

Prospective study of asthma in relation to smoking habits among 14 729 adults

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ABSTRACT The prevalence and incidence of asthma in relation to cigarette smoking habits was studied in a population of 14 729 Finnish adult men and women who participated in a postal health survey in 1975. Of those invited to participate in a new survey in 1981, 89.7% replied. Asthma was diagnosed on the basis of self reporting of asthma diagnosed by a physician and by record linkage to a national register of hospital admissions to all general and tuberculosis hospitals during 1972 and 1983. The prevalence of diagnosed asthma in 1975 was significantly higher among male smokers than among male non-smokers (relative risk (RR) = 1.73); no significant difference was observed for women (RR = 1.33). People with asthma were slightly but not significantly more likely to stop smoking during the six year follow up period (RR = 1.23). The incidence of asthma among those who had neither reported asthma in 1975 nor been admitted to hospital for asthma before the 1975 questionnaire study was not significantly higher among smokers than among non-smokers during follow up. Although possible mechanisms exist to explain how smoking could have a role in the aetiology of asthma, this study suggests that smoking is not a strong risk factor for asthma.

Introduction

There are some data on the smoking habits of patients with asthma 15-20 years ago,¹⁻³ but no recent studies from Finland that reflect the changes in smoking habits over the past decade. To study the prevalence and incidence of asthma in Finland in relation to smoking habits, we have carried out a prospective study of unrelated individuals chosen from the population based Finnish Twin Cohort.

SUBJECTS

The Finnish Twin Cohort study is a prospective study of genetic and environmental influences on chronic diseases in adults. The cohort consists of over 17 000 same sex twin pairs, with both members alive in 1967 and born before 1958. It was compiled from the Finnish Central Population Registry in 1974 by selecting all "pairs" of individuals with the same surname at birth, the same birth data, the same sex, and the same place of birth.⁴ Because this procedure meant that both biological twins and non-biological "pseudotwins"—that is, singletons—were selected, the question of twinship was resolved on the basis of the 1975 questionnaire study (see below) and inquiries to local parishes.

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Accepted 20 April 1988

QUESTIONNAIRE STUDIES

In 1975 a questionnaire was mailed to everyone in the cohort. Questions covered twinship, medical history, symptoms, state of health, and social and psychological traits.

The medical questions included one that asked whether asthma had ever been diagnosed by a physician. Smoking was assessed in detail. Respondents were classified with respect to cigarette smoking as never smokers if they had never smoked more than 10 packs of cigarettes in their lifetime and occasional smokers if they had smoked more than this but had never smoked on a daily or almost daily basis. Regular (daily) smokers were classified as current smokers if they smoked at the time of the questionnaire study and as former smokers if they reported that they had stopped smoking. The age of starting smoking was asked and former smokers were asked at what age they had stopped and how much they had smoked before stopping. Current smokers were asked how much they currently smoked (less than five cigarettes daily, five to nine, 10-14, 15-19, 20-24, 25-29, or 40 or more) and the type of cigarette smoked (filter or non-filter or both). Because regular smokers of pipes or cigars were rare they were disregarded.

The overall response rate was 89%.⁴ In this analysis only one member of each pair of twins was included to eliminate correlations between observations. When

Table 1 Comparison of reported asthma in 1975 and 1981 questionnaires

		Asthma in 1975 study		
		No	Yes	Total
Asthma in 1981 study	No	10 184	41	10 225
	Yes	102	89	191
	Total	10 286	130	10 416

both members of a pair had replied, one was chosen at random. In all, 14 729 responses were received from people aged 18–64; 370 individuals had not replied to the question on whether a physician had ever diagnosed asthma, so that 14 359 questionnaires remained for analysis.

Six years after the 1975 questionnaire a second questionnaire was mailed to all the twins in the cohort who were alive and had an adequate address. The 2160 non-twins in the sample were not contacted again, so the sample size of the questionnaire responders is smaller in 1981 than in 1975. The purpose of the second questionnaire was to examine changes in risk factors and to obtain data on the incidence of diseases and symptoms not available from medical registries. In the questionnaire smoking history and a history of asthma were ascertained from questions that were identical in form to those in the 1975 study. There were 10 741 responders among the people in this analysis. Reasons for non-participation were incomplete response ($n = 61$, 0.5%), death ($n = 210$, 1.7%), non-response ($n = 1084$, 8.6%), illness ($n = 38$, 0.3%), refusals ($n = 47$, 0.4%), no address ($n = 91$, 0.7%), and living in institutions, etc. that were not contacted ($n = 297$, 2.4%). The net response rate—that is, the proportion responding among those contacted—was 89.7%. The item on asthma was not answered by 137, so that there were 10 604 responses.

