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Smoking, changes in smoking habits, and rate of decline in FEV_1: new insight into gender differences

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Smoking, changes in smoking habits, and rate of decline in FEV_1: new insight into gender differences. X. Xu, S.T. Weiss, B. Rijcken, J.P. Schouten. ©ERS Journals Ltd 1994.

ABSTRACT: We wanted to test the hypothesis that gender differences in effects of smoking on the rate of decline in pulmonary function may be related to gender differences in the frequency of smoking.

Data from the Vlagtwedde-Vlaardingen study in The Netherlands were analysed, to investigate the rate of decline in forced expiratory volume in one second (ΔFEV_1) in relation to smoking status and gender. 4,554 participants, initially aged 15–54 yrs, provided 16,900 pairs of observations at 3 yr intervals over 24 yrs of follow-up.

Lifetime nonsmokers accounted for 11% of male participants and 45% of female participants. Compared with lifetime nonsmokers, estimated excess ΔFEV_1 for light, moderate, and heavy continued smokers was 4.4, 9.5 and 13.5 ml·yr^{-1} for men and 6.1, 10.8 and 18.8 ml·yr^{-1} for women, respectively. Female former smokers had a significantly more rapid ΔFEV_1 (β=-4.4, SE=1.6 ml·yr^{-1}) than lifetime nonsmokers; but male former smokers had a slower rate of decline (β=4.1, SE=2.3 ml·yr^{-1}) than lifetime nonsmokers. Overall gender difference in smoking effects on ΔFEV_1 was statistically significant.

Among subjects who smoked an identical amount at the beginning of the study period those who quit smoking during the period had a significantly slower ΔFEV_1 than those who continued smoking, for both men (β=20.6, SE=3.9 ml·yr^{-1}) and women (β=15.7, SE=3.4 ml·yr^{-1}). Younger quitters (<45 yrs) benefited significantly more from smoking cessation than older quitters (≥45 yrs).

We conclude from the data obtained in this study and from other studies that part of the gender difference in smoking effect on ΔFEV_1 may be related to gender difference in the proportion of smokers.

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There is overwhelming evidence that cigarette smoking is the major cause of chronic obstructive lung disease both for men and women [1, 2]. However, the findings on gender differences in effects of smoking on pulmonary function remain controversial. For example, studies in six US cities [3, 4], Tucson, USA [5], Los Angeles, USA [6], Italy [7], and Denmark [8] showed increased rate of decline and reduced level of pulmonary function associated with cigarette smoking in men to be greater than in women. However, reports from other studies [9–13] are inconsistent with these results. The hypothesis tested by this study is that the observed gender differences in smoking effect may be related to gender differences in the frequency of smoking, which create differences between the sexes in the proportion of unhealthy nonsmokers in nonsmoker reference groups.

Cross-sectional analyses in the Six Cities Study showed that, in comparison with ex-smokers of identical total pack-years, current smokers had lower forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) levels. The amount of the deficit was proportional to the number of cigarettes currently smoked each day; thus, implying that heavy smokers will regain more lung function than light smokers after quitting smoking [3]. In contrast, a longitudinal study from Copenhagen, Denmark found that the beneficial effect of smoking cessation on FEV_1 decline was more pronounced among light smokers than among heavy smokers [12]. However, this analysis did not account for the cigarette consumption during the interval between lung function tests, which is linearly associated with increased rate of decline in FEV_1 [4].

Longitudinal analyses from the Six Cities Study [4] indicate that age-adjusted rates of decline in FEV_1 were greater in subjects who started smoking than in lifetime nonsmokers. However, the Denmark study [12] found no significant difference between starters and lifetime nonsmokers. Neither of the two studies separated new smokers from recidivist smokers in the analyses. It is possible that lifetime nonsmokers and former smokers

may have different biological responses when they start to smoke.

Data obtained from a 24 year follow-up of a large cohort in The Netherlands provide an opportunity to study longitudinal changes in pulmonary function in relation to smoking status. The data also enable us to make a comprehensive assessment of gender differences in smoking effects on rate of change in FEV_1.

