

## Comparative safety and effectiveness of long-acting inhaled agents for treating chronic obstructive pulmonary disease: a systematic review and network meta-analysis

### Summary

This rapid review and network meta-analysis was conducted to determine the comparative safety and efficacy of inhaled corticosteroids (ICS) and long-acting-beta-agonists (LABA) in patients with COPD. Ranking analysis of the results of an NMA restricted to patients with moderately severe COPD found that budesonide+formoterol and mometasone+formoterol had the highest probability of reducing the risk of exacerbations. Fluticasone in combination with salmeterol or vilanterol was most likely to increase the risk of pneumonia while Mometasone+formoterol was less likely to cause pneumonia. No differences in risk of arrhythmia were found across any of the agents compared in the review.

### Implications

Combined ICS+LABA therapies such as budesonide+formoterol and mometasone+formoterol are likely effective in preventing exacerbations in patients with moderately severe COPD and mometasone+formoterol is 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, Veroniki AA, et al. Comparative safety and effectiveness of long-acting inhaled agents for treating chronic obstructive pulmonary disease: a systematic review and network meta-analysis. *BMJ open*. 2015 Oct 1;5(10):e009183.

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### What is the current situation?

- Evidence suggests that therapy with inhaled corticosteroids (ICS) and long-acting beta-agonists (LABA) for patients with chronic obstructive pulmonary disease (COPD) is promising
- However, it is not clear which combinations of ICS and LABA are safest and most effective for these patients

### What is the objective?

To determine the comparative safety and efficacy of long-acting inhaled agents (ICS, LABA) 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- 3 electronic databases and unpublished literature were searched for randomized controlled trials (RCTs) of long-acting inhaled agents in adults with COPD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 that experienced exacerbations overall and secondary outcomes included pneumonia and arrhythmia
- 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?

- 183 published RCTs with 56 companion reports were identified for inclusion in the review
- Budesonide+formoterol and mometasone+formoterol had the greatest probability of decreasing the risk of exacerbation in patients with moderately severe COPD (68 RCTs)
- Fluticasone+salmeterol and fluticasone+vilanterol increased risk of pneumonia and were the least safe agents in patients with all COPD severities (33 RCTs)
- There were no significant differences in risk of arrhythmia across all treatment groups (17 RCTs)

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