Is CRP-guided antibiotic treatment a safe way to reduce antibiotic use in severe hospitalised patients with exacerbations of COPD?

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From the authors:

We thank M. Miravitlles and colleagues for their interest in our work [1]. They express concern about our failure rate: 24% at 10 days, and 45% at day 30; they feel that 31% of patients of the C-reactive protein (CRP) group and 46% of patients of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy group treated with antibiotics for acute COPD exacerbation is low in this high-risk population of hospitalised patients. Although treatment failure is high in our study, it reflects the severity of our population. Indeed, the proportion of patients on antimicrobials is lower than the outpatient study population in a recently published trial from the UK [2]; however, our COPD population is more severe and consists of hospitalised patients. Their concern is safety: have we caused harm in our patients by withholding antimicrobial treatment? First, in our study population, there was no significant difference in failure rates at days 10 and 30 between the CRP and GOLD group, which strongly argues against their point that antimicrobial treatment might have prevented harmful events (table 1). Neither failure during admission, nor relapse was significantly different between both study arms. Indeed, relapses among patients with acute exacerbation of COPD admitted to hospital are common [3], especially among individuals with a low forced expiratory volume in 1 s, but antimicrobial treatment may not necessarily prevent this, in particular among those that had low inflammatory markers. Slow recovery and early relapse have also been associated with increased inflammation, *e.g.* reflected by persistently increased CRP, and in patients characterised by chronic bronchitis [4], but whether these individuals might benefit from antimicrobial treatment if their CRP is below a given threshold has not been addressed in clinical studies [5]. An earlier study suggested that patients with CRP >50 $mg \cdot L^{-1}$ benefit more from antibiotic treatment compared to patients with CRP below this threshold [6]. Second, they argue that perhaps the active study arm treated with co-amoxiclav as the primary antimicrobial agent might have been inadequate. Although antimicrobial susceptibility data have not been listed in our paper, *Pseudomonas* spp. or other high-risk

pathogens were covered if retrieved from sputum, and patients known to have colonisation with high-risk pathogens were provided with tailored antimicrobial regimens.