EVIDENCE ON SMOKING AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Purpose

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic obstruction of lung airflow. COPD is a major and increasing global health problem. The WHO predicts that COPD will become the third most common cause of death and the fifth most common cause of disability in the world by 2020 [1]. The most important risk factor for COPD is tobacco smoking and it has been estimated that tobacco smoking accounts for up to 70-95% of COPD in Western populations although pollution and occupational exposure to dusts and chemicals are also significant risk factors for this disease.

The objective of this study is to collect and summarize published epidemiological evidence relating smoking to COPD prevalence, incidence or mortality, with a view to assessing how the strength of the association varies by the index of smoking considered and by the characteristics of the study reporting the findings.

Methods

The methods of collecting and summarizing published epidemiological studies relating smoking to COPD are described below.

Identification of the studies

Attention was restricted to epidemiological case-control, prospective, or cross-sectional studies which provide data on prevalence or incidence of COPD or mortality from COPD, and to papers published up to the end of 2006.
Studies were selected which satisfied three criteria:
(a) the outcome is COPD (i.e., excluding studies of chronic bronchitis [CB] or of emphysema specifically),
(b) data are available for one or more defined major smoking indices or dose-related indices, and
(c) the study is conducted in a population which was not at specially high risk of respiratory disease.

Setting up databases to allow entry of relevant data

In-house software has been used. The structure involves two linked databases, one containing study details, with a record for each study, and the other containing relative risk details, with a record for each relative risk (RR). The study database contains details of the study itself (e.g., location, timing, design), the disease definition, and the potential confounding variables considered. The relative risk database contains all RRs for selected indices of exposure, with sufficient detail stored to define the RR precisely.

Entry and checking of data

For the selected indices of exposure, data were entered for COPD prevalence, incidence, or mortality; for males and females separately if available, otherwise for the sexes combined. For prospective studies, data were generally entered only for the longest follow up period.

Methods for analysis

Preliminary analyses were performed to describe the characteristics of the studies considered and the quantity and type of data available.

The overall risk from the major smoking indices and dose-related indices were estimates using meta-analytic methods [2]. Both fixed-effect and random-effects meta-analysis have been carried out to form combined estimates of the individual independent risks.

Meta-regression analyses were conducted to study the variation in risk by level of a range of factors

Results

Based on papers published up to the end of 2006, 132 relevant studies were identified. There were 117 independent "principal" studies, with 15 "subsidiary studies" with data only used in meta-analyses where equivalent results were not available from the principle studies. Some major characteristics of the 132 studies are shown in table 1.

Table 1 Characteristics of the 132 studies

Characteristic / level	Study type				
	Principal			Subsidiary	Total
	Case Control	Prospective	Cross-Sectional		
Total	14	34	69	15	132
Study type					
case/control	14	0	0	1	15
prospective	0	34	0	6	40
cross-sectional	0	0	69	7	76
nested case/control	0	0	0	1	1
Study sex					
both	11	18	63	11	103
male	2	15	4	4	25
female	1	1	2	0	4
Region					
USA	2	11	13	4	30
Canada	0	0	3	0	3
S/C America	2	0	5	0	7
UK	2	6	3	3	14
Western Europe	2	2	5	0	9
Scandinavia	0	5	14	4	23
E Europe	2	1	6	1	10
SE Europe/Balkans	0	0	3	2	5
SE Asia/Pacific	0	1	1	0	2
Far East	3	5	12	1	21
Australia/NZ	1	1	2	0	4
multi	0	2	2	0	4
Type of outcome					
prevalence	10	2	69	9	90
mortality	3	24	0	5	32
incidence	1	8	0	1	10

Results from a variety of meta-analyses are presented for five variants of the major indices of smoking status. Based on RRs for any valid COPD definition (e.g. using ICD codes or lung function criteria), and (where the study provides a choice) preferring RRs for smoking any tobacco product to those for cigarette smoking and preferring RRs adjusted for the most potential confounding variables, an association is clearly evident, with random-effects estimates as follows:

	RR (95% CI, no study)
Ever smoking	2.85 (2.60 – 3.13; n = 127)
Current smoking	3.48 (3.07 – 3.94; n = 120)
Ever (or current) smoking	2.99 (2.70 – 3.30; n = 139)
Current (or ever) smoking	3.40 (3.03 – 3.82; n = 140)
Ex smoking	2.36 (2.12 – 2.62; n = 110)

There is a clear tendency for overall RR estimates to be higher where the diagnosis was based on mortality than if based on lung function alone or other definitions of COPD.

		RR (95% CI; no studies)
Ever smoking	Mortality	4.00 (3.00 – 5.33; n = 29)
	Lung function	2.34 (2.12 – 2.58; n = 59)
	Other COPD	3.05 (2.56 – 3.64; n = 45)
Current smoking	Mortality	4.73 (3.52 – 6.36; n = 32)
	Lung function	2.77 (2.40 – 3.20; n = 55)
	Other COPD	3.55 (2.97 – 4.24; n = 40)

Comparing with never smokers, the risk increases monotonically for amount smoked (with RRs of 2.77, 5.91, and 8.76 for smoking around 5, 20, and 45 cigarettes per day) and for pack-years (with RRs of 1.25, 2.51, and 3.88 for around 5, 20, and 45 pack-years).

For age of starting, the risk is higher for starting around age 14 (RR 3.12), but little different between ages 18 and 26 (RRs 1.91 and 2.11).

Comparing the highest with the lowest category of exposure from each study, the association with each measure of exposure is as follows.

	RR (95% CI; no studies)
Amount smoked	2.28 (1.86 – 2.81; n = 42)
Age of starting to smoke	1.49 (1.26 – 1.76; n = 14)
Pack-years	2.85 (2.43 – 3.34; n = 33)
Duration of quitting	2.18 (1.28 – 3.71; n = 10)

Variation in risk by level of a range of factors was studied. These factors include continent, national cigarette tobacco type, start year of study, publication year, study type, lowest age in RR, highest age in RR, midpoint age, population/setting, study weakness, type of outcome, COPD definition, asthma, bronchodilator/reversibility, number of cases, number of adjustment variables, smoking product. No single factor explains the marked between studies heterogeneity of RR, which remained even after fitting a multiple regression model.

References

1. Lopez AD, Murray CC. The global burden of disease, 1990-2020. Nat Med. 1998 Nov;4(11):1241-3.

2. Fleiss JL, Gross AJ. Meta-analysis in epidemiology, with special reference to studies of the association between exposure to environmental tobacco smoke and lung cancer: a critique. J Clin Epidemiol. 1991;44(2):127-39.

Conclusion

The meta-analyses carried out have clearly demonstrated a highly significant association between COPD and smoking. The association is evident for all types of COPD studied, and whether ever, current or ex smoking is considered. However, the magnitude of the observed association varies.

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