NATIONAL TRAINING AND RESEARCH APPRAISAL GROUP

Critical Appraisal of an Overview

1. METHODS	
1.1 Is the question clear? a) What is the population? b) What is the exposure/intervention? c) What is/are the outcome(s)?	The study considers the potential benefit of adding anticholinergics to beta2 antagonists in acute asthma. The populations involved studies in most ethnic groups worldwide and in several language groups. The main outcomes considered were hospital admission after presenting at A&E and in short term improved respiratory function.
1.2 Is the search thorough? a) Bibliographic database; years covered? b) References in relevant articles? c) Grey literature (unpublished research reports etc.)?	Appears to be thorough. Uses databases other than Medline (Cinahl, Embase) and looks for recent registered clinical trials that might not yet be published as well as hand searching 'top' (undefined) respiratory journals. Also considers references in relevant articles. Considers unpublished research identified from Boehringer Ingelheim, but does not consider abstracts. This may lead to publication bias but they may have been unwilling to consider these because they could not assess quality.
1.3 Is the validity of included studies adequately assessed? a) Are the inclusion criteria appropriate? b) Has methodological quality been assessed? c) Is assessment reproducible, blind? d) Was missing information obtained from investigators? e) Is publication bias an issue?	Inclusion criteria of the studies appears appropriate – target populations clearly described – refers to acute asthma (not defined but baseline severity has been defined in each study that suggested that most patients would fall into that group. Outcomes were information about hospital admission and improvement of respiratory function over two hours. Javad scoring used to assess quality of studies (randomisation, blinding and drop-outs) and only randomised controlled trials considered. Assessment was independent and made by two reviewers who were in total agreement about the studies to be included and their relative quality. No missing information was searched for – this could have included going to the researchers in any studies published only in abstract form. This could produce a publication bias but none was detected in the collected studies when a funnel plot was examined.

Critical Appraisal of an Overview (continued)

2. RESULTS	
2.1 Effect: a) On what scale is the effect measured? e.g., odds ratio b) How big is the overall effect?	Hospital admission is shown as a relative risk suggesting that treatment reduces hospital admission by around (1 – 0.73) = 27% in children and 32% in adults. Respiratory function improvement is shown as a difference in FEV_1 in children, the improvement being 0.75 on average, and as a difference in PEFR in adults, the improvement being 44 l/minute. Increased dosing produced higher benefits.
2.2 Consistency: a) Are the results consistent between studies? b) How sensitive are the results to changes in the way the review is done?	Heterogeneity was assessed overall and between subgroups. Significant heterogeneity was observed in spirometry parameters until the data was stratified according to dose and then the heterogeneity disappeared. Sensitivity analyses were done to look at whether the inclusion of low quality studies, or the inclusion of studies where the criteria for hospital admission was unknown, was affecting the conclusion, but no effect was seen.
2.3 Precision: a) Does the lower confidence limit include clinically relevant effects? b) Does the upper confidence limit exclude clinically relevant effects?	In all of the outcomes presented in figures 1 to 4 we are interested in the upper confidence limit as this is the one that approaches the 'no difference' level. The upper end of RR for hospital admission is 0.85 for children and 0.86 for adults – meaning that we are 95% confident that the treatment reduces admission by at least 14% (1-0.86).
3. INTERPRETATION OF RESULTS	
3.1 Are subgroup analyses interpreted cautiously?	Heterogeneity is considered for all subgroup analyses. The subgroup analyse suggest greater improvement of treatment in terms of respiratory function with increased dose and hospital admission with greater severity and with increased dose.
3.2 a) Can the conclusions and data be generalised to other settings? b) Is NNT (numbers needed to treat) stated or able to be calculated?	Although the authors have highlighted their doubts about generalisability, because of the unknown criteria for hospital admission in some of the studies, removal of this data does not alter the conclusion. This study also is better than many as it includes studies from the major ethnic groups (investigation of the primary articles would be needed to see if individuals of African origin were included in any of the studies). NNT can be calculated from 1/absolute risk reduction. Hospital admission for children is 0.215 on treatment, 0.298 on control, difference = 0.083. 1/0.083 = 12.05 NNT = 13 (always round up so that result is more conservative). This means that use of treatment will mean one less child is hospitalised for every 13 children treated. This has important cost implications.
3.3 Are recommendations linked to the	The conclusion in the abstract is adequately supported by the

strength of the evidence?	evidence. This is a good systematic review that has supported previous observations, as well as adding information about the importance of multiple dosing.