

ERS and UKCTAS protocol for a content based website on smoking and lung health in Europe

Aim of the website

The website aims to provide content based on a review of contemporary estimates of the magnitude of effect for the association between active and passive smoking on a range of health outcomes, primarily focussing on respiratory-related outcomes. The review was conducted adhering to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Types of studies

Systematic reviews (meta-analysis/reviews/reviews of reviews) were included for each health outcome where possible. Longitudinal studies and nested case control studies were identified to update existing reviews or where reviews had not been performed.

Types of populations

Populations primarily included adults; however, for the effect of passive smoking, studies focussing on in utero, infants, children and adolescents were also included.

Types of exposures

All studies which assessed active smoking were included, including those defined as, current smoker, ever smoker, ex- or former smoker, never smokers or non-smoker. Biochemically verified measures of smoking (for example exhaled carbon monoxide/saliva cotinine levels), when available, were used in preference to self-reported smoking status. Studies assessing levels of exposure to smoke based on cigarette consumption (e.g pack/years) were also included.

All studies that assessed passive smoking or environmental tobacco smoke exposure were included – defined as being in contact with second-hand smoke from any source (domestic, occupational or other sources). Biochemically verified measures of smoking, when available, were used in preference to self-reported smoking status. Studies that assessed passive smoking in non-smokers, or where smoking status of the individual exposed to passive smoking had been adjusted for in the statistical analyses were also included.

Studies which only looked at passive smoke exposure relating to cooking fuels were excluded. Studies looking at exposure to active and passive smoking from illegal substances were also excluded.

Types of outcomes

All studies that assessed the effects of smoking on the incidence of disease were included.

Active and passive smoke exposure on:

- Lung cancer
- Chronic obstructive pulmonary disease (COPD)
- Asthma and wheeze (to also include asthma exacerbations)
- Sleep apnoea
- Tuberculosis

Passive smoke exposure on:

- Respiratory infections
- Lung function

Search methods

The most recent definitive systematic review was taken for all health outcomes. If the last definitive systematic review was deemed out of date (depending on the health outcome and the amount of literature available), all prospective studies since this systematic review were screened and added to this existing review. In circumstances where there was no systematic review identified for a certain health outcome, prospective studies were identified from 1985 onwards. The literature searches were performed by a .

Electronic database search

Three electronic databases were systematically searched (Medline, EMBASE and Web of Science).

Examples of the Medline search terms used for systematic reviews into active smoking and lung cancer are given here:

<u>Medline</u>
1. Smoking/
2. "Tobacco Use Disorder"/
3. Smoking Cessation/
4. smok\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
5. tobacco\$.mp.
6. cigarette\$.mp.
7. nicotine\$.mp.
8. cotinine.mp.
9. cigar\$.mp.
10. or/1-9
11. Lung Neoplasms/
12. Carcinoma, Non-Small-Cell Lung/
13. Carcinoma, Small Cell/
14. Small Cell Lung Carcinoma/
15. lung cancer\$.mp.
16. SCLC.mp.
17. NSCLC.mp.
18. or/11-17
19. Meta-Analysis/
20. metaanaly\$.mp. concept, unique identifier] [TW]
21. "Review Literature as Topic"/
22. (systematic adj (review\$1 or overview\$1)).tw.
23. or/19-22
24. 10 and 18 and 23

A 'search diary' was developed and maintained detailing the names of the databases searched, the keywords used and the search results. Search terms used for different health outcomes were saved on individual databases. Titles and abstracts of studies to be considered for retrieval were recorded on a database (Endnote), along with details of where the reference had been found. Inclusion/exclusion decisions were recorded on an Excel database. Retrieved studies were filed according to inclusion/exclusion decisions.

No language restrictions were imposed and translations were sought where necessary.

Websites

The following five websites were searched to identify further potentially eligible studies:

- UK Centre for Tobacco and Alcohol Studies <http://www.ukctas.ac.uk>
- European Respiratory Society <http://www.ersnet.org/>
- European Lung Foundation <http://www.europeanlung.org>
- Action on Smoking and Health (ASH) <http://www.ash.org.uk>
- Society for Research on Nicotine and Tobacco <http://www.srnt.org>

Conference proceedings

The following three conference proceedings were electronically searched for the last 3 years to identify further potentially eligible papers:

- European Respiratory Society (ERS) Congress, search back till 2009
- Society for Research on Nicotine and Tobacco (SRNT) Annual Conference, search back till 2009
- World Conference on Tobacco or Health (WCTOH), proceedings in years 2009 and 2012

Contact experts in the field

ERS and UKCTAS members were contacted for published and unpublished trials relating to the list of health outcomes being covered.

Reference screening

The reference lists of all included studies were screened to identify further potentially eligible studies.

Study selection

The titles and abstracts identified from the searches were examined by one reviewer to select relevant articles. The full texts of the potentially eligible studies were sought and one reviewer checked each paper against the eligibility criteria. A second reviewer independently screened titles and abstracts (minimum 10%) and full text (30%) papers, and disagreements were resolved through discussion with a third reviewer.

See Appendix A for the full text inclusion criteria used

Data extraction and management

Two authors independently extracted data from included studies, and recorded data on a previously piloted data extraction form. Discrepancies were resolved through discussion or with a third reviewer. The information relating to study design, participants, exposures, study setting, outcomes and timing of outcomes were collected.

See Appendix B for data extraction and quality assessment forms used for systematic reviews and longitudinal studies

Quality assessment

Two authors independently extracted data relating to quality assessment from the included studies using the Newcastle-Ottawa Scale for longitudinal studies, and the Assessment of Multiple Systematic Reviews (AMSTAR) Scale for systematic reviews.

Statistical analysis

Measure of effect for the association between exposure to smoking and the risk of disease was extracted using either odds ratios (OR), risk ratios (RR), hazard ratios (HR) or incidence rate ratios

(IRR), with 95% confidence intervals (CI). Estimates adjusted for potential confounders were used in preference to crude estimates. Where possible, random effect meta-analytic methods were performed to pool studies that were deemed to be similar.

Heterogeneity between the studies was assessed using the I^2 statistic. Meta-analytic methods were not performed when extreme levels of heterogeneity were detected within a meta-analysis ($I^2 > 85\%$). Subgroup analyses were performed to expose reasons for heterogeneity between the studies, based on gender, European comparisons (studies conducted in Europe compared to the rest of the world), dose response, and age of children (in passive exposure studies). Assessments of publication bias were made using funnel plots. The statistical analysis was performed using STATA version 11 and Review Manager 5.1 software.