

## CORRESPONDENCE

Authors' response to Walker *et al.*

The research letter by Walker *et al.*<sup>1</sup> questions the generalisability of the results of the 4-year UPLIFT trial comparing tiotropium versus placebo based on potential eligibility for UPLIFT at time of discharge of a COPD patient population in New Zealand hospitalised for an exacerbation. The authors state that 38% of their study population would have been excluded from UPLIFT. The authors' assertion regarding the limited generalisability of UPLIFT's findings to clinical practice is not valid for several reasons.

First, patients hospitalised for COPD exacerbations are not representative of the general COPD population. An epidemiological analysis from The Netherlands<sup>2</sup> reported that 2.1% and 4.4% of COPD patients (mean age, 68 years) starting treatment with HandiHaler and Respimat, respectively, had a COPD-related hospitalisation in the year preceding the analysis. Analysis of an elderly Canadian COPD population<sup>3</sup> showed that 9.8% were recently hospitalised for acute respiratory conditions. These epidemiological data suggest that the COPD population studied by Walker *et al.* is not representative of the general COPD population.

Second, UPLIFT used liberal inclusion/exclusion criteria and allowed all COPD medications except other inhaled anticholinergics. The exclusion from UPLIFT of patients with unstable or life-threatening cardiac arrhythmias, recent acute myocardial infarction (MI) or severe heart failure requiring hospitalisation is consistent with most long-term COPD trials designed to evaluate the benefit/risk of pharmacotherapy, including those evaluating long-acting beta-agonist±inhaled corticosteroid. Furthermore, the Canadian COPD database analysis cited above reported 1.3% of patients hospitalised for acute coronary syndrome, including MI, 0.2% for arrhythmias and 2.2% for heart failure during the 6 months preceding the analysis. The proportion of patients excluded from UPLIFT because of these conditions is therefore very limited and would not limit the generalisability of UPLIFT's findings.

Third, patients studied in UPLIFT, who therefore did not have these conditions at baseline, could experience such adverse events in a real-world manner as prevalence increases with age (mean age at baseline, 65 years) during the conduct of the 4-year trial. This further supports the

generalisability of UPLIFT's findings to clinical practice. The respective events tended to occur later in the group treated with tiotropium versus placebo. Most patients did not withdraw due to these events, allowing for a robust analysis of serious adverse cardiac events. No findings of concern were detected and a manuscript of the respective analysis is in preparation.

For these reasons, we believe that Walker *et al.*'s assertion regarding the limited generalisability of UPLIFT's findings is not valid.

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**Contributors** DPT contributed to the analysis and interpretation of a post hoc analysis of 'patients excluded from UPLIFT at baseline'. DPT also conceived, drafted, read and approved the letter. NM contributed to the analysis and interpretation of a post hoc analysis of 'patients excluded from UPLIFT at baseline'. NM also conceived, drafted, read and approved the letter. NM is the guarantor for the overall content of the letter. CH contributed to the analysis and interpretation of a post hoc analysis of 'patients excluded from UPLIFT at baseline'. CH also conceived, drafted, read and approved the letter. IL generated new data based on a post hoc analysis of 'patients excluded from UPLIFT at baseline'. IL also, conceived, drafted, read and approved the letter. TL contributed to the analysis and interpretation of a post hoc analysis of 'patients excluded from UPLIFT at baseline'. TL also, conceived, drafted, read and approved the letter. MD contributed to the analysis and interpretation of a post hoc analysis of 'patients excluded from UPLIFT at baseline'. MD also, conceived, drafted, read and approved the letter.

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