

$\beta$ -agonists and 27 (14%) subjects were taking  $\beta$ -blockers. Only one (0.5%) patient was taking both.

$\beta_1$ -receptors are much more prevalent in the heart, while  $\beta_2$ -receptors are prevalent in bronchial smooth muscle [3]. The original evidence of adverse effects of  $\beta$ -blockers on airways was based on early case reports of acute bronchospasm associated with high doses of nonselective  $\beta$ -blockers [1]. Since then, cardioselective  $\beta$ -blockers have been developed that have >20 times the affinity for  $\beta_1$ - than  $\beta_2$ -receptors and are therefore less likely to cause bronchospasm. It is valid to use cardioselective  $\beta$ -blockers in low-risk respiratory patients with high-risk cardiac conditions, but this should be done with close monitoring [4]. As cardioselective  $\beta$ -blockers are increasingly prescribed, it is not surprising that 67% of patients in our survey were using them. However, 33% of patients were taking nonselective  $\beta$ -blockers, which have not been shown to be safe in airways disease. Eight (30%) of the patients in our survey were on a  $\beta$ -blocker solely for hypertension, even though  $\beta$ -blockers are no longer regarded as first-line treatment for hypertension [5].

Concomitant use of  $\beta$ -agonist and  $\beta$ -blocker drugs does not appear to be common. The in-patient point prevalence was 0.5% and over a 2-yr period, in a variety of settings, we encountered only 34 examples (27 analysed). Our survey suggests that co-prescription of these drugs may often be inadvertent and that in some patients with airways disease,  $\beta$ -blockers could be stopped or a cardioselective  $\beta_1$ -antagonist substituted.

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#### STATEMENT OF INTEREST

None declared.

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## Meta-analysis may not be practicable for guiding antibiotic therapy

To the Editors:

We read with interest a meta-analysis by SIEMPOS *et al.* [1] that showed that macrolides, quinolones and amoxicillin/clavulanate might be considered equivalent for treating acute bacterial exacerbation of chronic bronchitis. Despite meticulous adherence to the methodology of meta-analysis and a comprehensive discussion of the major limitations of their study, the investigators might have used an inappropriate tool for addressing a common clinical problem.

Although meta-analysis has been placed at the pinnacle of the hierarchy of clinical evidence [2], caution is required for clinical scenarios in which targeted pathogens and their drug sensitivity patterns may vary with geographical location and time. One such scenario is the antibiotic treatment of lower respiratory tract infection, including pneumonia and chronic bronchitis, for which the clinical decision is often empirical and heavily dependent upon timely and relevant epidemiological data, as well as the patient's clinical characteristics [3, 4]. Fundamental differences in these major factors that existed between the study populations from different locations and

periods would have rendered it meaningless to find summary estimates with meta-analysis.

The only valid finding may be their conclusion about the significantly higher association between adverse effects and amoxicillin/clavulanate in comparison with quinolones, since adverse events may be subject to less variation due to time, place and person. That notwithstanding, the choice of antibiotic for empirical treatment must also take into account the inherent diagnostic uncertainty and long-term implications for resistance profiles. In this regard, fluoroquinolones have been incriminated in causing a delay in the diagnosis of tuberculosis [5]. Thus, fluoroquinolones have been reserved for use only in certain settings in some tuberculosis-endemic populations.

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#### STATEMENT OF INTEREST

None declared.

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From the authors:

We thank K.C. Chang and C.C. Leung for their interest in our meta-analysis [1] and we welcome their comments.

As our respectful colleagues acknowledged, a well-designed and carefully performed meta-analysis is graded at the highest level of scientific quality by evidence-based movement [2]. It has been stated that a systematic review “faithfully summarizes the evidence from all relevant studies on a topic, and it does so concisely and transparently” [3]. Thus, meta-analyses are consistently used as the basis for a grade A recommendation in clinical practice guidelines, including those dealing with antimicrobial therapy [4]. Convinced by the principles of evidence-based medicine, we attempted to perform several meticulous meta-analyses in the field of antimicrobial treatment for acute bacterial exacerbations of chronic bronchitis (ABECB) [1, 5], as well as for other lower respiratory tract infections [6, 7].

We are aware that simple pooling of data is not sufficient to ensure the internal validity and, therefore, the generalisability of the findings of a meta-analysis [8]. Thus, we have critically appraised the evidence derived from systematic reviews [9]. For example, in our meta-analysis of the various antimicrobials for ABECB, we insisted on assessing its potential limitations [1]; a great proportion of the Discussion section is devoted to this. We emphasised that “antimicrobial resistance is a moving target and only data from local surveillance studies on this major clinical and public health problem provide information that helps the clinician in decision making regarding the choice of the appropriate antibiotic for a given patient with ABECB” [1]. In addition, in table 1 of the manuscript we carefully listed the characteristics of the subjects included in the individual randomised controlled trials, in order to help the reader determine

whether its findings are applicable to his/her patient population [1]. Taking these issues into consideration, we believe that clinicians will find our meta-analysis results valuable while treating patients with ABECB.

Finally, we agree with K.C. Chang and C.C. Leung that several concerns have arisen regarding the usage of fluoroquinolones for the treatment of patients with lower respiratory tract infections in areas with endemicity of tuberculosis [10]. Actually, it could be argued that this fact further underscores the usefulness of the present meta-analysis. Indeed, if clinicians acknowledge that fluoroquinolones are equivalent to macrolides or amoxicillin/clavulanate for the treatment of patients with acute bacterial exacerbations of chronic bronchitis in terms of their short period of effectiveness, they may prefer to use macrolides or amoxicillin/clavulanate rather than fluoroquinolones in areas with endemicity of tuberculosis.

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## STATEMENT OF INTEREST

None declared.

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