Rates of Decline in Lung Function Among Subjects Who Restart Cigarette Smoking

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Several studies have demonstrated that smokers who are able to break the habit generally experience reductions in respiratory symptoms and improvement in pulmonary function; however, far less attention has been given to smokers who are unsuccessful in their attempts at quitting. Recent reports have suggested that these subjects (restarters) may have steeper rates of decline in pulmonary function than subjects never attempting to quit smoking. In this study, we compared rates of decline in FEV\textsubscript{1} between restarters and subjects who remained current, ex-smokers, or never-smokers throughout the observation period. The results showed that, in both sexes, subjects who attempt to quit the habit and then restart have significantly steeper rates of decline in their FEV\textsubscript{1} than subjects who continue smoking uninterrupted. Female restarters also have significantly steeper rates of decline in FEV\textsubscript{1} than ex-smokers. These effects were independent of the amount smoked and respiratory diseases. (CHEST 1996; 109:1001-05)

Key words: epidemiology; longitudinal; pulmonary function; smoking cessation

Since the Surgeon General’s report on the harmful effects of cigarette smoking in 1964, there have been numerous scientific investigations detailing such effects and showing subsequent benefits of smoking cessation.\textsuperscript{1} With the assistance of educational and smoking cessation programs and the advent of nicotine substitutes, such as nicotine gum and epidermal patches, the number of adult smokers attempting to stop the habit has been increasing in the United States.\textsuperscript{2-4} Those smokers who are able to break the habit generally experience reductions in respiratory symptoms and improvement in pulmonary function, but sex differences and a strong association with age have been demonstrated.\textsuperscript{5-10} The adverse effects in smokers who are unsuccessful in their attempts at quitting smoking have received far less attention. Preliminary results from the “Lung Health Study” suggested that subjects who quit and restart smoking have steeper mean single year changes in percent predicted FEV\textsubscript{1} than subjects never attempting to quit smoking and those who were successful at quitting (Lung Health Study, communication).

To examine this association, we compared rates of decline in pulmonary function between restarters and subjects who remained current, ex-smokers, or never-smokers throughout the observation period. Subjects for this study were participants of the Tucson Epidemiology Study of Airways Obstructive Disease.\textsuperscript{11}

Materials and Methods

Study Population

Subjects were participants in the Tucson Epidemiological Study of Airways Obstructive Disease, aged 20 years and older. Detailed description of the study design and methods of data collection have been reported previously.\textsuperscript{11} Briefly, the population in this ongoing study is a random stratified cluster in Tucson, Ariz, starting with 3,905 individuals in 1,655 households, enrolled in 1972 to 1973, with new enrollees added by marriage and births.

Data were available for this analysis through the 12th survey, spanning a period of up to 20 years. Pulmonary function tests from 11 of the 12 surveys were included in the analysis. The fourth survey was excluded because pulmonary function testing was not done. Selected subjects had to have 5 years follow-up or at least three surveys with pulmonary function test to ensure sufficient follow-up for accurate slope estimates.\textsuperscript{12} In addition, to ensure that subjects in the different smoking categories had similar lengths of follow-up as restarters, consistent smokers, ex-smokers, and never-smokers were included in the analysis only if their duration of follow-up was within a selected interval, defined as the mean follow-up of restarters ±4 years (eg, 2.74 to 10.74 and 2.77 to 10.77 years, for male and female subjects, respectively). Ex-smokers were current smokers who were successful in stopping the habit. Since ex-smokers tended to be older than subjects in the other smoking categories, they were matched to ages of the restarters. Restarters were subjects who either entered the study as ex-smokers and later reported active smoking, or were active smokers who reported quitting on at least one survey, then again reported active smoking. Subjects who “flip-flopped” between categories were included only if they had a restart period that met the inclusion criteria. As a measure of total cigarette consumption, we computed the self-reported average of number of cigarettes per day smoked each sur-
very, termed the "usual number of cigarettes per day." Subjects also reported during each survey if they ever had respiratory symptoms or diseases for which they saw a physician (ie, was diagnosed by the physician as having asthma, emphysema, or chronic bronchitis).

