e-Appendix 2

Risk of bias assessment tool

The risk of bias tool was developed by the authors for the purposes of this review and is based on the Newcastle–Ottawa scale. It is structured around three domains which represent the three main sources of bias in observational studies. Each domain comprises a number of items or "signalling questions" responses to which allow reviewers to assign a risk of bias category as follows: red for moderate-to-high risk of bias, green for low risk of bias and amber where there is sufficient information to make a judgement.

Some signalling questions were dropped from the risk of bias assessment of cross-sectional studies, as they were not appropriate (e.g. item B3).

DOMAIN A: Selection of participants (selection bias)	
A1	**Is the study (source or sample) population appropriate and representative of the population of interest (i.e. the general population)?** Yes (green), No (red), Not clear (amber)
A2	**Is the exposed group/cases (e.g. people with COPD) representative of the condition under study?** Yes (green), No (red), Not clear (amber)
	NOTE: This question is study design specific; different considerations apply for cross-sectional, case–control/nested case–control, and longitudinal cohort studies.
A3	**Is the selection of the unexposed group/controls (e.g. people without COPD) appropriate?** Yes (green), No (red), Not clear (amber)
	NOTE: This question is study design specific; different considerations apply for cross-sectional, case–control/nested case–control, and longitudinal cohort studies.
DOMAIN B: Appropriate measurement/ascertainment of exposure and outcome variables	
B1	**Is the methodology of the exposure assessment explicitly stated and is ascertainment/ measurement of the main exposure(s) adequate and appropriate (i.e. how is COPD defined/established; is it objective)?** Yes (green), No (red), Not clear (amber)
B2	**Is the methodology of the outcome assessment explicitly stated and is ascertainment/ measurement of the main outcome(s) adequate and appropriate (i.e. how is stroke defined/established; is it objective)?** Yes (green), No (red), Not clear (amber)

B3	**Was follow-up long enough for the outcomes of interest to occur?** Yes (green), No (red), Not clear (amber)
	NOTE: Excluded from the risk of bias assessment of studies which estimate prevalence ratios and prevalence odds ratios for stroke.
DOMAIN C: Statistical analyses (including appropriate control of confounding)	
C1	**Did the study identify and appropriately adjust for potential confounders that might influence the findings?** Yes (green), No (red), Not clear (amber)
	NOTE: Excluded from the risk of bias assessment of studies which estimate prevalence ratios for stroke.
C2	**Is the sample size adequate and is there sufficient power to detect a meaningful difference in the outcome of interest?** Yes (green), No (red), Not clear (amber)
C3	**Is there evidence that adequate precautions had been taken to ensure that the outcome was not present in study subjects at the start of the study?** Yes (green), No (red), Not clear (amber)
	NOTE: Excluded from the risk of bias assessment of studies which estimate prevalence ratios and prevalence odds ratios for stroke.
C4	**Are there missing data and if so did the study handle the missingness in an appropriate manner?** Yes (green), No (red), Not clear (amber)
DOMAIN 4: Other	
D1	**Anything else of concern in terms of potential sources of bias (study specific)** Yes (green), No (red), Not clear (amber)