Methods

A detailed description of The Netherlands Study has been published elsewhere [14]. In brief, this is a longitudinal study of host factors and environmental determinants of chronic obstructive pulmonary disease, based on a random sample of populations from Vlagtwedde and Vlaardingen. Vlaardingen is an urban community in the south-west Netherlands, and Vlagtwedde a rural community in the north-east Netherlands. The Vlagtwedde cohort consists of 450 subjects, 40–44 yrs of age, who were enrolled in 1965; and 1,793 subjects, 15–39 yrs of age, who were enrolled in 1967. The Vlaardingen cohort consists of 859 subjects, 40–54 yrs of age, who were enrolled in 1965; and 1,590 subjects, 15–39 yrs of age, who were enrolled in 1969. After the baseline survey, the two cohorts were re-examined every 3 yrs, beginning in 1970 in Vlagtwedde and 1972 in Vlaardingen. The Vlaardingen subjects make up a fixed cohort, in which only those persons enrolled initially have been followed subsequently. In the Vlagtwedde cohort, all original subjects and any new subjects in the initial age range have been seen at each follow-up examination. In this analysis, data through the 1990 follow-up were considered.

Pulmonary function was measured with a water-sealed spirometer (Lode Spirograph D53, Lode Instruments, Groningen, The Netherlands) whilst the subjects were seated and wearing noseclips. After a deep expiration, inspiratory vital capacity (IVC) and then FEV_1 were measured. Subjects repeated the manoeuvre until two technically satisfactory tracings were produced. For a trial to be acceptable, the difference between the two FEV_1 measurements could not be more than 150 ml. The larger of the two values was analysed. All examinations took place in October in the same facility. All values were recorded at ambient temperature and pressure, saturated with water (ATPS).

Lifetime nonsmokers were defined as those who reported no smoking history at the beginning and the end of the interval between pairs of pulmonary function measurements; former smokers as reporting a smoking history but no smoking during the interval; continued smokers as reporting cigarette smoking throughout the interval; quitters as smoking at the beginning but stopped in the interval; new starters as not smoking at the beginning but starting during the interval; recidivist smokers as being a former smoker at the beginning but resuming smoking during the interval; brief smokers as not smoking at the beginning, but starting and then stopping during the interval; consistent pipe/cigar smokers as reporting pipe/cigar smoking throughout the interval; and inconsistent pipe/cigar smokers as shifting from pipe/cigar to any other smoking status, or from any other smoking status to pipe/cigar smoking during the interval. Continued smokers were further divided into light, moderate and heavy smokers, according to cigarettes·day^{-1} smoked at the beginning and the end of the interval. Light smokers were defined as those who smoked fewer than 15 cigarettes·day^{-1} at the beginning and the end of the interval. Heavy smokers were defined as 25+ cigarettes·day^{-1} at the beginning and the end of the interval; 25+ cigarettes·day^{-1} at the beginning of the interval, and 15–24 cigarettes·day^{-1} at the end of the interval; or 15–24 cigarettes·day^{-1} at the beginning of the interval, and 25+ cigarettes·day^{-1} at the end of the interval. The remainder of the continued smokers were defined as moderate smokers. For new smokers and recidivist smokers, light, moderate and heavy smokers were defined according to the cigarette consumption reported at the end of the interval (light=<15 cigarettes·day^{-1}; moderate=15–24 cigarettes·day^{-1}; heavy=25+ cigarettes·day^{-1}).

Each subject contributed up to seven pairs of FEV_1 measurements, and the data were expressed as the annual changes in FEV_1 (ΔFEV_1 ml·yr^{-1}) during the intervals. The subjects in the sample ranged from 15–75 yrs of age. Graphic analysis showed that the change in pulmonary function with age was not a linear function within the age range. Thus, a single equation does not completely describe pulmonary function change from adolescence to ageing subjects. SHERRILL *et al.* [15] have used nonparametric polynomial smoothing splines to describe lung function growth in children. This study used regression spline models [16, 17], which allow pulmonary function change to depend linearly on height, with age dependent intercepts and slopes. These methods provide a flexible family of nonlinear models, are fully parametric, and permit the use of familiar regression techniques for the assessment of covariates. The regression model for subject i at interval t can be written as:

