Has Risk Associated with Smoking Increased? Results from the Copenhagen Center for Prospective Population Studies

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Background. Two recent much cited publications have raised the concern that risk associated with cigarette smoking has so far been underestimated. In this study we wish to determine whether excess all-cause mortality associated with smoking has increased during the last 20–30 years in a study population representative of the general Danish population and whether any such changes relate to changes in smoking behaviour.

Methods. Pooled data from three prospective population studies conducted in Copenhagen with detailed information on smoking habits. A total of 31 194 subjects, 17 669 males and 13 525 females, initially examined between 1964 and 1992 with examinations repeated at intervals from 1–10 years, were followed until 1995 for all-cause mortality. Relative mortality risk in smokers versus never-smokers was calculated within periods of five calendar years and compared throughout the study period.

Results. Male smokers’ exposure did not change during the study period whereas female smokers’ exposure to tobacco increased in terms of age at smoking onset, quantity smoked and depth of inhalation. During follow-up 5744 males and 2900 females died. In males, death rate ratios (comparing continuous smokers with never-smokers) did not change in the study period. In females, ratios increased from 1964–1978 to 1979–1994 by a factor of 1.3 (95% confidence interval 1.0–1.8).

Conclusions. In agreement with the observed changes in smoking habits, excess mortality in male smokers did not increase whereas excess mortality in female smokers increased slightly.

Keywords: mortality, methods, prospective study, women, time trend

The often-cited study on male British doctors followed for 40 years demonstrated that the excess mortality associated with smoking had doubled between 1951 and 1971 and 1971 and 1991 and it was concluded that the hazards of long-term use of tobacco have been underestimated.¹ It was suggested that this was caused by changes in smoking habits during the study period with smokers having a more intensive exposure to the harmful contents of tobacco smoke in the second half of the study: e.g. through higher consumption and younger age at smoking onset. Similar results were reported in a prospective study from the American Cancer Society² but it is not clear whether these findings can be extrapolated to the general population.

Based on data from three longitudinal population studies conducted in Copenhagen, this study aims to determine whether excess mortality associated with smoking has increased during the last 20–30 years in a study population representative of the general Danish
population and whether any such changes relate to changes in smoking behaviour.

METHODS
The study is based on pooled data from three longitudinal population studies conducted in the Copenhagen area: the Copenhagen City Heart Study (CCHS), the Glostrup Population Studies (GPS) and the Copenhagen Male Study (CMS), which have all been described in detail previously.3–6 The combined study population consisted of 31 194 subjects, 17 669 males and 13 525 females. Most subjects were recruited in the 1970s (first examination between 1964 and 1992) and examinations were repeated at intervals of 1–10 years. Mean response rate was 77% (range 69–88%). Subjects were followed until the end of 1994 for all-cause mortality by record linkage with the central death register. The only possible loss to follow-up was through emigration (less than 0.5%).

Statistical Analysis
Subjects were examined repeatedly and contributed person-years of observation to the smoking category in which they had most recently described themselves. Thus, a subject who reported changing his or her smoking habits during follow-up contributed person-years to several smoking categories.

Each subject’s person-years of observation from study entry until death or censoring were split into several observations by expanding data by 5-year bands of calendar time and 5-year bands of age using a Lexis-programme.7 Time trends in risk associated with smoking were thereafter analysed in a Poisson regression model for each gender separately assuming equal effect of age (categorical in 5-year age-bands) and study population (five study groups, that differed in adjusted level of mortality) over the six calendar periods under study. The model was:

\[
\log(\text{hazard rate}) = \alpha + p_2 \text{period}_{69-74} + p_3 \text{period}_{74-79} + \ldots + p_6 \text{period}_{89-94} + z_1 \text{period}_{64-69, smoker} + z_2 \text{period}_{69-74, smoker} + \ldots + z_6 \text{period}_{89-94, smoker} + a_2 \text{ageband}_{25-30} + a_3 \text{ageband}_{30-35} + \ldots + a_{16} \text{ageband}_{95+} + c_2 \text{studynop}_{2} + c_3 \text{studynop}_{3} + \ldots + c_5 \text{studynop}_{5}.
\]

The parameter \(\alpha\) describes baseline hazard rate (i.e. the hazard rate for never-smokers in the period 1964–1969, younger than 25 belonging to study population 1), \(p_2-6\) parameter estimates for never-smokers in the corresponding 5-year period, \(z_1-6\) parameter estimates for smokers in the corresponding 5-year period, and \(a_{2-16}\) and \(c_{2-6}\), respectively, effects of age and study population. In this model, time trends in smokers’ excess risk can be analysed without assumptions regarding baseline mortality rates of never-smokers. For each gender it was tested whether period estimates for smokers (\(z_1-6\)) was adequately described by a linear function. All statistical analyses were performed using the Stata Statistical package.8

RESULTS
To illustrate the changes in smoking that have taken place during the study period, results from two examinations 15 years apart (in 1977 and 1992) in the largest study (CCHS) are shown in Table 1. Adjusted for age, the average female smoker in 1992 was more exposed to tobacco than in 1977 in terms of depth of inhalation, age at smoking onset and quantity smoked daily, whereas the average male smokers’ exposure remained almost unchanged. Changes in smoking habits were similar in the two other studies.