### Pulmonary Function Testing

Spirometric tests were performed using American Thoracic Society criteria, using the same pneumotachograph in all surveys.\(^{13}\) Percent predicted values were calculated using our continuous prediction equation.\(^{14}\)

### Statistical Methods

In this report, we used the simple linear regression slope of the FEV\(_1\) with age as an estimate of the rate of decline in pulmonary function. FEV\(_1\) slopes for subjects who were consistent current or never-smokers (eg, never reported changing their smoking habit), and ex-smokers, were estimated using all available FEV\(_1\) observations, while for restarters only those FEV\(_1\) measures taken after restarting and while then continuing to smoke were used. This means that the restarters had to have either 5 years follow-up or at least three FEV\(_1\) measures after restarting. Comparisons between smoking categories were made using one-way analysis of variance, with Student-Newman-Keuls multiple comparisons, or unpaired Student's t test when only two groups were compared. All statistical tests were done at the \(\alpha=0.05\) significance level and \(p\) values greater than 0.05 and less than 0.1 were reported as borderline significant.

### RESULTS

There were 477 subjects who met the inclusion criteria of age older than 20 years, at least three FEV\(_1\) observations or 5 years' follow-up of FEV\(_1\) measurements, and duration of follow-up within the selected range. More female subjects (n=301) than male subjects (n=176) were included in the analyses, but the number of restarters was similar in each group (34 men and 37 women). Table 1 lists the number of subjects in each smoking category and the average of several baseline and final measures, stratified by sex and smoking status. Among male subjects, the mean percent predicted FEV\(_1\) (FEV\(_1\)%) values for restarters were higher, but not statistically significantly different compared with consistent smokers, although the FEV\(_1\) % means for both groups were significantly lower than those for never-smokers and ex-smokers. This was true for both the initial and last survey estimates. Male restarters also had significantly lower initial FEV\(_1\)/FVC ratios than never-smokers, but did not differ from ever-smokers. Female restarters differ from consistent smokers only in the number of pack-years of smoking, 42.9 vs 33.5, for consistent smokers and restarters, respectively. Their FEV\(_1\)% and FEV\(_1\)/FVC were between those of ex-smokers and consistent smokers. Female consistent smokers also had lower FEV\(_1\)% values than never-smokers and ex-smokers, both at the initial and last surveys.

The mean slopes for the different smoking categories by sex are listed in Table 2. Female restarters had significantly steeper rates of decline in FEV\(_1\) than consistent, ex-, and never-smokers. Male restarters also had steeper rates of decline in FEV\(_1\) than consistent and never-smokers, but did not differ significantly from ex-smokers. The difference between restarters and consistent smokers was larger for male than female subjects, 37 mL/yr and 25 mL/yr differences, respectively. To test if this increased rate of FEV\(_1\) loss was associated with the quantity of cigarettes smoked, we examined the mean slopes stratified by the usual number of cigarettes, with 20 cigarettes per day selected as the dividing point (Table 2). The mean slopes for restarters were statistically different than those estimated for consistent smokers who smoked at least 20 cigarettes per day. However, these differences were not statistically significant for subjects whose usual number of cigarettes per day was less than 20. The inability to demonstrate significant differences among those who smoked less than 19 cigarettes per day, as compared with those who smoked greater than

### Table 1—Baseline Characteristics and Duration of Follow-up*

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never-Smoker</td>
<td>Consistent Smoker</td>
</tr>
<tr>
<td>Cases</td>
<td></td>
</tr>
<tr>
<td>Initial age, yr</td>
<td>47.6±21.4</td>
</tr>
<tr>
<td>Initial FEV(_1)%</td>
<td>98.9±19.3</td>
</tr>
<tr>
<td>Last FEV(_1)%</td>
<td>103.7±22.5</td>
</tr>
<tr>
<td>FEV(_1)/FVC initial, %</td>
<td>79.8±6.9</td>
</tr>
<tr>
<td>Duration, yr</td>
<td>7.5±2.0</td>
</tr>
<tr>
<td>No. of observations</td>
<td>4.1±1.3</td>
</tr>
<tr>
<td>Pack-years</td>
<td>—</td>
</tr>
</tbody>
</table>

*Values are mean±SD. Initial mean values for age, FEV\(_1\), FEV\(_1\)% (percent prediction), and FEV\(_1\)/FVC were calculated at the first survey included in estimating FEV\(_1\) slope. For restarters this would correspond to the first observation in the restart period.