$$E(\Delta FEV_{it}) = b_1 \times (\text{Height})_{it} + b_2 \times (\text{Age terms})_{it} + b_3 \times (\text{smoking variables})_{it} + b_4 \times (\text{area})_i$$

where $\Delta FEV_{it}=(FEV_{i,t+1} - FEV_{i,t})/(Age_{i,t+1} - Age_{i,t})$; b_1, b_2, b_3, and b_4 are the vectors of the coefficients for height, age, smoking and residential areas, respectively. The age knots were [15, 18, 20, 22, 25, 30, 50, 55, 60, 65, 70, 76]. A negative ΔFEV_{it} implies that pulmonary function declined during the interval. The b_3 represents the difference in the rate of decline in pulmonary function between smokers and the nonsmoking reference group. A negative b_3 implies that smokers had a greater rate of decline in pulmonary function than lifetime nonsmokers. The regression coefficients are estimated assuming independence among all observations. Then, robust variance estimates [18] were calculated for the estimated regression coefficients to accommodate repeated measures on subjects. Wald Chi-squared test was used to test the global difference in pulmonary function changes between lifetime nonsmokers and former/consistent smokers.

Results

The sample cohort consisted of 6,386 participants, aged 15–55 yrs at entry, of whom 3,294 (52%) were male and 3,092 (48%) were female. 3,147 men (96%) and 2,855 women (92%) had a satisfactory pulmonary function test at the initial visit. Of 3,080 men and 2,796 women who enrolled before the final visit, 2,417 men (78%) and 2,137 women (76%) had at least one complete follow-up, and contributed a total 16,900 pairs (men 55%; women 45%) of observations to the analysis. Table 1 presents sex-specific descriptive statistics on age, FEV_1 level and rate of decline by smoking status. Fewer men than women were lifetime nonsmokers (11% *versus* 45%). Age distribution varied with smoking status and is potentially an important confounding factor in the analysis of smoking effects. Smokers tend to have a greater rate of decline in FEV_1 than lifetime nonsmokers.

The effects of smoking were estimated by a piecewise quadratic spline model described in the Methods, with adjustment for age and height. Table 2 presents the effect estimates for those whose smoking status was constant during the interval, *i.e.* continued and former smokers. Estimated excess ΔFEV_1 for light, moderate and heavy continued smokers compared with those for lifetime nonsmokers was 4.4, 9.5 and 13.5 ml·yr^{-1} for men, and 6.1, 10.8 and 18.8 ml·yr^{-1} for women, respectively. Women former smokers had a significantly more rapid ΔFEV_1 than lifetime nonsmokers (4.4±1.6 ml·yr^{-1}); but among men, former smokers had a slower ΔFEV_1 than lifetime nonsmokers (4.1±2.3 ml·yr^{-1}). The effects of cigarette smoking on ΔFEV_1 appeared to be greater in women than in men in all smoking categories, despite the fact that women had smaller lungs than men. The overall gender difference among continued and former smokers was statistically significant (χ^2= 11.0; df=4; p=0.026) by Wald chi-squared test.

Table 1. – Descriptive statistics on age, FEV_1 level, and rate of decline in FEV_1 by smoking status and sex in subjects aged ≥25 yrs in the Vlagtwedde-Vlaardingen study

