

## Comparative safety and effectiveness of muscarinic antagonists for chronic obstructive pulmonary disease (COPD): A rapid review and network meta-analysis

### Summary

This rapid review and NMA examined the comparative safety and efficacy of inhaled corticosteroids (ICS) and long-acting muscarinic antagonists (LAMA) in patients with COPD. In patients with moderately severe COPD tiotropium+formoterol and GSK961081 were most likely to reduce the risk of exacerbations. In patients with all severities of COPD glycopyrronium, aclidinium, glycopyrronium+indacaterol, and tiotropium were found to be safer across a variety of harms including mortality and pneumonia.

### Implications

Tiotropium+formoterol and GSK961081 are likely effective in preventing exacerbations in patients with moderately severe COPD. In patients with all severities of COPD glycopyrronium and aclidinium are likely to have the least risk for all-cause mortality, glycopyrronium and glycopyrronium+indacaterol likely have the least risk for cardiovascular-related mortality, and glycopyrronium and tiotropium are less likely to cause pneumonia. These inhalers likely don't increase the risk of cardiac arrhythmia. As this is a rapid review, our results should be interpreted with caution.

**Reference:** Tricco AC, Striffler L, Yazdi F, et al. Comparative Safety And Effectiveness Of Long-Acting Muscarinic Antagonists For Chronic Obstructive Pulmonary Disease (COPD): A Rapid Review And Network Meta-Analysis. Toronto: Ontario Drug Policy Research Network, 2014.

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### What is the current situation?

- Evidence suggests that therapy with long-acting muscarinic antagonists (LAMA) for patients with chronic obstructive pulmonary disease (COPD) is promising
- However, it is not clear which combinations of therapies are safest and most effective for these patients

### What is the objective?

- To determine the comparative safety and efficacy of LAMA for patients with COPD through a rapid review of the literature

### How was the review conducted?

- The protocol (or plan) for the review was developed and revised with input from researchers, clinicians, industry stakeholders, and the Ontario Ministry of Health and Long Term Care
- 3 electronic databases and unpublished literature were searched for randomized controlled trials (RCTs) of long-acting inhaled agents in adults with COPD
- The primary outcome of interest was the proportion of patients with moderately severe COPD experiencing exacerbations and secondary outcomes included mortality, pneumonia, arrhythmia, and cardiovascular related mortality
- Screening of literature search results was conducted independently by two reviewers, data abstraction was completed by one reviewer and independently verified by a second, and risk of bias assessment was independently assessed by one reviewer
- Random-effects network meta-analysis (NMA) was conducted based on the availability of evidence

### What did the review find?

- 186 published articles reporting on 190 RCTs were identified for inclusion in the review
- Tiotropium+formoterol and GSK961081 had the greatest probability of decreasing the risk of exacerbation in patients with moderately severe COPD (68 RCTs)
- Glycopyrronium and aclidinium had the greatest probability of decreasing the risk of mortality for patients with all severities of COPD (79 RCTs)
- Glycopyrronium and tiotropium had the greatest probability of being safest for pneumonia for patients with all severities of COPD (33 RCTs)
- Glycopyrronium and glycopyrronium+indacaterol had the greatest probability of being safest for cardiovascular-related mortality (32 RCTs)
- There were no significant differences in risk of arrhythmia across the compared agents (17 RCTs)