\(p<0.05\) significantly different from never and ex-smokers.

\(p<0.05\) significantly different from never-smokers.

\(p<0.05\) significantly different from restarters and ex-smokers.

\(p<0.05\) significantly different from consistent smoker.
20, reflects both the reduced sample size and the large amount of scatter in the slope estimates.

To examine the influence of subjects with respiratory diseases, we also ran the analysis excluding subjects with asthma (physician diagnosed) or emphysema. After excluding subjects with emphysema (n=51), the restarters still had statistically significantly steeper rates of decline in FEV₁ than consistent smokers; and for female subjects, greater than ex-smokers, with magnitudes that were similar to those from analyses including emphysema patients (Table 2). Male restarters did not differ significantly from ex-smokers, even after removing subjects with emphysema. Removal of asthmatics (n=61) yielded similar results.

The relationships between smoking categories are illustrated in Figure 1 for a hypothetical male reverter (using slope estimates from Table 2). This plot demonstrates how FEV₁ starts to improve following cessation, but then exhibits a "catch up" period after restarting smoking, and will even drop below the level of consistent smokers for this particular individual.

The calculation of FEV₁ slope estimates for restarters included only the FEV₁ observations after the subjects reported restarting the habit. We verified the importance of only including observations after restarting the habit by repeating the analysis, including all of the available FEV₁ observations for each subject (Table 2, Restart [all]). For some restarters, this meant including values during periods of active smoking and nonsmoking, while for others, it meant including values from a period of nonsmoking (ie, those who were ex-smokers at the first survey). Comparisons between these new slope estimates showed no significant differences between rates of decline in FEV₁ between restarters and consistent smokers.

To compare the respiratory status between restarters and consistent and ex-smokers, we examined symptoms reported at the initial and last surveys. The symptoms included any wheeze, cough, dyspnea, or phlegm. There were no statistically significant differences in the reported initial symptoms between restarters and consistent smokers; however, consistent smokers did report significantly more dyspnea during the last survey, 62% vs 35% in restarters (p<0.05 χ²). Similar rates were also found in female subjects. Comparing female restarters with ex-smokers, there were no significant differences between reported symptoms, either initially or at the last survey. In contrast, male restarters initially reported more cough than ex-smokers (53% vs 19%, respectively), and in the last survey more phlegm (47% vs 15%) than ex-smokers (p<0.05 χ²).

**Discussion**

In this report, we have demonstrated that subjects
who attempt to quit smoking, then start again, have more rapidly declining FEV\textsubscript{1} than continuously smoking and ex-smoking subjects, when one only considers the observations after restarting. This result was independent of level of initial and final function and of effects due to asthma and emphysema (as demonstrated by excluding these subjects in separate analyses). The results of stratifying on “usual number of cigarettes” were statistically significant for subjects who smoked more than 20 cigarettes per day, but not significant for those who smoked less than 20 cigarettes per day. In all strata, the magnitude of the slope differences was similar to those found in the unstratified analyses; however, the SEs were larger because of the reduced sample sizes, particularly for restarters.

These findings have two likely implications; one would be that individuals who attempt to quit the habit, then restart, have increased their susceptibility during the cessation period, perhaps related to immunologic changes. This interpretation is supported by recent findings showing transient increases in total serum IgE level immediately following smoking cessation. The second would be that by selecting those individuals who are attempting to quit the habit, we have defined a group of smokers who initially had an increased sensitivity to tobacco. Although restarters did not differ significantly from consistent smokers in their initial levels of percent predicted FEV\textsubscript{1} or prevalence of respiratory symptoms, neither of these would be considered a perfect surrogate for sensitivity. In addition, the rates of decline in FEV\textsubscript{1} in consistent smokers do not differ significantly from those of never-smokers (Table 2), suggesting that individuals who are cigarette tolerant are less likely to attempt quitting the habit, which supports the latter theory/hypothesis.