FOLLOW UP

Follow up information was obtained from linkage of the cohort to computerised medical registries. Data on deaths and causes of death were available from 1967 to 1984 from the Central Statistical Office of Finland. Data on inpatient admissions to general and tuber-

culosis hospitals and hospitals for mental illness have been obtained from the National Board of Health hospital discharge registry for 1972–83. These two data sources were used to identify hospital diagnoses of asthma (ICD-8 rubric 493). The year of the first admission for asthma was used in the analysis. The reliability of the hospital diagnoses in the registry has been assessed for alcohol related diagnoses⁵ and cardiovascular diagnoses⁶ and found to be adequate for epidemiological purposes. Follow up data were almost complete for death certificates. For hospital records the probability that any single record was missing was 10–15%; thus if a person had only a single admission for asthma, this is the probability that the diagnosis would be missed in the record linkage. When there is more than one hospital admission for any person, the probability that the diagnosis is missed becomes very small, the event of non-recording of the diagnosis being independent and due mainly to clerical mistakes. Thus the overall missing data rate for hospital admissions will be much less than 10% when the entire follow up period is considered.

The validity of the reporting of asthma in the questionnaire studies was examined by comparing the reporting of asthma in 1975 and in 1981 (table 1) and by comparing the results of both questionnaires with hospitalisation data (table 2). When the responses to the two questionnaires were compared 31.5% (41/130) of those who reported asthma in 1975 no longer reported it in 1981. Of those who had been in hospital because of asthma before the questionnaire studies, 68% (30/44) reported it in the 1975 questionnaire and 75% (55/73) in the 1981 study. Most people reporting asthma in the questionnaires had not been admitted to hospital during the follow up period (1972–83). Only 0.1% of those who reported that they did not have asthma in 1975 had been admitted to hospital for asthma before the 1975 study. For the 1981 study the corresponding figure was 0.2%.

STATISTICAL METHODS

Age and gender adjustment of continuous variables was done by analysis of covariance with the BMDP statistical software package.⁷ Relative risks and their

Table 2 Comparison of asthma reported in 1975 and 1981 questionnaires with data on hospital admissions for asthma during 1972–83

Hospital data on year of first admission for asthma	Asthma in 1975 study			Asthma in 1981 study		
	No	Yes	Total	No	Yes	Total
No admission	14 073	145	14 218	10 370	137	10 507
Before study*	14	30	44	18	55	73
After study†	78	19	97	21	3	24
Total	14 165	194	14 359	10 419	195	10 604

*For 1975 study 1972–5; for 1981 study 1972–81.

†For 1975 study 1976–83; for 1981 study 1982–3.

Table 3 Distribution of cigarette smoking habits among asthmatic and non-asthmatic subjects in the questionnaire study of 1975

Age (y)	Smoking*	Men (No (%))		Women (No (%))	
		No asthma	Asthma	No asthma	Asthma
18-29	Non-smokers	1267 (39.2)	10 (35.7)	1749 (51.8)	8 (30.8)
	Former smokers	494 (15.3)	3 (10.7)	473 (14.0)	4 (15.4)
	Current smokers	1468 (45.5)	15 (53.6)	1154 (34.2)	14 (53.8)
30-49	Non-smokers	890 (32.1)	5 (16.7)	1906 (71.7)	26 (74.3)
	Former smokers	687 (24.8)	8 (26.7)	267 (10.0)	3 (8.6)
	Current smokers	1194 (43.1)	17 (56.7)	484 (18.2)	6 (17.1)
50-64	Non-smokers	207 (23.5)	4 (12.9)	970 (85.3)	38 (88.4)
	Former smokers	345 (39.1)	16 (51.6)	65 (5.7)	2 (4.7)
	Current smokers	330 (37.4)	11 (35.5)	102 (9.0)	3 (7.0)
Total †	Non-smokers	2364 (32.5)	19 (22.5)	4625 (66.9)	72 (60.8)
	Former smokers	1526 (25.0)	27 (27.3)	805 (10.6)	9 (10.4)
	Current smokers	2992 (42.5)	43 (50.3)	1740 (22.4)	23 (28.9)
	Total	6882	89	7170	104

Relative risks for asthma with respect to smoking habit adjusted for age in men and women with 95% confidence limits:

	Non-smokers	Former smokers	Current smokers	
Men	1.0	1.69 (0.88, 3.23)	1.73 (1.01, 2.96)	Tests for trends and heterogeneity over age gave non-significant results
Women	1.0	1.05 (0.52, 2.14)	1.33 (0.78, 2.26)	

*Information on smoking was missing for 113 individuals without asthma and for one with asthma.

