We appreciate the comments made by Tashkin et al regarding the limited generalisability of the Understanding Potential Long-term Impacts of the Use of Tiotropium (UPLIFT) trial findings. In this study, we excluded patients with cardiac arrhythmias or other serious cardiac conditions. This is in line with the UPLIFT inclusion criteria. The UPLIFT study did not report patients hospitalised for acute coronary syndrome or myocardial infarction during the trial. We believe that these patients would have been excluded from the UPLIFT trial.


For these reasons, we believe that the study of the Canadian COPD database would not have been reported in a manuscript of the respective findings. To our knowledge, the Canadian COPD database analysis cited above reported 1.3% of patients hospitalised for acute coronary syndrome or myocardial infarction during the trial. DPT also conceived, designed, and drafted, read and approved the letter. NM contributed to the analysis and interpretation of a post hoc analysis of the findings. MD contributed to the analysis and interpretation of a post hoc analysis of the findings. MD reports personal fees from Pﬁzer Inc., grants from AstraZeneca, grants from GlaxoSmithKline, outside the submitted work. TL reports personal fees from Pﬁzer, outside the submitted work. MD reports personal fees from Pﬁzer, grants from Boehringer Ingelheim, outside the submitted work. NM reports grants from AstraZeneca, grants from Boehringer Ingelheim, outside the submitted work. DPT reports personal fees from Pﬁzer, outside the submitted work. TL reports personal fees from Pﬁzer, outside the submitted work. MD reports personal fees from Pﬁzer, grants from Boehringer Ingelheim, outside the submitted work. NM reports grants from AstraZeneca, grants from Boehringer Ingelheim, outside the submitted work. DPT reports personal fees from Pﬁzer, outside the submitted work. TL reports personal fees from Pﬁzer, outside the submitted work.


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In contrast, the Canadian data related to arrhythmias requiring hospital admission in the last 6 months. Third, the cardiovascular and renal comorbidity exclusion criteria in UPLIFT were not used in major long-term COPD trials evaluating LABAs±ICS, such as the landmark TOwards a Revolution in COPD Health study, which had no specific cardiovascular or renal comorbidity exclusion criteria.

In our view, the efficacy/safety profile of a COPD medication can only be determined if those patients who are at greatest risk of serious adverse events are studied. If this has not been done, then failing to list the characteristics of patients who were excluded from trial participation in the medication data sheet is unsatisfactory. We propose that the tiotropium data sheet is amended to state that the favourable efficacy/safety profile of tiotropium HandiHaler established in the UPLIFT study applies only to patients without recent cardiovascular or renal comorbidity, as these patients were excluded from the study.

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Contributors SW and JF undertook the data collection that was analysed by MW. All authors contributed to both the drafting of the manuscript and this letter.

Competing interests RB has been a member of the GlaxoSmithKline (NZ) advisory board, consulted for Cytos Biotechnology and Pharmaxis, received research grants from AstraZeneca, Cephalon, Chiesi, Genentech, GlaxoSmithKline and Novartis, and payment for lectures or support to attend meetings from Boehringer Ingelheim, GlaxoSmithKline, Novartis, Nycomed and Otsuka Pharmaceuticals. JF has received payment for lectures or support to attend meetings from AstraZeneca, Boehringer Ingelheim and Novartis. SW and MW have no competing interests to declare.

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