High Cumulative Risk of Lung Cancer Death among Smokers and Nonsmokers in Central and Eastern Europe

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The authors have calculated cumulative risks of lung cancer from a case-control study conducted between 1998 and 2002 involving 2,633 lung cancer cases and 2,884 controls in Hungary, Poland, the Czech Republic, Slovakia, Romania, and Russia. The odds ratios for smoking history were combined with national lung cancer mortality rates to obtain the cumulative risk of lung cancer. The cumulative risk of death from lung cancer by the age of 75 years among current male smokers was 14.6% in Romania and Russia and 15.8% in Poland, similar to levels reported in Western Europe, although higher risks were found in the Czech Republic (19.8%), Hungary (21.9%), and Slovakia (28.2%). Cumulative risks of lung cancer death among never smokers of over 1% were observed in Hungary among both men and women and among men in Poland. The effect of quitting smoking on the lifetime cumulative risk was substantial, with between 67% and 83% of lung cancer risk among men being avoided by quitting before the age of 50 years. This substantial reduction in risk among former smokers confirms that lung cancer mortality in Central Europe over the next three decades will be determined by the extent to which current smokers can successfully quit smoking.

case-control studies; Europe, Eastern; lung neoplasms; mortality; risk; smoking

Very high lung cancer mortality rates have been observed in Central Europe over the last decade, with cumulative risks among men by the age of 75 years in the region of 10 percent in several countries including Hungary, Poland, Russia, and the Czech Republic (figure 1) (1). These risks are similar to the peak cumulative risks observed in the United Kingdom during the 1960s and 1970s, and they far exceed the peak rates observed in the United States. Indeed,

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the current national lung cancer mortality rate in Hungary represents the highest ever observed in a national setting.

Measures of the effect of tobacco on lung cancer among smokers relative to nonsmokers are not informative regarding their role in the high mortality rates and, in order to understand the role of tobacco in causing the lung cancer epidemic in Central Europe, absolute risks of lung cancer by smoking habit are essential. Obtaining an accurate measure of the absolute risk of lung cancer for different smoking habits typically requires information on large cohorts with extensive baseline information on smoking and long-term follow-up. An alternative and more efficient approach is to combine estimates of risk ratios from case-control studies with national incidence or mortality data. In a recent example of this approach in southwest England, the cumulative risk of death from lung cancer by age 75 years among lifetime smokers in the United Kingdom was estimated at 15.9 percent for men and 9 percent for women, rising to 24.4 percent among men and 18.5 percent among women for lifetime smokers who reported smoking at least 25 cigarettes per day (2). Moreover, the benefit of quitting smoking at various ages was demonstrated with cumulative risks of lung cancer death of 10 percent, 6 percent, 3 percent, and 2 percent for men who stopped smoking at ages 60, 50, 40, and 30 years, respectively. The cumulative risk of lung cancer death among never smokers was estimated at 0.2 percent, slightly less than estimates obtained from several large cohort studies including the American Cancer Society cohort of over one million Americans, which suggests a cumulative risk of 0.44 percent for men and 0.42 percent for women (3). In the absence of other cofactors, one would expect similar levels of cumulative risk among men in other countries where the male lung cancer epidemic has matured, such as in Central Europe.

Using a large multicenter case-control study of lung cancer in Central Europe, we have investigated whether the higher overall lung cancer mortality rates in this region are due to higher cumulative risks of lung cancer death in lifetime smokers, implicating the presence of other lung carcinogens. We also aimed to provide measures of the reduction in cumulative risk for smokers who quit smoking in these countries.

**MATERIALS AND METHODS**

The analysis is based on a case-control study that was conducted according to an identical protocol in 15 centers in Romania, Hungary, Poland, Russia, Slovakia, and the Czech Republic. In each center, cases included subjects with histologically confirmed lung cancer who were living in the study areas for at least 1 year and who were interviewed within 3 months of diagnosis between 1998 and 2002. Controls were frequency matched by age (±3 years), sex, and
study area. Hospital controls were included in 14 of the study areas from an extensive list of nonneoplastic, non- 
tobacco-related diseases, with no more than 10 percent of 
controls coming from any particular diagnostic group. Pop-
ulation controls were recruited in one center (Warsaw) by 
randomly selecting age- and sex-matched subjects from the 
electronic register of Polish residents.