†Percentages age standardised by 1975 Finnish general population.

confidence limits (CL) were computed on EPILOG (Epicenter Software, Pasadena, California) with the Mantel-Haenszel⁸ test and the Mantel extension test.⁹

Results

A total of 194 people (1.35%) reported that they had asthma in the 1975 questionnaire. Of those who also replied in 1981, 191 (1.80%) reported asthma at that time, the prevalence slightly increasing as the cohort aged.

The prevalence of cigarette smoking among asthmatic and non-asthmatic subjects in the 1975 questionnaire data is shown in table 3. The age adjusted prevalence of current smoking was higher among those reporting a history of asthma diagnosed by a physician both for men (50.3% v 42.5% in non-asthmatics; RR = 1.73, 95% CL 1.01-2.96) and for women (28.9% v 22.4%; RR = 1.33, 95% CL 0.78-2.26) (table 3). The difference was significant for men but not for women. Those with asthma, both men and women, were less often never smokers. Among current smokers the number of cigarettes smoked daily did not differ ($p = 0.48$) between individuals without asthma (mean 14.9) and with asthma (mean 14.3) after adjustment for sex and age by analysis of covariance. Furthermore, the mean number of years of smoking did not differ ($p = 0.73$); individuals without asthma had smoked for an average (sex and age adjusted) of 13.0 years, compared with 13.1 years for those with asthma.

Cessation of smoking was compared among those with and without asthma by comparing those who smoked in 1975 with those who smoked in 1981. In both groups about one quarter had stopped smoking six years later (12 out of 47 asthmatics and 876 out of 3318 non-asthmatic subjects). Stopping smoking was slightly though not significantly more common among those reporting asthma (age and gender adjusted RR = 1.23, 95% CL 0.65-2.31). Resumption of smoking among former smokers was much less common among those with asthma. Only three of the 25 ex-smokers with asthma in 1975 reported that they smoked in 1981—a proportion of 12% compared with 20.5% of all ex-smokers in 1975 (303/1482) (NS).

The incidence of new cases of diagnosed asthma reported in the 1981 questionnaire study is given in table 4 broken down by sex, age, and smoking habit. The crude incidence was eight per 1000 for men and 10.6 per 1000 for women, a yearly rate of 1.3/1000 in men and 1.7/1000 in women. There were no significant differences in incidence rates by smoking habit for either men or women.

A similar analysis was carried out for those who were admitted to hospital with asthma after 1975 but who had not reported asthma in the 1975 questionnaire nor been admitted to hospital with asthma during 1972-5 (table 4). The crude incidence was 5.6/1000 for men and 5.2/1000 for women overall, corresponding to a yearly incidence of about 0.7 per 1000. Again smoking habit did not predict the incidence of asthma.

Table 4 Incidence of asthma among those not reporting asthma in the 1975 questionnaire and with no previous admission to hospital for asthma (1972-5) by smoking habit

		Non-smokers	Former smokers	Current smokers	Total
Population at risk*	M	1744	1075	2039	4858
	F	3457	598	1327	5382
Incident cases	M	13	11	15	39
	F	38	4	15	57
Age adjusted relative risk and 95% confidence limits†	M	1.0	0.93 (0.44, 1.97)	0.92 (0.44, 1.93)	
	F	1.0	0.76 (0.28, 2.05)	1.29 (0.69, 2.40)	

*Persons respondent to both questionnaires without asthma in 1975 either in questionnaire data or prior hospital (data on smoking missing for 36 persons).

†Age adjusted over age-groups (18-29, 30-39, 40-49 and 50-64) Chi-square tests for trends and homogeneity of relative risk all non-significant.

B Hospital admission for asthma 1976-83

		Non-smokers	Former smokers	Current smokers	Total
Population at risk	M	2364	1550	2992	6906
	F	4617	803	1739	7159
Incident cases	M	15	7	17	39
	F	25	3	9	37
Age adjusted relative risk and 95% confidence limits*	M	1.0	0.56 (0.22, 1.42)	0.84 (0.42, 1.71)	
	F	1.0	0.85 (0.24, 2.98)	1.32 (0.60, 2.94)	

*Age adjusted over age groups (18-29, 30-39, 40-49, and 50-64 y); results of χ^2 tests for trends and heterogeneity of relative risk all non-significant (data on smoking missing for 86 persons without asthma in 1975).

Discussion

Validity of data on smoking The prevalence of smoking in this study may be compared with that in studies of the general population in Finland.¹⁰ In the autumn of 1975 population based interview studies found the proportion of smokers of all kinds of tobacco to be 46% for men and 22% for women. As nearly all tobacco in Finland is consumed in the form of cigarettes, these figures correspond very closely to our figures, shown in table 3: 42.5% of men and 22.4% of women were current cigarette smokers.

