A Difficult Step in Meta-analysis

Refining the Search

To the Editor:

I found the meta-analysis performed by Edmonds et al (June 2002) to be very instructive, but in some areas it needs to be refined.

The inclusion in the meta-analysis of patients who had been treated with a combination of corticosteroids (CS) and long-acting β₂-agonists clearly should have been avoided in a meta-analysis in which the primary outcome was the relapse rate. It has been demonstrated that this rate is lower when using a combination of long-acting β₂-agonists and CS, compared with studies using short-acting β₂-agonists and CS.

Some of the outcomes described are too heterogeneous. In my view, to give the same significance and to pool together the “treatment failures” during the first 3 days and to pool together the relapses at 7 days and after is a mistake. While the first pooling might be due to specific triggers, the latter could have a more complex causality, including noncompliance.

In the face of significant heterogeneity, reviewers need to be mindful; they should refrain from the statistical pooling of data and should refine their search, focusing more on the exploration and description of the sources of heterogeneity.

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REFERENCES

2 Markham A, Jarvis B. Inhaled salmeterol/fluticasone propionate combination: a review of its use in persistent asthma. Drugs 2000; 60:1207–1233

To the Editor:

We are pleased to respond to the points raised by Dr. Jalba about our article in CHEST (June 2002). First, we feel the concern about long-acting β₂-agonists (LABAs) is misleading for...
a number of reasons. It is unlikely that any of the trials included in the review would employ therapy with the combination of LABAs and corticosteroids (CS). However, even if they had, one would imagine the distribution would be similar across the groups in a randomized controlled trial, and their effect would be of limited concern. The trials in the review are older, and these drugs are infrequently used, even today. Furthermore, Dr. Jalba’s claim of benefit from LABAs only relates to the treatment of patients with chronic asthma, since there is no evidence that adding LABAs to therapy for patients with acute asthma is beneficial.

When trials using similar designs (ie, randomized controlled trials), comparisons (ie, inhaled CS vs CS), populations (ie, acute asthma), and outcomes (ie, relapse) exist, pooling is justified. In our review, where there was no significant clinical or statistical heterogeneity, pooling was clearly appropriate. If the results of pooling demonstrate heterogeneity, then limited exploration is warranted, and pooling may not be appropriate. Conversely, searching for subgroup differences has been shown to generate erroneous results and should be considered far more carefully than Dr. Jalba would suggest.3

We further believe that the timing of relapse needs to be more fully evaluated before assigning the blame to patients for “late relapses.” We clearly appreciate the fact that the timing of relapse is important. That is precisely why we separated the outcomes based on time in the review.1

Finally, we challenge Dr. Jalba on the need for a better search and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. Cochrane reviews pride themselves on comprehensive, exhaustive (even exhausting!) and more exploration of heterogeneity. 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