A total of 2,893 cases and 3,161 controls satisfied initial 
eligibility criteria and were requested to participate in the 
study. Of the eligible cases, 260 (9.0 percent) were not in-
cluded in the study (27 had been discharged from hospitals 
before the interview, 26 were too ill to be interviewed, six 
had died before the interview, and 201 refused to partici-
)pate). In addition, 277 (8.8 percent) eligible controls were 
not included in the study (16 had been discharged from the 
hospital before the interview, 20 were too ill to be inter-
viewed, 239 refused to participate, and two were excluded 
before analyses because of missing data). The final study 
population included in analyses comprised 2,633 cases and 
2,884 controls. Further details of the study areas have been 
reported elsewhere (4–7).

A lifestyle questionnaire to elicit information on basic 
demographic characteristics, outdoor air pollution, medical 
history of occupational diseases, family history of cancer, 
history of tobacco consumption, passive smoke exposure, 
and other potential lung cancer carcinogens was adminis-
tered by trained interviewers. All subjects who had regularly 
smoked at least one cigarette per day for at least 1 year 
were considered ever smokers. Current smokers were those who 
still smoked at the time of interview or who had quit less 
than 2 years previously, while former smokers were those 
who had quit smoking 2 or more years previously. When 
information on different time periods was available for cur-
rent smokers, the most recent number of cigarettes smoked 
was used. Information on other tobacco-smoking products 
was also included after weighting for the amount of tobacco 
(1 g of pipe tobacco = one cigarette, one cigarillo = two 
cigarettes, one cigar = four cigarettes, and one papyroso 
(unfiltered cigarette) = 0.7 cigarette).

Country-specific relative risks of lung cancer were esti-
mated separately for men and women by means of odds 
ratios and 95 percent confidence intervals by use of uncondi-
tional logistic regression (8) and adjustment for age and 
center. Smoking categories were introduced as dummy var-
iables, and odds ratios were estimated for each smoking 
category compared with never smokers.

The cumulative risks were estimated by multiplying the 
relative risks for different smoking categories by a unique 
common factor, calculated so that the combination of these 
risks with the prevalence of smoking habits among study 
controls resulted in the age-specific cancer incidence rate in 
each country for that age group (refer to the Appendix for 
further details on these calculations). Our assumption was 
that within each age group the smoking distribution of each 
national population was represented by our control distribu-
tion. Finally, we calculated the cumulative rate (C) for the 
different categories of smoking by adding age-specific ab-
solute rates (in 5-year age groups) and then the lifetime 
cumulative risk by age 75 years using the standard formula 

$$100(1 - \exp(-5 \times C/10^5))$$

(9). The cumulative risk may be interpreted as the probability that an individual will die from lung cancer before the age of 75 years in the absence of competing causes of death; 95 percent confidence intervals for odds ratios and cumulative risks were calculated by use of floating absolute risks to obtain the variance of the log-

arithm of the odds ratio (var(log r)) (10) and subsequently 
incorporating a Taylor series expansion. The method of floating absolute risks leads to confidence intervals that 
are approximately independent and are therefore readily 
interpreted (11). As accurate, age-specific lung cancer in-
cidence data are not available from the majority of the par-
ticipating countries, we used national lung cancer mortality 
figures instead. Our cumulative estimates should therefore 
be interpreted as the lifetime risk of death from lung cancer. 
Given that 5-year relative survival from lung cancer is gen-

erally less than 10 percent (12), the cumulative risk of de-
volving lung cancer may be up to 10 percent higher than 
our calculated figures. Sampling variations in smoking prev-
alone estimates are also not included in the calculation of 
the confidence intervals, resulting in intervals that may be 
somewhat too narrow. The extent of this underestimation 
is likely to be inversely related to the size of the control group 
and is therefore more of a concern for the calculations of 
cumulative risk among women.

RESULTS

The country-specific odds ratios and floating 95 percent 
confidence intervals for never, former, and current smokers 
among men and women are shown in table 1. Cumulative 
risks of lung cancer among never smokers were generally 
higher than the risks estimated for men and women in the 
United Kingdom of 0.2 percent and 0.4 percent, respec-
tively. Among men, high cumulative risks of 0.7 percent 
(95 percent confidence interval: 0.1, 1.4), 0.9 percent (95 
percent confidence interval: 0.3, 1.5), 1.1 percent (95 
percent confidence interval: 0.4, 1.7), and 1.1 percent (95 
percent confidence interval: 0.3, 1.9) were observed in the 
Czech Republic, Russia, Poland, and Hungary, respectively. 
Among women, a particularly high cumulative risk of 1.2 
percent (95 percent confidence interval: 0.9, 1.5) was ob-
erved in Hungary. For current male smokers, the cumula-
itive risk of death from lung cancer was 14.6 percent (95 
percent confidence interval: 8.9, 19.9) in Romania, 14.6 
percent (95 percent confidence interval: 12.4, 16.6) in Rus-