Smoking	Pairs n	Age yrs	FEV_1 *l*	ΔFEV_1 ml·yr^{-1}
Male				
Lifetime NS	1069	32 (11)	3.94 (0.66)	-5.8 (103.7)
Former	2099	45 (12)	3.46 (0.76)	-20.0 (81.9)
Pipe/cigar	400	44 (11)	3.37 (0.75)	-32.7 (82.9)
Continued cigs·day^{-1}				
Light	1172	39 (13)	3.45 (0.75)	-18.8 (95.1)
Moderate	2014	38 (11)	3.44 (0.71)	-26.3 (98.0)
Heavy	1293	38 (10)	3.49 (0.70)	-33.2 (91.1)
New	66	21 (10)	3.83 (0.69)	74.9 (172.9)
Recidivist	169	36 (11)	3.68 (0.77)	-28.6 (103.6)
Quitting	622	40 (13)	3.42 (0.81)	-6.1 (93.2)
Brief	38	29 (11)	3.75 (0.79)	-29.5 (108.2)
Inconsistent pipe/cigar	418	40 (11)	3.54 (0.72)	-29.6 (90.5)
Female				
Lifetime NS	3391	43 (12)	2.57 (0.49)	-14.8 (66.0)
Former	1066	42 (11)	2.71 (0.50)	-19.2 (68.7)
Continued cigs·day^{-1}				
Light	1300	35 (11)	2.78 (0.48)	-15.0 (75.5)
Moderate	696	35 (10)	2.76 (0.46)	-20.4 (69.4)
Heavy	296	38 (10)	2.66 (0.48)	-30.1 (67.9)
New	131	28 (11)	2.83 (0.49)	6.9 (75.1)
Recidivist	152	35 (10)	2.85 (0.49)	-19.7 (62.5)
Quitting	428	37 (11)	2.76 (0.47)	-2.7 (65.7)
Brief	80	37 (11)	2.78 (0.48)	-18.6 (65.4)

Data are presented as mean and SD in parenthesis. FEV_1: forced expiratory volume in one second; ΔFEV_1: annual change in FEV_1; NS: nonsmoker.

Table 2. – Sex-specific effects of smoking on decline of FEV_1 (ml·yr^{-1}); lifetime nonsmokers were the reference group

Category of smoker	Male		Female		Gender difference	
	Coeff	(SE)	Coeff	(SE)	Coeff	(SE)
Former	4.1	(2.3)	-4.4	(1.6)#	8.5	(2.8)#
Continued cigs·day^{-1}						
Light	-4.4	(2.8)	-6.1	(1.8)#	1.7	(3.3)
Moderate	-9.5	(2.5)#	-10.8	(2.2)#	1.2	(3.3)
Heavy	-13.5	(2.7)#	-18.8	(3.0)#	5.1	(4.0)

Coeff: coefficient. *: p<0.05; #: p<0.01. Test for gender difference: Wald Chi-squared=11.0; df=4; p=0.026. FEV_1: forced expiratory volume in one second.

Table 3 presents effects of smoking cessation on ΔFEV_1 during the interval between lung function tests. Among subjects who smoked an identical amount at the beginning of the interval, those who quit smoking during the interval had a slower ΔFEV_1 than those who continued smoking. The reduced declines among the quitters were, on average, 20.6±3.9 ml·yr^{-1} for men and 15.7±3.4 ml·yr^{-1} for women, and were significant for both sexes. Heavy smokers appeared to benefit more from smoking cessation than light smokers, especially women, in whom a 1.7 fold difference was noted; however, the difference between light and heavy smokers was not significant. When the quitters were divided into younger (<45 yrs) and older (≥45 yrs) groups,

Table 3. – Effects of smoking cessation on change of FEV_1 (ml·yr^{-1}), current smokers were the reference group

Subgroup of cohort	Male		Female	
	Coeff	(SE)	Coeff	(SE)
All	20.6	(3.9)#	15.7	(3.4)#
Smoking pattern				
Light	19.6	(5.1)#	13.8	(3.6)#
Heavy	21.8	(5.8)#	23.5	(8.7)#
Difference	-2.2	(7.7)	-9.8	(9.4)
Age				
<45 yrs	28.2	(5.3)#	20.0	(4.3)#
45+ yrs	10.4	(5.2)*	5.4	(4.5)
Difference	17.8	(7.3)*	14.7	(5.9)*

Coeff: coefficient; *: p<0.05; #: p<0.01. FEV_1: forced expiratory volume in one second.

Table 4. – Effects of smoking on decline of FEV_1 ($ml \cdot yr^{-1}$) among new, recidivist and brief; lifetime nonsmokers were the reference group

Smoking group	Male		Female	
	Coeff	(SE)	Coeff	(SE)
New	0.6	(11.0)	1.3	(5.7)
Recidivist	-13.5	(5.3)*	-8.7	(3.8)*
Brief	-28.5	(17.1)	-8.1	(7.2)

Coeff: coefficient; *: $p<0.05$; #: $p<0.01$. FEV_1: forced expiratory expiratory volume in one second.

younger smokers were seen to benefit more from smoking cessation than older smokers (2.7 fold for men and 3.7 fold for women). The difference between younger and older smokers was significant for both sexes.