Validity of asthma diagnoses The overall prevalence of reported asthma corresponds to that found in other Scandinavian studies—1-2% of the adult population, with an increase with age and an excess of women with asthma.¹¹ It also agrees with the prevalence of asthma based on the numbers of those receiving fully reimbursed drugs for asthma from the National Pensions Institute. Only a minority of those reporting asthma in the questionnaires had been admitted to hospital for it. Frequently the diagnosis is established from an outpatient consultation. Over two thirds of those who had been admitted to hospital for asthma before the studies reported it in the questionnaires. Thus the validity of the questionnaire based diagnosis can be considered adequate at least for assessing differences in smoking habits between groups of individuals.

Earlier studies have examined the degree of agreement of the diagnosis of asthma on two different occasions. In a questionnaire study on allergy in 7000 twin pairs in Sweden, Edfors-Lubs¹² found that the

questionnaire diagnosis and clinical diagnosis were in good agreement. For 39 people who were examined the clinical and questionnaire diagnoses agreed for seven with asthma and 30 without asthma; in two cases the diagnoses conflicted. She points out that "the material included many individuals that had been symptom-free for many years, since allergic symptoms become less frequent in older years."¹² Thus the history taken by a physician is then comparable to information provided by the patient on a questionnaire. Kiviloog *et al*¹¹ also found good agreement between prior interview diagnosis of asthma and interviews with tests of bronchial hyperreactivity six years later. In the Tecumseh total community study, interview diagnoses four years apart were in very good agreement; 97% of those diagnosed as having asthma on the first interview satisfied the diagnostic criteria in the second interview.¹³ In the present analysis some 30% of those who reported asthma in the first questionnaire study did not report it in the second study six years later. This may be due in part to reporting errors or changes of diagnosis and in part to remission of the disease, causing patients to forget to report that they had once had asthma. Broder *et al*¹³ reported remission of asthma in 24% of men and 16% of women during four years.

Asthma and smoking habits In the present study, covering more than 14 000 adults, the prevalence of asthma was significantly higher among male smokers than among men who had never smoked. There was a similar but non-significant trend for women. There were, however, no differences between smokers with

and without asthma with respect to the amount smoked or the duration of smoking. Kiviloog *et al*¹¹ found that female smokers had significantly more asthma than female non-smokers, with a similar but non-significant trend for men. In a random sample of 1209 Norwegian adults, Gulsvik¹⁴ found no relationship between the prevalence of asthma and smoking habit in either men or women. Similarly, no relation between smoking habit and asthma prevalence was found for 4699 people in the Tecumseh study.¹⁵ Huhti *et al*³ studied rural men and women in Finland and found no relation between smoking and asthma prevalence; the number of asthma cases among men was small ($n = 15$) and smoking among women was rare. Alanko¹ reported a higher prevalence of smoking among male asthmatics aged 30–59 than among controls.

Changes in smoking habit among those with asthma and the entire population From 1975 to 1981 more adults stopped than started smoking in Finland,¹⁰ in part as a result of the 1978 Tobacco Act and tobacco price increases. Among those with asthma in this study there seemed to be a larger proportion stopping and a lower rate of starting again than in the non-asthmatic population, even though the differences were non-significant. Of 125 asthmatic patients seen during two months, Hillerdahl and Rylander¹⁶ report that 44% had never smoked or had stopped at least one year before the disease had caused symptoms. Only 8.8% were current smokers and 47% had stopped. Of those who had stopped smoking, equal numbers had noticed improvement, no change, and deterioration in their symptoms. Lebowitz¹⁷ found that, although the prevalence of asthma did not consistently relate to smoking habits, former smokers reported asthma more often than current or never smokers.

Incidence data The incidence of new cases of asthma was higher when the questionnaire data were used than the hospital admission data. The incidence rate was 5.5 per 1000 for hospital admissions over eight years, and for events ascertained by questionnaire six years later 9.4 per 1000. Broder *et al*¹³ reported a four year incidence rate of somewhat under 1% for adults, with no sex difference. In the present study we found no differences in incidence rate depending on smoking habit; for women a slightly higher but non-significant incidence was found among current smokers. Dodge and Burrows¹⁸ found that smokers had a higher incidence of asthma than non-smokers, with a relative risk of nearly 2 in people under 40 and of 1.5 in those aged 40 or more. The overall 3.5 year incidence was 49 new cases in 3432 disease free subjects (0.4%/year). Incidence rates in adults were higher for women than for men.¹⁸

Thus, although several mechanisms exist that could explain effects of smoking in the aetiology of asthma,

this epidemiological study in a large population suggests that the relation between smoking and asthma is fairly weak, and that the smoking habits of people with asthma do not greatly differ from those of the general population.

EV has been supported by the Finnish Allergy Research Foundation, and the Finnish Twin Cohort by the Council for Tobacco Research, USA, Inc, and the Medical Research Council of the Finnish Academy.

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