sia, and 15.8 percent (95 percent confidence interval: 13.2, 
18.2) in Poland, similar to levels reported in the United 
Kingdom, although these risks of 19.8 percent (95 percent 
confidence interval: 14.9, 24.5), 21.9 percent (95 percent 
confidence interval: 16.8, 26.6), and 28.2 percent (95 
percent confidence interval: 21.7, 34.0) were higher in the 
Czech Republic, Hungary, and Slovakia, respectively. The 
cumulative risk among heavy smokers was particularly 
high, reaching over 40 percent (95 percent confidence in-

terval: 32.8, 48.6) among men in the Czech Republic. 
Among women, cumulative risks among current smokers 
were less than 10 percent in all countries with the exception 
of Hungary, where they were 13.2 percent (95 percent con-
fidence interval: 6.2, 19.7). As expected, cumulative risks
among former smokers were intermediate for both men and women.

The effect of quitting on the cumulative risk of lung cancer death was analyzed further among men after stratification on the age at quitting and calculation of age-specific cumulative risk for each category of smoking (given the small number of female former smokers, cumulative risk estimates among women for different ages at quitting tended to be unstable and are not presented). A strong decreasing trend in the cumulative risk was observed with an earlier age at quitting smoking in all six countries (figure 2). The cumulative risk of lung cancer death ranged between 5.1 percent and 12.0 percent for those who quit smoking at the ages of 50–59 years, between 3.5 percent and 7.4 percent for those who quit at the ages of 40–49 years, and between 1.0 percent and 3.0 percent for those who quit before the age of 40 years. Furthermore, based on estimates of cumulative risk from figure 2, the proportion of excess cumulative risk of lung cancer death, compared with never smokers, that was avoided by quitting smoking at age 40 years was over 90 percent in all six countries, ranging between 67 percent in Russia and 84 percent in Poland for those who quit between 40 and 49 years and between 38.4 percent in Poland and 67.9 percent in Romania for those who quit between the ages of 50 and 59 years.

The cumulative risks for male current smokers according to the number of cigarettes smoked per day are presented in table 2. With the exception of Romania, extremely high cumulative risks were observed for those who smoked more than 30 cigarettes/day, ranging from 27 percent in Hungary to 41.2 percent in the Czech Republic. The reduced cumulative risk in Romania is likely explained by the small numbers of cases and controls who smoked more than 30 cigarettes/day.

**DISCUSSION**

Based on an analysis similar to that reported here, the lifetime risk of death from lung cancer among male never smokers was high, but...
former, and current smokers in the United Kingdom was calculated as 0.2 percent, 5.5 percent, and 15.9 percent, respectively, reaching 24.4 percent among heavy smokers (>5 cigarettes/day) (1). Corresponding estimates for women were 0.4 percent, 2.6 percent, and 9.5 percent, respectively, reaching 18.5 percent among current heavy smokers. These risks were substantially higher than corresponding risks calculated from a case-control study conducted in the United Kingdom in 1950, reflecting the fact that current smokers in 1990 were likely to have started smoking in their teens or early 20s, which was not the case for the majority of current smokers in earlier periods. Similarly, the higher lung cancer cumulative risks among men as opposed to women were thought likely to be due to a greater proportion of women who started smoking at a later age.

The primary aim of the current analysis was to determine whether the cumulative risks of developing lung cancer for various groups of smokers in Central European countries are similar to those previously reported for other countries where cigarette smoking habits have been established for several decades. Overall, the cumulative risks among never smokers appeared to be higher than those previously reported, particularly in Hungary, with only men in Slovakia and women in Poland providing estimates...
consistent with those in the United Kingdom and the United States. Regarding current smokers, cumulative risks among men in Romania, Russia, and Poland were similar to those observed in the United Kingdom and the United States, although they were substantially higher in the Czech Republic, Hungary, and Slovakia. Cumulative risks among women current smokers were generally low in all countries except Hungary.

Similar lifetime cumulative risks have also been estimated from large case-control studies of lung cancer for male smokers in Italy (14.3 percent) and Germany (13.8 percent), although they were somewhat lower in Sweden.