Subjects who recently took up smoking were further grouped into new smokers, recidivist smokers and brief smokers. The values, 0 (lifetime nonsmokers), 1 (<15 cigarettes·day^{-1}), 2 (15–24 cigarettes·day^{-1}), and 3 (25+ cigarettes·day^{-1}), and were assigned to each smoking level, respectively, for new smokers and recidivists, and were then used in the regression analysis. As shown in table 4, new smokers had a comparable ΔFEV_1 with lifetime nonsmokers. The excess ΔFEV_1 for recidivist smokers was 13.5±5.3 ml·yr^{-1} in men and 8.7±3.8 ml·yr^{-1} in women, suggesting that recidivists may be subject to greater lung tissue damage than new smokers, due to previous sensitization. The brief smokers had a significantly increased ΔFEV_1 (14.9±7.4 ml·yr^{-1}) when the men and the women were pooled.

The effects of pipe/cigar smoking on lung function were estimated for men only, because no women in this sample were pipe/cigar smokers. The excess ΔFEV_1 for consistent and inconsistent pipe/cigar smokers was 8.2± 4.1 and 8.9±4.4 ml·yr^{-1} compared with those for lifetime nonsmokers, respectively.

Discussion

The results of this study are consistent with those from other longitudinal studies on smoking effects [1, 2], which show that continued cigarette smokers have a more rapid ΔFEV_1 than lifetime nonsmokers, and that the effect is dose-dependent. In addition, our study, with a large sample and 24 yr follow-up, provides a comprehensive and longitudinal assessment of gender differences in the effects of smoking on lung function. Our analyses suggest that female smokers overall tend to have faster ΔFEV_1 than male smokers. We have consistently observed such gender differences among former smokers and continued smokers.

The findings on gender differences are consistent with several earlier reports [9–13]. Beijing Respiratory Health Study [9] on 1,618 male and 1,669 female adults, aged 40–69 yrs found that female smokers suffered an additional loss of 26.2 (SEM=12.6) ml·m^2 and 37.4 (SEM=13.6) ml·m^2, respectively, for FEV_1 and FVC compared with male smokers, after adjusting for smoking year, smoking status, and other related confounding factors. A recent analysis of a random sample of 1,149 adults, 25–59 yrs of age, in a rural community in Saskatchewan, Canada, shows that FEV_1 and maximal mid-expiratory flow rate decreased and the slope of Phase III of the single breath nitrogen test ($\Delta N_2 \cdot l^{-1}$) increased with increasing pack-years more rapidly in women than in men [10]. The French Co-operative Study, PAARC, on 1,898 male and 1,345 female subjects, aged 40 yrs or more, indicated that the deficits in forced mid-expiratory flow (FEF_{25-75}) associated with smoking were greater in women than in men [11]. A 5 yr follow-up study on 7,764 men and women, aged 20 yrs and over, in Copenhagen showed that the effects of smoking on ΔFEV_1 were greater in women than in men both for heavy smokers and transitional smokers, and both for younger and older groups [12]. A three city study conducted in Montreal and Winnipeg, Canada, and Portland, Oregon suggested that the number of cigarette-years was significantly associated with a lower FEV_1/FVC among women, but not among men [13].

However, the findings from other studies [3–8] are inconsistent with these results. Reports from a random sample of 8,191 adults, between 25–74 yrs of age, in six US cities found that the estimated loss of FEV_1 level in cross-sectional analysis was 7.4 and 4.4 ml for each pack-year smoked, in men and in women, respectively, [3]. The longitudinal analysis of data collected during the 6 yr follow-up again indicates that the accelerated ΔFEV_1 associated with smoking was greater in men (12.6 ml·yr^{-1} per pack/day) than in women (7.2 ml·yr^{-1} per pack/day) [4]. Data from a random sample of 1,705 adults in Tucson, Arizona, suggest that observed-minus-expected declines in FEV_1 for smokers younger than 70 yrs of age were significantly greater in men than in women [5]. A study of residents, 25–64 yrs of age, from three communities in the Los Angeles area showed that adjusted mean deficit in FEV_1 was 320 ml for male continued smokers and 210 ml for female continued smokers, and the accelerated ΔFEV_1 was 14 ml·yr^{-1} for male smokers and 12 ml·yr^{-1} for female smokers [6]. A cross-sectional study on 3,289 inhabitants, aged 8–64 yrs, in Northern Italy found a significant difference in FVC, FEV_1, and FEF_{25-75} between lifetime nonsmokers and current smokers in men, but not in women [7]. More interestingly, when the data from the Copenhagen study were analysed by using different exclusion criteria in another report, the effects of smoking on ΔFEV_1 became greater in men [8], in contrast to the results discussed previously [12].

