11st of Oct 2021

Dear Editor,

We would be grateful for the opportunity to resubmit our manuscript titled “Carriage and transmission of macrolide resistance genes in patients with chronic respiratory conditions and their close contacts”, originally submitted last year. While the editorial comments were favourable for this submission, a relatively small sample size was highlighted as a primary limitation for this study. We have since expanded our study cohort, almost doubling the number of participants, from 53 pairs of patients and close contacts to 93 pairs.

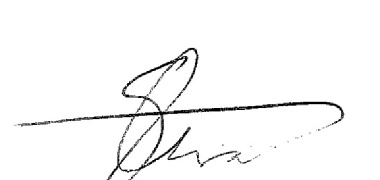
In summary, we address concerns that macrolide maintenance therapy might contribute to community-level antibiotic resistance (*Lancet Respir Med* 2013;1(3):262-74). Long-term treatment with macrolides is increasingly central to care for those with bronchiectasis, cystic fibrosis, uncontrolled asthma, and uncontrolled COPD. While treatment appears to be safe and effective, the potential for increased carriage and dissemination of antibiotic resistance has not been resolved. Given the increasing use of macrolide therapy, there is a growing need to investigate the propensity for therapy to select for antibiotic resistance genes in both recipients and the wider population.

In our cross-sectional cohort study, we hypothesised that the carriage of macrolide resistance genes would be more frequent within the oropharyngeal microbiota of patients receiving long-term macrolide therapy compared to macrolide-naïve patients. We further hypothesised that any differences in resistance carriage between recipient and non-recipient patients would be reflected in resistance carriage in close contacts of patients, consistent with interpersonal transmission.

We report long-term macrolide exposure to be associated with increased macrolide resistance carriage within patients. Importantly, however, no increase in resistance carriage was observed in close-contacts of patients, supporting the continued safe use of macrolide maintenance therapy in chronic respiratory disease.

We have included the original editorial comments in this submission. Our Research Article is not under consideration by any other journal. Thank you for your consideration of our work.

Sincerely,



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