TABLE 2. Odds ratios and cumulative risks of death from lung cancer by age 75 years among men who were current cigarette smokers, stratified by amount smoked per day (most recent estimate), by Central European country, 1998–2002

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases/controls (no.)</th>
<th>Odds ratio*</th>
<th>Floating 95% confidence interval</th>
<th>Cumulative risk</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romania</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>4/50</td>
<td>1.0</td>
<td>0.4, 2.8</td>
<td>0.6</td>
<td>0.01, 1.3</td>
</tr>
<tr>
<td>&lt;10/day</td>
<td>10/9</td>
<td>19.5</td>
<td>7.6, 50.0</td>
<td>11.1</td>
<td>11.2, 17.5</td>
</tr>
<tr>
<td>10–19/day</td>
<td>54/38</td>
<td>25.7</td>
<td>16.6, 39.8</td>
<td>14.4</td>
<td>11.2, 17.5</td>
</tr>
<tr>
<td>20–29/day</td>
<td>37/15</td>
<td>51.7</td>
<td>25.8, 103.8</td>
<td>26.9</td>
<td>19.8, 33.3</td>
</tr>
<tr>
<td>≥30/day</td>
<td>9/8</td>
<td>20.6</td>
<td>7.6, 55.4</td>
<td>11.7</td>
<td>7.6, 15.7</td>
</tr>
<tr>
<td>Russia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>9/92</td>
<td>1.0</td>
<td>0.5, 2.0</td>
<td>0.9</td>
<td>0.3, 1.5</td>
</tr>
<tr>
<td>&lt;10/day</td>
<td>36/46</td>
<td>8.1</td>
<td>5.3, 12.5</td>
<td>7.2</td>
<td>6.2, 8.1</td>
</tr>
<tr>
<td>10–19/day</td>
<td>275/156</td>
<td>18.8</td>
<td>15.6, 22.6</td>
<td>15.9</td>
<td>14.2, 17.6</td>
</tr>
<tr>
<td>20–29/day</td>
<td>98/58</td>
<td>20.4</td>
<td>14.3, 28.8</td>
<td>17.1</td>
<td>15.1, 19.1</td>
</tr>
<tr>
<td>≥30/day</td>
<td>21/7</td>
<td>35.2</td>
<td>14.7, 83.8</td>
<td>27.7</td>
<td>23.1, 32.0</td>
</tr>
<tr>
<td>Czech Republic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>5/92</td>
<td>1.0</td>
<td>0.4, 2.5</td>
<td>0.7</td>
<td>0.1, 1.4</td>
</tr>
<tr>
<td>&lt;10/day</td>
<td>5/9</td>
<td>14.4</td>
<td>4.5, 45.7</td>
<td>8.3</td>
<td>5.4, 11.0</td>
</tr>
<tr>
<td>10–19/day</td>
<td>71/44</td>
<td>41.3</td>
<td>27.7, 61.6</td>
<td>21.9</td>
<td>18.1, 25.6</td>
</tr>
<tr>
<td>20–29/day</td>
<td>59/36</td>
<td>39.8</td>
<td>25.9, 61.3</td>
<td>21.3</td>
<td>17.3, 25.0</td>
</tr>
<tr>
<td>≥30/day</td>
<td>25/8</td>
<td>88.6</td>
<td>38.3, 205.0</td>
<td>41.2</td>
<td>32.8, 48.6</td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nonsmoker</td>
<td>9/71</td>
<td>1.0</td>
<td>0.5, 2.0</td>
<td>1.1</td>
<td>0.3, 1.9</td>
</tr>
<tr>
<td>&lt;10/day</td>
<td>11/9</td>
<td>9.4</td>
<td>3.9, 23.0</td>
<td>9.7</td>
<td>7.5, 11.9</td>
</tr>
<tr>
<td>10–19/day</td>
<td>104/40</td>
<td>25.1</td>
<td>16.8, 37.4</td>
<td>23.8</td>
<td>19.8, 27.6</td>
</tr>
<tr>
<td>20–29/day</td>
<td>80/30</td>
<td>26.0</td>
<td>16.4, 41.3</td>
<td>24.6</td>
<td>20.3, 28.6</td>
</tr>
<tr>
<td>≥30/day</td>
<td>18/6</td>
<td>28.9</td>
<td>10.8, 77.4</td>
<td>27.0</td>
<td>21.0, 32.4</td>
</tr>
<tr>
<td>Poland</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nonsmoker</td>
<td>11/102</td>
<td>1.0</td>
<td>0.5, 1.9</td>
<td>1.1</td>
<td>0.4, 1.7</td>
</tr>
<tr>
<td>&lt;10/day</td>
<td>8/16</td>
<td>4.9</td>
<td>2.1, 11.5</td>
<td>3.6</td>
<td>2.6, 4.7</td>
</tr>
<tr>
<td>10–19/day</td>
<td>168/143</td>
<td>11.8</td>
<td>9.5, 14.8</td>
<td>8.6</td>
<td>6.3, 10.9</td>
</tr>
<tr>
<td>20–29/day</td>
<td>184/78</td>
<td>24.3</td>
<td>18.4, 32.1</td>
<td>16.9</td>
<td>12.7, 20.9</td>
</tr>
<tr>
<td>≥30/day</td>
<td>44/9</td>
<td>50.8</td>
<td>24.6, 105.1</td>
<td>32.0</td>
<td>27.7, 32.0</td>
</tr>
<tr>
<td>Slovakia</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nonsmoker</td>
<td>4/93</td>
<td>1.0</td>
<td>0.4, 2.7</td>
<td>0.4</td>
<td>0.01, 0.8</td>
</tr>
<tr>
<td>&lt;10/day</td>
<td>4/4</td>
<td>53.4</td>
<td>11.8, 242.2</td>
<td>11.3</td>
<td>6.2, 16.1</td>
</tr>
<tr>
<td>10–19/day</td>
<td>86/41</td>
<td>79.0</td>
<td>57.0, 109.6</td>
<td>16.2</td>
<td>4.8, 25.3</td>
</tr>
<tr>
<td>20–29/day</td>
<td>82/26</td>
<td>143.2</td>
<td>86.4, 237.1</td>
<td>27.4</td>
<td>9.0, 42.2</td>
</tr>
<tr>
<td>≥30/day</td>
<td>22/5</td>
<td>181.4</td>
<td>64.2, 513.2</td>
<td>33.4</td>
<td>3.3, 54.2</td>
</tr>
</tbody>
</table>

