

APPENDIX

Systematic review

Search strategy

We started the literature search in Pubmed using the following keywords: COPD OR emphysema OR “chronic bronchitis” AND exacerb* AND (diary OR “symptom* increase OR “symptom* decrease” OR “symptom*-based” OR “symptom* recording” OR “symptom* score” OR “worsening symptom*” OR “daily symptom*” OR “symptom* algorithm” OR “symptom* reduction” OR “symptom* defined” OR “symptom* chart”). Where possible the MESH-terms for concepts were inserted.

For all relevant articles the records retrieved with the “related articles” link in PubMed were screened and reference lists were checked for other relevant studies. The bibliographic details of all retrieved articles were stored in a Reference Manager file (version 12). Duplicate records resulting from the various database searches were removed. Two members of the review team independently screened the titles and abstracts. Studies were selected for inclusion using the following predetermined criteria: 1) Study participants are diagnosed with COPD 2) the study uses exacerbation rate as an end point (primary, secondary or exploratory) and 3) the study uses a symptom-based definition in assessing exacerbations. Cross-sectional, longitudinal and intervention trials were included. We did not apply any language restrictions. After the first selection, the two reviewers independently evaluated the full text of all retrieved papers, applied the in- and exclusion criteria and discussed the decisions. Any disagreement was resolved by consensus with close attention to the in- and exclusion criteria.

Data extraction

We used the following questions to retrieve data from the full-text articles:

- 1) How are exacerbations defined in terms of symptoms and time?
- 2) Is exacerbation recovery / recovery time included in the definition?

- 3) Did the investigators attempt to distinguish relapsed from recurrent exacerbations?
- 4) How was exacerbation severity assessed?
- 5) Which method was used to record patient's symptoms?
- 6) Were symptom-based exacerbations matched (concurrency) with event-based (a minimal change in regular treatment) exacerbations?
- 7) Was there blinding for adjudication while counting the exacerbations?
- 8) Did the investigators report how to handle missing diary data?
- 9) Did the investigators report on methods to measure and enhance validity of symptom registration?