% reduction (from 14.6% to 4.1%) was found in the proportion requiring an unscheduled physician visit during the 45 days after 1st September compared to placebo OR 0.25 (0.08-0.79) (9). Neither a second larger trial of montelukast (10) nor pooled data from both studies, however, found evidence for a significant between-group difference. There was no evidence that the proportion of participants who had at least one unscheduled medical contact for a respiratory diagnosis between September and December differed between those randomised to receive a medication reminder letter and those in the control group (OR 1.13, 95% CI 0.95 to 1.33) (8).

There was no evidence that the total proportion of participants experiencing adverse events differed significantly between intervention and usual care groups. In the PROSE trial, significantly more participants experienced local administration site reactions in the omalizumab group in comparison to the usual care group (15.3% vs. 6.5%, p = 0.03) (7).

What are the implications of this review for practice and research?

The review identified evidence from a relatively small study suggesting that add-on seasonal omalizumab treatment, commencing four to six weeks before children return to school might reduce asthma exacerbations in allergen-sensitised children. Although results from one study suggest seasonal montelukast might reduce autumn exacerbations, there was no evidence for a reduction in exacerbations from either two subsequent trials based on LTRA therapy or pooled data from trials of montelukast. There was no evidence that a medication reminder letter is associated with reduced unscheduled contacts during the autumn months.

Further investigation of interventions to reduce the risk of asthma exacerbations in children after they return to school in the autumn is needed to reduce clinical impact and disease burden and also to better understand the mechanisms underlying asthma exacerbations. Whilst omalizumab appears effective in those at greatest risk of exacerbation and a seasonal approach would be cheaper than year round treatment, this intervention remains expensive and can be painful to administer. There is a need to identify relatively low expense interventions which could be useful to all those with asthma. Currently, only a limited number of pharmacological and non-pharmacological strategies have been evaluated. In future studies, definitions of exacerbations should be provided, and where possible standardised. In order to support subgroup analysis according to asthma severity, participants in future trials should be well characterised with respect to baseline asthma severity and previous exacerbation history, as well as age and gender.

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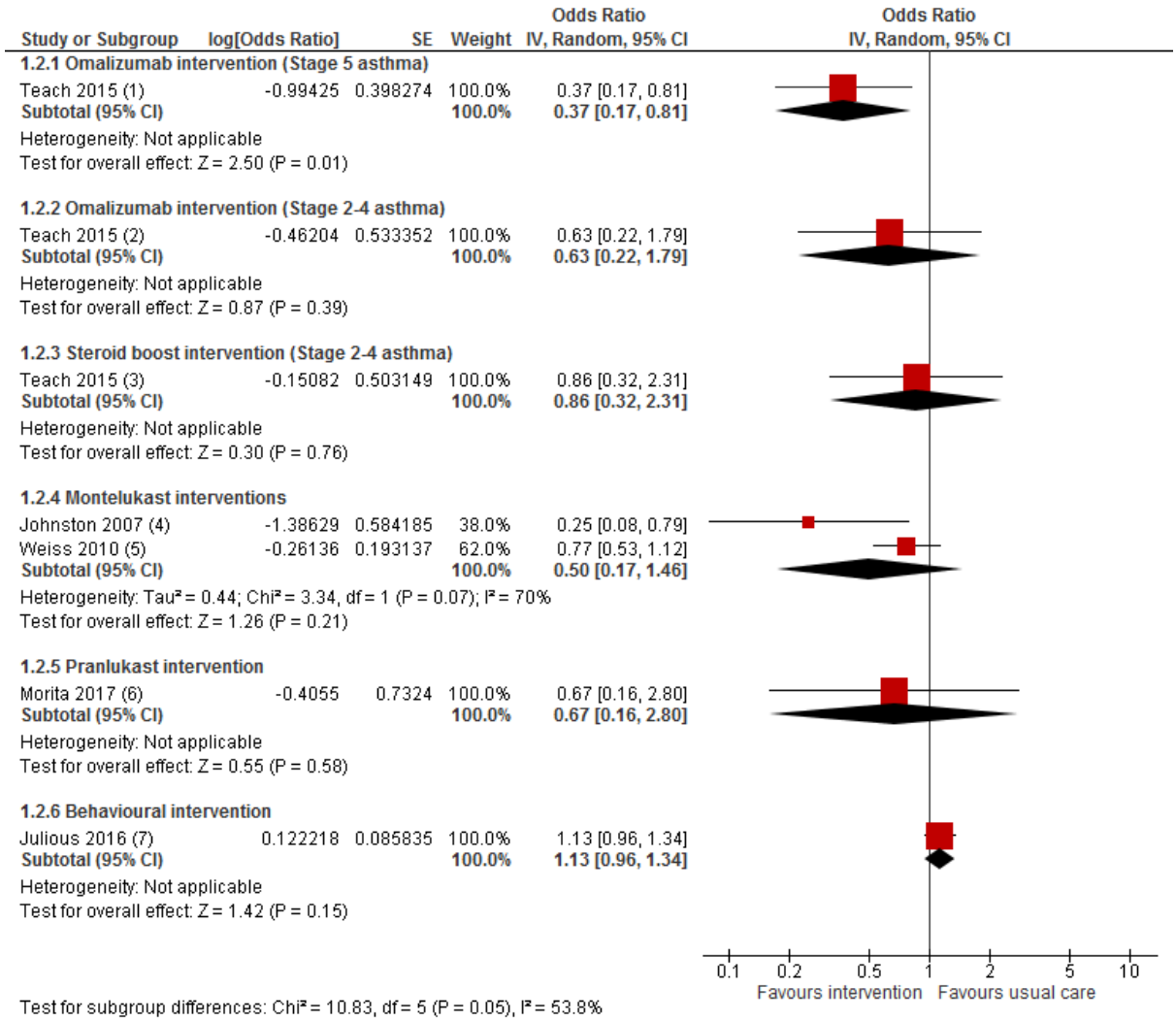


