

# Cochrane review of mucolytics for chronic obstructive pulmonary disease (COPD)

Poole P<sup>1</sup>, Sathananthan K<sup>2</sup>, Normansell R<sup>3</sup>

1. Department of Medicine, University of Auckland, Auckland, New Zealand UK 2. Cochrane Airways, Population Health Research Institute, St George's, University of London, London 3. Cochrane airways, Population health research institute, St George's, University of London, London, UK

## Introduction

Individuals with chronic bronchitis or chronic obstructive pulmonary disease (COPD) may suffer recurrent exacerbations with an increase in volume or purulence of sputum, or both. Personal and healthcare costs associated with exacerbations indicate that therapies that reduce the occurrence of exacerbations are useful.

Mucolytics are oral medicines, given daily, that are believed to increase expectoration of sputum by reducing its viscosity, thus making it easier to cough it up. Improved expectoration of sputum may lead to a reduction in exacerbations of COPD.

## Methods

We searched the Cochrane Airways Trials Register, trial registries and reference lists of primary studies. We extracted outcome data and assessed risk of bias in duplicate and used current Cochrane methodology throughout. We analysed dichotomous data as odds ratios (OR) or risk differences (RD), and continuous data as mean differences (MD), all with a fixed-effect model. We presented effect estimates with their 95% confidence interval (CI). We described skewed data narratively.

## Results

38 studies met our inclusion criteria, including a total of 10,377 participants with exacerbations of COPD. Six new records, linked to four new unique studies were added to the review (Dal Negro 2017; Fukuchi 2016; Johnson 2016; Xu 2014).

### Key Points:

- Majority of studies were conducted in high-income countries
- The mean age of participants ranged from 40 to 71 years
- Participants must have received regular treatment with oral mucolytics or placebo for at least two months.

### Primary outcomes:

- Participants given a mucolytic agent for an average of nine months are more likely to be exacerbation-free during that time (Peto OR 1.73, 95% CI 1.56 to 1.91).
- For one participant to be exacerbation-free, eight (95% CI 7 to 10) need to be treated for at least nine months
- Mucolytics may be associated with a reduction of approximately half a day of disability per participant per month, but the result is heterogeneous (MD -0.43, 95% CI -0.56 to -0.30; I<sup>2</sup> = 61%).

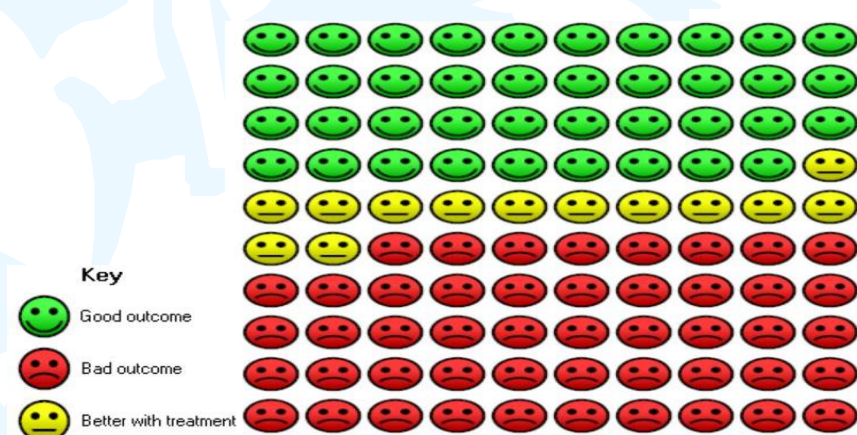


Figure 1: In the control group, 39 of 100 people were free from exacerbations over 9 months (represented by green faces) compared with 52 (95% CI 49 to 55) of 100 for the mucolytic group (represented by green plus yellow faces).