During follow-up 5744 males and 2900 females died. Adjusted relative mortality risk for smokers versus never-smokers within 5-year calendar periods and 95% confidence interval are depicted in Figures 1 and 2. In both males and females mortality risk in smokers was approximately twice that of never-smokers. In both genders time trends were adequately described by a linear function with a slope that did not differ significantly from zero. In other words, neither males nor females showed any significant time trend in the excess risk associated with smoking from 1964 to 1994. However, when the study period was split into two periods of equal length (analogous to the analyses by Doll et al.1) with cutoff point in 1979, the excess risk in female smokers compared to never-smokers was higher in the second period by a factor of 1.3 (95% confidence interval 1.0–1.8). For males, excess risk for smokers in the two study periods did not differ (RR 1.1 [0.8–1.5]).

To decide whether time trends differed with socio-economic status, data were stratified by three levels of school education. The results from these analyses did not differ from the ones given above (results not shown).

DISCUSSION
Based on a large population study representative of the general population of Copenhagen with a high prevalence of smoking throughout the study period, we found no temporal trend in excess mortality for male smokers from 1964 to 1994 and only a small increase in excess mortality for female smokers.

In the study on male British doctors, excess mortality among smokers increased between 1951 and 1971 and 1971 and 1991. Cigarette smokers were studied as one
group without adjustment for changes in the distribution of light versus heavy smokers, inhalation habits or for duration of smoking. It was thought that the relatively increased risk in smokers was caused by a ‘maturing of the epidemic’; that males who reached middle and old age in the second half of the study period had started smoking at a younger age and perhaps smoked differently than males who reached middle and old age in the first part of the study period. Similar results were reported in an American study.2

In the present study, where we primarily describe changes from the early 1970s to late 1980s, excess

### Table 1

**Smoking characteristics in the Copenhagen City Heart Study (CCHS) in 1977 and 1992 by gender and age (changes in the other two studies were similar)**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Women</th>
<th></th>
<th></th>
<th>Men</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;45</td>
<td>45–60</td>
<td>&gt;60</td>
<td></td>
<td>45–60</td>
<td>&gt;60</td>
</tr>
<tr>
<td>1977</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 1898</td>
<td></td>
<td></td>
<td></td>
<td>n = 1696</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex-smokers %</td>
<td>13</td>
<td>14</td>
<td>17</td>
<td>14</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>Current smokers %</td>
<td>62</td>
<td>62</td>
<td>47</td>
<td>69</td>
<td>74</td>
<td>65</td>
</tr>
<tr>
<td>Heavy smokers (%&gt;15 g/day)*</td>
<td>54</td>
<td>47</td>
<td>38</td>
<td>70</td>
<td>69</td>
<td>57</td>
</tr>
<tr>
<td>Age at debut (years) (SD)</td>
<td>19.4 (4.8)</td>
<td>24.2 (8.5)</td>
<td>32.3 (12.8)</td>
<td>17.3 (4.4)</td>
<td>18.0 (6.2)</td>
<td>19.4 (8.7)</td>
</tr>
<tr>
<td>Percentage inhaling*</td>
<td>88</td>
<td>73</td>
<td>41</td>
<td>95</td>
<td>84</td>
<td>58</td>
</tr>
<tr>
<td>1992</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 1120</td>
<td></td>
<td></td>
<td></td>
<td>n = 968</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex-smokers %</td>
<td>21</td>
<td>18</td>
<td>27</td>
<td>20</td>
<td>24</td>
<td>38</td>
</tr>
<tr>
<td>Current smokers %</td>
<td>46</td>
<td>53</td>
<td>40</td>
<td>46</td>
<td>57</td>
<td>51</td>
</tr>
<tr>
<td>Heavy smokers (%&gt;15 g/day)*</td>
<td>55</td>
<td>65</td>
<td>43</td>
<td>63</td>
<td>77</td>
<td>61</td>
</tr>
<tr>
<td>Age at debut (years) (SD)</td>
<td>17.1 (3.8)</td>
<td>20.3 (7.0)</td>
<td>24.4 (10.5)</td>
<td>16.9 (4.2)</td>
<td>17.6 (5.9)</td>
<td>18.2 (8.0)</td>
</tr>
<tr>
<td>Percentage inhaling*</td>
<td>95</td>
<td>86</td>
<td>65</td>
<td>95</td>
<td>86</td>
<td>75</td>
</tr>
</tbody>
</table>

* Including only current smokers.

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**Figure 1** Mortality ratio for male smokers versus never-smokers by calendar period (dotted line is 95% confidence interval)
mortality in male smokers did not increase. This could be because the epidemic had already ‘matured’ in Danish males—reflected in the fact that the average male smokers’ exposure to tobacco did not change from 1977 to 1992—and thus the studies may not be directly comparable. However, another explanation is also possible. In the American and, perhaps especially, the British study population, a large number of subjects had quit smoking and changed their general lifestyle in a beneficial direction. The remaining smokers constituted a diminishing proportion of the study populations (only 7% of the British doctors were smokers in 1991) and were probably also characterized by more adverse health behaviour, more stress, poor social network etc. factors that are all independently related to mortality. In other words, the attrition rate among smokers in the British doctors’ study may lead to the accumulation of a selectively unhealthy smoking population which is not the case in a population such as the Danish. The same time trend was evidently not seen in Danish males representative of the general population where the prevalence of smoking remained high throughout the study period.

For females the picture was different. The average female smoker in 1992 smoked more and started smoking at a younger age than in 1977, and a small but significant increase in excess mortality in smokers in the last part of the study period was found, reflecting a ‘maturation’ of the epidemic of smoking related diseases for females.

In conclusion, we naturally do not question the fact that the smoking epidemic will change with evolution in smoking patterns. In the present study, the risk associated with smoking for females increased in accordance with the demonstrated changes in female smoking habits. However, we wish to point out that smoking habits among male smokers representative of the general population may in fact have changed very little in the past few decades, that risk associated with smoking has not changed, and that choice of study population is very important.

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REFERENCES


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