The findings of gender differences in smoking effects could have many bases, ranging from inherently different susceptibility and different smoking behaviour to environmental and occupational confounding factors. Another possibility is the incomparability of the reference group between men and women. Lifetime nonsmokers were always used as the reference group to estimate the effects of smoking on pulmonary function. Therefore, assuming no heterogeneity in airway responses to smoking across different populations and

genders, the reference values of lifetime nonsmokers would directly affect the estimates of smoking effects. Generally, there is a healthy-smoking effect in population-based studies; *i.e*. smokers were initially healthier on average than otherwise comparable people who never started to smoke. People who had cardiovascular disease, or respiratory diseases during early life are more likely to have a reduced level or increased decline in pulmonary function, and are also more likely to be lifetime nonsmokers than are initially healthy people. Given a relative fixed proportion of "unhealthy lifetime nonsmokers" in a population, the higher the prevalence of smoking, the higher the proportion of "unhealthy lifetime nonsmokers" among the lifetime nonsmoker referent group. Therefore, the reference value of pulmonary function will change with the prevalence rate of smoking; thus, implying that the comparison of smoking effects across different populations and between genders may be biased unless the comparisons are adjusted for smoking prevalence. Such incomparability in reference values for pulmonary function between the sexes will be most obvious when almost all the lifetime nonsmokers are "unhealthy lifetime nonsmokers" in one sex due to high smoking prevalence, whilst the majority of lifetime nonsmokers are "healthy life-time nonsmokers" in the other sex due to low smoking prevalence.

Our data and data published previously are consistent with this hypothesis. As seen in table 5, all the studies reporting greater smoking effects among women than among men had a low prevalence of male lifetime nonsmokers (11–25%). In contrast, studies reporting greater smoking effects among men than among women had a relatively higher prevalence of male lifetime nonsmokers (27–43%). Of note, the contrasting results in association of male lifetime nonsmoking prevalence with gender difference was even observed in the same study [8, 12]. The first report [8] from the Copenhagen 5 yr follow-up study indicated a greater smoking effect in women than in men when the prevalence of male lifetime nonsmokers was 15%. However, the second report [12] from the same study indicated a reverse gender difference in smoking effects when a different exclusion criteria was used, which led to a higher prevalence of male lifetime nonsmokers (43%). We therefore conclude that part of the observed gender difference in this longitudinal study was attributed to a varying proportion of unhealthy subjects between the sexes in the lifetime nonsmoker reference group.

Table 5. – Association of percentage of lifetime smokers in the samples with gender difference in smoking effects on level or decline of pulmonary function in various studies

Study [Reference]	Design	% Lifetime NS		Smoking effects
		Male	Female	
Six Cities [3]	CX	27	51	M > F
Six Cities [4]	LN	27	51	M > F
Tucson [5]	LN	28	42	M > F
Los Angeles [6]	LN	38	56	M > F
Northern Italy [7]	CX	32	66	M > F
Copenhagen [8]	LN	43	48	M > F
Beijing [9]	CX	22	65	M < F
Saskatchewan [10]	CX	25	46	M < F
Seven French cities [11]	CX	25	72	M < F
Copenhagen [12]	LN	15	31	M < F
Three Cities [13]	CX	19	40	M < F
Present	LN	11	45	M < F

NS: nonsmoker; LN: longitudinal study; CX: cross-sectional study; M: male; F: female.