* Odds ratios and 95% confidence intervals calculated by logistic regression analyses, adjusted for age and center.
† Confidence intervals based on floating variance.
controls recruited in 14 of the 15 centers. The effects of such
mates, bias may have resulted from the use of hospital con-
based results not shown). Indeed, the only form of bias that
could result in systematic inflation of cumulative risk for all
exposure groups is overestimation of the national mortality
rates and, as explained above, there is no reason to expect
this to have occurred.

If the cumulative risks among men have not been system-
atically biased upward, then this would argue for a real
higher cumulative risk in these countries, especially in Hun-
gary, the Czech Republic, and Slovakia. One possible
explanation for this would be that smokers in these countries
start smoking at an earlier age. The average age of initiating
smoking among male controls was 17.1 years in Hungary,
18.5 years in Romania, 18.7 years in Poland, 18.6 years in
the Czech Republic, 19.5 years in Slovakia, and 19.1 years
in Russia. This compares with 17.1 years among male con-
trols who were current smokers in the study from the United
Kingdom (Sarah Darby, University of Oxford, personal
communication, 2005). The age at initiating smoking would
therefore not appear to explain the higher cumulative risks
observed in some Central European countries.

An alternative explanation for the high cumulative risks
among smokers could be a greater carcinogenic potency
associated with cigarettes in some Central European coun-
tries. Although the risk of developing lung cancer does ap-
tear to be greater among smokers of higher tar than medium
or lower tar cigarettes (15), firm data are lacking on histor-
cal tar levels of cigarettes in these countries. Furthermore,
nitrosamine levels are known to vary widely between coun-
tries, even for the same brand of cigarette, and may also
depart from different lung cancer risks. In a survey of three
popular cigarette brands in 27 countries, over ninefold dif-
f erences were found between the highest and lowest nitro-
samine levels for the same brand of cigarettes (16). No clear
trends were observed, however, with different regions of
Europe.