The fact that there was no significant difference in mean FEV\textsubscript{1} slopes between restarters and continuous smokers when all observations for restarters were used to calculate the slopes suggests that the more harmful effects are related to actual restarting, and that subjects who were unsuccessful at stopping the habit were no worse off initially than those continuing to smoke. This is also evident in the percent predicted FEV\textsubscript{1} in which enrollment FEV\textsubscript{1} % and FEV\textsubscript{1}/FVC, in male and female subjects did not differ significantly between restarters and those continuing to smoke (Table 2).

The importance of using FEV\textsubscript{1} slope estimates to demonstrate the impact of restarting the habit can be illustrated also by examining the initial and last FEV\textsubscript{1} % values for restarters (Table 1), where for either sex there were no significant differences. The explanation for this apparent discrepancy is as follows; even though FEV\textsubscript{1} in restarters is declining at a faster rate than in consistent smokers (Figure 1), the duration of follow-up is not long enough to completely offset the beneficial effects of cessation. Therefore, if the analysis were done using only initial and final FEV\textsubscript{1} % values, no effect would be detected.

After stratifying subjects by their usual number of cigarettes (Table 2), the mean slope of FEV\textsubscript{1} for male consistent smokers was much lower than expected. Inspection of the slope distribution for this subgroup revealed three subjects who actually had high positive slope estimates (>100 mL/yr). Inspection of these individuals’ raw data did not yield any outlying values or errors in the slope calculations. Thus, we could not justify removing them from subsequent analysis. However, to assess their influence on our conclusions, we reran the analysis of variance of FEV\textsubscript{1} slopes, excluding their data. Although the new mean slope for male consistent smokers was less (−34 mL/yr compared with −19 mL/yr), as expected, it was still statistically significantly different than that of restarters.

The results of the analysis of symptoms at initial and last surveys would suggest that even though restarters have the steepest rates of decline in FEV\textsubscript{1}, they are less symptomatic than consistent smokers, who reported significantly more dyspnea at the last survey. (Excessive initial symptoms not included in the questionnaire may have been a motivation for temporary cessation.) Results may indeed reflect that despite the lower rates of decline in FEV\textsubscript{1}, consistent smokers are experiencing more respiratory side effects than restarters. It could also result from a reporting bias in which subjects who restart may be less likely to admit to symptoms that resulted from their inability to quit the habit. However, they did report more phlegm than ex-smokers in the last survey.

Male ex-smokers being more symptomatic than re-
starters indicates that this subgroup (ex-smokers) contains subjects who quit the habit after developing symptoms that for the most part were not reversible. This is also supported by the fact that male ex-smokers’ mean FEV₁ slope did not differ significantly from that of restarters.

In a recent report, Xu et al. investigated the rate of decline in FEV₁ in relation to smoking in 4,554 participants from the Netherlands, found that restarted had more rapid rates of decline than new starters. The excess change in FEV₁ was 13.5 mL/yr in men and 8.7 mL/yr in women. Based on this result, they suggested that the restarters may be subject to greater lung tissue damage than new smokers, due to previous sensitization. Their restarters (n=321) had slope estimates of -28.6 mL/yr and -19.7 mL/yr for male and female subjects, respectively, which are less than the slopes of our restarters (Table 2). For male restarters, their slope estimate was greater than we found in moderate smokers (-26.3 mL/yr), but not as steep as that for heavy smokers (-33.2 mL/yr). For female restarters, their FEV₁ slope was greater than we found for light smokers (-15.0 mL/yr), but less than that for moderate or heavy smokers.

In summary, we have demonstrated that subjects who attempt to quit the smoking habit, and then restart, have significantly steeper rates of decline in their FEV₁ than subjects who continue smoking uninterrupted, when one only considers the observations after restarting. For female subjects, restarters also have significantly steeper rates of decline than ex-smokers. These effects were independent of the amount smoked, respiratory diseases, and sex, and stress the importance of convincing quitters not to restart the habit.

REFERENCES


