12st of Oct 2021

**Chest**

Dear Professor Mazzone,

We submit a manuscript entitled “***Carriage and transmission of macrolide resistance genes in patients with chronic respiratory conditions and their close contacts***” for consideration as an original article in Chest.

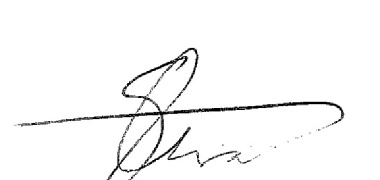
In summary, we address concerns that macrolide maintenance therapy might contribute to community-level antibiotic resistance (*Lancet Respir Med* 2013;1(3):262-74). Long-term treatment with macrolides is increasingly central to care for those with bronchiectasis, cystic fibrosis, uncontrolled asthma, 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.

This work is not under consideration for publication by any other journal and no author has any relevant conflict of interest. We thank you in advance for your consideration of our work.

Yours sincerely,



**Dr. Steven Taylor**

NHMRC Emerging Leader Fellow,

Head of the Respiratory Health Group,

South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia

E-mail: steven.taylor@sahmri.com