Biological differences between men and women may also account for the significant gender differences observed here. Women have smaller lungs and larger airways than men of comparable size [19]. Since airway size may influence smoke distribution and lung size may be related to decline in lung function, mechanical factors may favour an increased sensitivity of females to cigarette smoke. Hormonal factors may also play a role. Animal studies suggest that female rats have a greater increase both in the number and size of goblet cells on exposure to cigarette smoke than male rats [20, 21]. Hormonal factors may also influence other aspects of epithelial cell function. These biological differences, as well as possible differences in inflammatory responses and the distribution of atopy and airway responsiveness, deserve further investigation.

Because of the huge difference in smoking prevalence between men and women in this study, we can expect that women would have had a much greater chance to be exposed to the passive smoking from their husbands than men from their wives. In addition, men smoked more cigarettes per day than women; therefore, the dose of exposure to passive smoking in wives should also be higher than that in husbands if both husband and wife were smokers. Thus, passive smoking may be one of the environmental factors which could reduce the apparent effect of active smoking among women. Unfortunately, the potential confounding effect of passive smoking could not be adjusted for in this report, because the study did not collect passive smoking information.

In addition, male lifetime nonsmokers appeared younger than male smokers, whilst female lifetime nonsmokers were older than female smokers, indicating an increasing trend for young women to take up smoking. The average age in male lifetime nonsmokers (32 yrs) was 10 yrs younger than that in female lifetime nonsmokers. Despite adjustment for age in the regression analysis, the contrasting age distribution in lifetime nonsmokers and smokers between two sexes may affect the observed gender difference in smoking effects on pulmonary function. The health records on physician-diagnosed cardiovascular and respiratory diseases may provide direct evidence for "unhealthy lifetime nonsmokers". However, such information was not available for the analysis.

Our study shows that quitters aged 15–45 yrs had greater recovery in FEV_1 than quitters aged 45 yrs and older. This age-dependent effect of smoking cessation confirms earlier work from the Tucson Study [5], and the Six Cities Study [4]. CAMILLI *et al*. [5] suggested

that the earliest effects of smoking should represent a bronchoconstrictive effect, which is reversible. In addition, older smokers are usually those who are less motivated to quit smoking; those highly motivated may have quit already. Therefore, the older quitters are more likely to include a greater proportion of "unhealthy quitters" who were forced to quit because of illness.

DOCKERY *et al*. [3] estimated the combined acute and cumulative effects of cigarette smoking on lung function levels. After accounting for total pack-years, they found that current smokers had lower levels of FEV_1 than ex-smokers. The deficits were in proportion to the number of cigarettes smoked each day; thus, suggesting that heavy smokers will regain their lung function to a greater extent after quitting than will light smokers. The finding from this study is consistent with the Six Cities study [3], in which heavy smoking quitters showed slower decline in lung function than light smoking quitters, especially among women. The opposite results were found in the Copenhagen longitudinal study [12], which may be due to failure to control for cumulative smoking.

Our study also shows a greater susceptibility to smoking in former smokers than in lifetime nonsmokers, which may be related to respiratory defence system damage by previous smoking or a sensitized immune response to smoking.

Few data are available on the effect of pipe and cigar smoking on rate of decline in pulmonary function [3, 8]. Cross-sectional analyses from the Six Cities Study showed that pipe/cigar smokers had pulmonary function levels similar to those of nonsmokers after adjustment for cigarette smoking [3]. A 5 yr follow-up study on 3,139 men and 4,986 women, aged 20 yrs and over, in Copenhagen found a significantly adverse effect of pipe and cigar smoking on the longitudinal decline in pulmonary function in inhaling smokers, but not in non-inhaling smokers [8]. Our results are consistent with this finding.

In summary, our analysis of the Vlagtwedde-Vlaardingen data suggest that females are more susceptible to cigarette smoking than males. Part of this effect is methodologically related to the prevalence of smoking in both genders, although biological differences, exposure to environmental tobacco smoking, and contrasting age distribution between lifetime nonsmokers and smokers may also contribute, and deserve further investigation. Recidivist smokers and pipe and cigar smokers were also at high risk in this analysis. Finally, our report also emphasizes the benefits of cessation, which was particularly apparent in younger and heavier smokers.

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