Effect of smoking cessation on major histologic types of lung cancer

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Authors' objectives
To assess the effect of smoking cessation on the rates of major histologic types of lung cancer.

Searching
MEDLINE and Cancerlit were searched using keywords pertaining to smoking and histologic type of lung cancer; the actual keywords used were not reported. The search identified articles prior to September 2000. The reference lists of the identified studies and review articles were checked for additional studies. Only studies published in English were included. Duplicate publications were excluded.

Study selection
Case-control and cohort studies were included. Studies were excluded if there was no risk comparison to non-smokers. Case series were also excluded.

Specific interventions included in the review
The interventions was smoking cessation.

Participants included in the review
Men and women who had stopped smoking (ex-smokers) were included. The years of abstinence from smoking in the included studies, where reported, ranged from less than one year to 10 years or more. The control groups of current smokers in the included studies were population-based, hospital-based and autopsy-based. The included studies were conducted in Europe, Asia and the Americas. One of the criteria for excluding studies was 'absence of risk comparison to nonsmokers'; the meaning of this was unclear.

Outcomes assessed in the review
The rate of major histologic types of lung cancer (squamous cell carcinoma, small-cell lung carcinoma, large-cell carcinoma and adenocarcinoma) was the outcome of interest. Studies were excluded if two or more histologic types were grouped together, or if they lacked measures for the relative risk.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The data presented in the review included: study; year; country; the number of men and women; the type of control, i.e. hospital, population, or dead; the histologic type of lung cancer; and the odds ratio (OR) and 95% confidence interval (CI). For investigation of the dose-response, where the 95% CI was not provided, the OR and standard error were calculated from the number of exposed cases and controls.
Methods of synthesis

How were the studies combined?

The outcome data were presented as ORs, which the authors defined as the estimator of the relative risk. A meta-analysis was used to pool the ORs from the case-control studies. The combined ORs for ex-smokers were presented separately from those for current smokers. A random-effects model was used if significant heterogeneity was detected, otherwise a fixed-effect model was used. The dose-response relationship was investigated using the number of years of abstinence. An exponential random-effects approach was used to assess the effect of the number of years since smoking cessation on the risk reduction of lung cancer (See Other Publications of Related Interest no.1). The cohort study was not included in the meta-analysis, but appears to have been included in the dose-response analysis.

Publication bias was investigated using funnel plots for each histologic type of lung cancer and a rank correlation test for the statistical significance.

How were differences between studies investigated?

The Cochran Q statistic was used to test for heterogeneity in the meta-analyses. The meta-analyses were stratified according to the type of control used in the case-control studies (hospital, population, all). Separate analyses were carried out for men and women.

Results of the review

Twenty-seven case-control studies (42,084 cases; the number of controls was not reported) and one prospective cohort study (n=31,738) were included.

There was significant heterogeneity between the studies in the data for current smokers; this applied to all histologic types of cancer and to hospital- and population-based controlled studies. Heterogeneity was less common in the data for ex-smokers. The highest OR was for current smokers and small-cell lung cancer (OR 72.5, 95% CI: 13.8, 379); the lowest was for ex-smokers and adenocarcinoma (OR 2.55, 95% CI: 0.82, 7.89). In current smokers, the combined OR for small-cell lung carcinoma and squamous cell carcinoma was higher among women. The ORs for all histologic types were consistently lower among ex-smokers, while women showed greater reductions than men for small-cell lung carcinoma and squamous cell carcinoma. The dose-response curve for intensity of smoking was steeper in women.

The statistical test for publication bias indicated no evidence of bias due to study size for all histologic types of lung cancer (results not shown).

Authors' conclusions

Smoking cessation was associated with a reduction in risk for all histologic types of lung cancer. The greatest reductions were for small-cell lung carcinoma and squamous cell carcinoma. The effect was most marked in heavy smokers, particularly among women.

CRD commentary

The observational study designs included in this review were appropriate to the question being addressed. However, the inclusion criteria for the participants, intervention and outcomes were not defined clearly. It is possible that relevant studies were missed because few sources were searched, the search strategy used was unclear, and only English language publications were included.

The included studies were not assessed for validity, and each included study was not presented in sufficient detail to allow the reader to judge the potential for bias and confounding. This is important because bias in the selection of cases and controls can produce a spurious association in case-control studies, and since the intervention was not randomly allocated, selection bias and confounding might have produced spurious results. It follows that a meta-analysis can produce precise but biased results when potential confounding factors in each study are not characterised and appropriate adjustments made in the analysis (See Other Publications of Related Interest no.2). The results of this review are based entirely on statistical pooling and statistical tests for heterogeneity, with no attention paid to bias or confounding or potential sources of heterogeneity between the included case-control studies. The pooling of data also
appears to have bypassed within-study comparisons, in that the odds for all ex-smokers appear to have been pooled then compared with the pooled odds for all smokers.

The results and conclusions of this review should be considered with caution because methodological rigour is lacking.

**Implications of the review for practice and research**

Practice: The authors’ implied implication is that stopping smoking reduces the risk of all histologic types of lung cancer.

Research: The authors state that cohort studies are needed to corroborate their findings from case-control studies and to delineate risk factors for adenocarcinoma other than smoking. Also, that further studies should be conducted to assess the effect of smoking cessation on the risk of large-cell carcinoma, and that these should be conducted in women in particular.

**Bibliographic details**


**PubMedID**

11713137

**DOI**

10.1378/chest.120.5.1577

**Original Paper URL**


**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Adenocarcinoma /epidemiology /etiology; Carcinoma, Large Cell /epidemiology /etiology; Carcinoma, Small Cell /epidemiology /etiology; Carcinoma, Squamous Cell /epidemiology /etiology; Female; Humans; Lung Neoplasms /epidemiology /etiology /pathology; Male; Odds Ratio; Risk; Smoking Cessation

**AccessionNumber**

12001002806

**Date bibliographic record published**

28/02/2003

**Date abstract record published**

28/02/2003

**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on
the reliability of the review and the conclusions drawn.