Test for subgroup differences: Chi² = 10.83, df = 5 (P = 0.05), I² = 53.8%

Footnotes

(1) Exacerbations defined as worsening asthma symptoms requiring hospitalisation or OCS within the 90 days following school return

(2) Exacerbations defined as worsening asthma symptoms requiring hospitalisation or OCS within the 90 days following school return

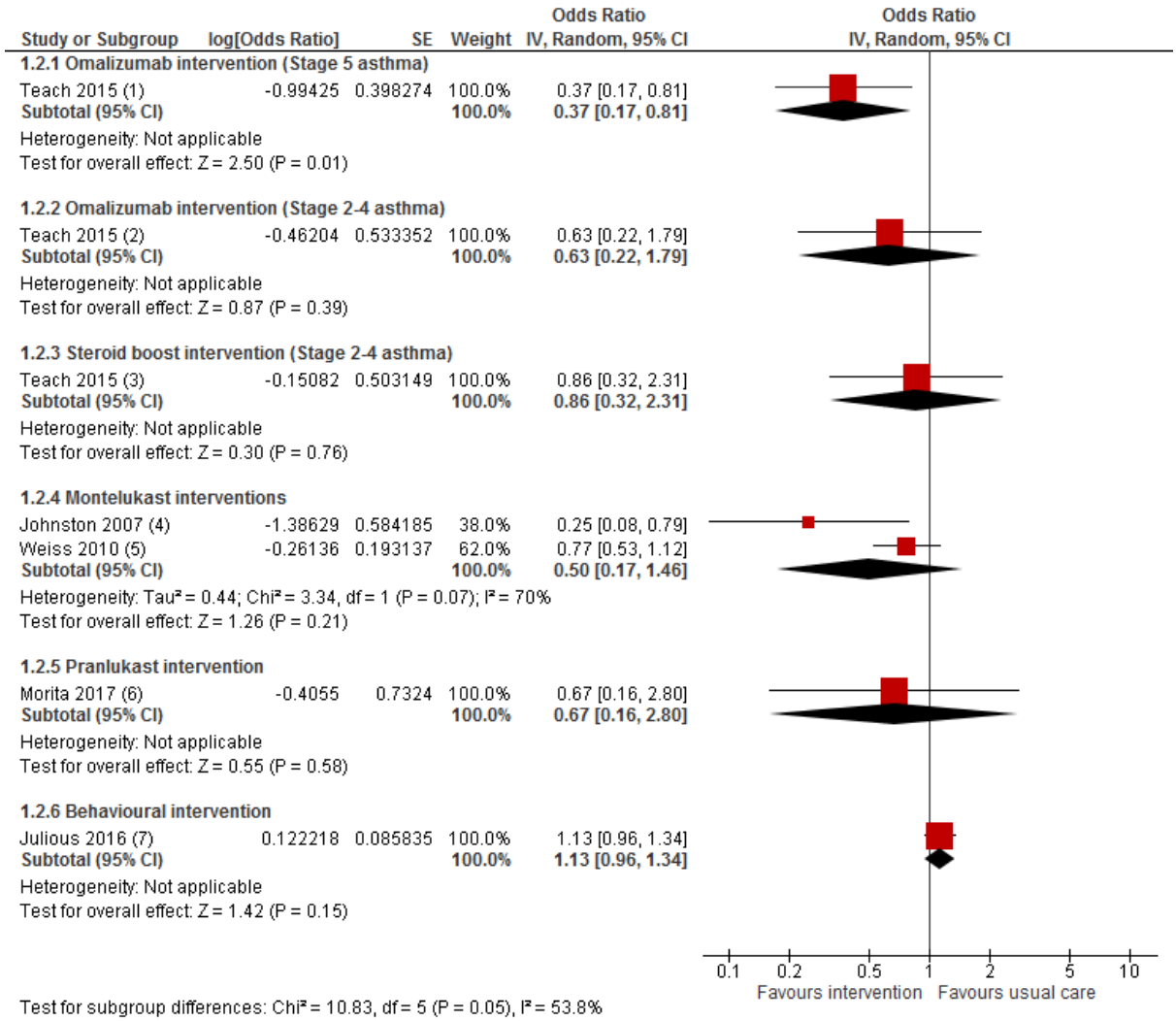
(3) Exacerbations defined as worsening asthma symptoms requiring hospitalisation or OCS within the 90 days following school return

(4) Eexacerbations defined as unscheduled visit to a doctor or treatment with OCS between 1 September and 15 October

(5) Exacerbations defined as unanticipated healthcare utilisation for asthma in the first eight weeks following school return

(6) Exacerbations defined as worsening asthma symptoms requiring an unscheduled visit to a physician or treatment with OCS between...

(7) Exacerbation defined as unscheduled contact for a respiratory diagnosis between 1 September and 31 December



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