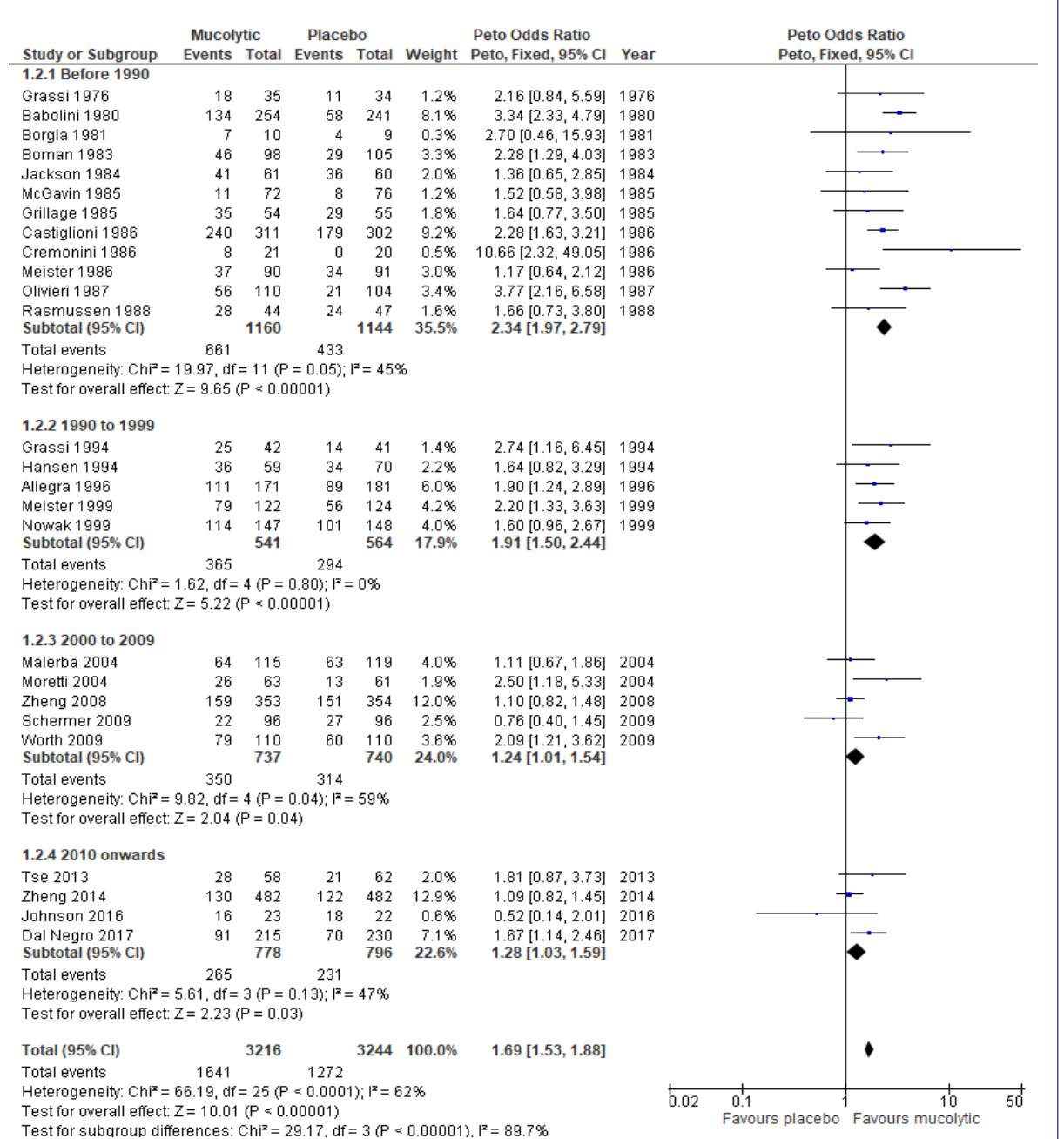


Figure 2: Forest plot of comparison showing participants with no exacerbation by decade, double-blind trials only.

### Secondary outcomes:

- Measures of lung function: Fourteen studies reported FEV1 in litres at the end of the study. The pooled effect favours mucolytics over placebo, however the effect size is small
- The meta-analysis of total numbers of adverse effects favours mucolytic treatment.
- Mucolytics may also be associated with a decrease in hospitalisations, although this finding is based on data from only four studies (Peto OR 0.68, 95% CI 0.52 to 0.89).
- Eleven studies reported on numbers of deaths in mucolytic-treated and placebo groups, revealing no significant differences, but the confidence interval is wide.

## Conclusions

- In participants with chronic bronchitis or COPD, we are moderately confident that treatment with mucolytics leads to a small reduction in likelihood of having an acute exacerbation, in days of disability per month and possibly hospitalisations, and is not associated with an increase in adverse events.
- There appears to be limited impact on lung function or health-related quality of life.
- Results are too imprecise to be certain whether or not there is an effect on mortality.
- Future studies could address whether specific subgroups of patients, for example, those with frequent exacerbations, experience greater benefit from mucolytics.

## References

Poole P, Chong J, Cates CJ. Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews (in press)