Although some estimates are based on small numbers, the
trend for higher cumulative risks among never smokers did
appear to be consistent over the six countries and also for
both men and women. This would argue for the presence of
other lung carcinogens in these countries, acting either on
their own or synergistically with tobacco. Occupational ex-
posures including exposure to asbestos, metals, and poly-
cyclic aromatic hydrocarbons could be suspected, although
they are likely to affect men primarily. Potential carcinogen
exposures that may also be relevant for women include in-
door and outdoor air pollution, high levels of alcohol con-
sumption, and also poor nutritional status. An overall
cumulative lifetime risk of between 0.5 percent and 1 per-
cent, as experienced by never smokers in our study, for
a specific cancer site is not negligible and, taking recent
rates in the United Kingdom as an example, is similar to
the lifetime cumulative risk of skin melanoma, pancreatic
cancer, or kidney cancer (17). While tobacco explains the
vast majority of the lung cancer burden in these countries,
the results for men are between those obtained in Sweden and other Western European countries.

The higher cumulative risks among male never and cur-
cent smokers in Central Europe could be explained by
a number of factors, the first being biased estimation. The
measures necessary in calculation of the cumulative risks
are the age-specific mortality rate, the relative risk for dif-
ferent smoking categories, and the estimated prevalence of
smoking by age group in the population. Bias in any of these
three measures could result in biased estimation of cumula-
tive risk. There is no reason to believe that national age-
specific mortality rates of lung cancer are likely to be
seriously biased and, given the large numbers on which they
are based, they are likely to be measured with little sampling
variation. Lung cancer diagnoses that are detected prior to
autopsy are usually confirmed by histology or cytology in
Central and Eastern European countries. Although it is un-
likely that lung cancer estimates are inflated by incorrect
diagnoses, it is possible that some lung cancers are not
detected or confirmed, although these are likely to predom-
inate in age groups older than 75 years.

Relative risks of the effect of smoking may also be biased,
because either the cases or the controls are not representa-
tive of the underlying populations, or the information col-
clected on smoking is not valid. Previous large case-control
and cohort studies would indicate a relative risk from around
10- to 20-fold for men and women, although there is sub-
stantial variation (14). The one estimate that seems to depart
from this in the current analysis among men is that of
Slovakia, with a reported relative risk of 82.7 among current
smokers. This anomalously high relative risk is unlikely,
however, to explain the high cumulative risk among current
smokers. This is because the cumulative risks in each expo-
sure group must add up to the overall cumulative risk, and
any overestimation in current smokers will have to be bal-
anced by an underestimation among nonsmokers and former
smokers, where the estimated cumulative risks do not ap-
pear conspicuously low.

Finally, estimates of the prevalence of smoking in the
population may be biased. Although we have little reason
to believe that the control smoking prevalence is likely to be
biased among men, given the coherent relative risk esti-
mates, bias may have resulted from the use of hospital con-
trols recruited in 14 of the 15 centers. The effects of such
a bias would be difficult to predict, although they would act
the role of non-tobacco-related carcinogens also deserves further attention. Within the current study population, we have recently reported an increased risk of lung cancer for multiple occupational x-rays, which was particularly prominent among never smokers, as well as an increased risk from the use of solid fuels for heating and cooking (5, 7). Further analysis of known and suspected lung carcinogens is underway, and the extent to which they explain the high cumulative lifetime risk among never smokers will be of much interest.

In summary, these results provide evidence of higher cumulative risks of lung cancer death among never smokers for both men and women from Central Europe than those observed in Western Europe and the United States and also among current smokers for men. Regarding women current smokers, the lung cancer epidemic is still maturing in Central Europe, and the cumulative risks presented here will increase in the future as later cohorts age. The effect of quitting smoking on the lifetime cumulative risk was also substantial and reinforces the conclusion that, for people who have been smoking for many years, giving up smoking in middle age means avoiding most of the subsequent risk of developing lung cancer. For the countries of Central and Eastern Europe, this has major public health implications, and tobacco-related mortality in these countries over the next three decades will be determined by the extent to which current smokers can be persuaded to quit smoking.

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REFERENCES


APPENDIX

The cumulative risk was calculated using methods similar to those described by Peto et al. (2). The following steps summarize the main measures used to obtain the cumulative risk.

\[ r_i = \text{the relative risk in the } i\text{th smoking category.} \] (step 1)

where the smoking categories are \(1 = \text{never smokers}; 2 = \text{former smokers subdivided in some analyses by age quit smoking} \quad (<40, 40–49, 50–59, \geq60 \text{ years}); \) and \(3 = \text{current smokers subdivided in some analyses by number of cigarettes per day} \quad (<10, 10–19, 20–29, \geq30 \text{ cigarettes}). \)

\[ p_{ij} = \text{the percentage of the controls in the } j\text{th age group and the } i\text{th smoking category,} \] (step 2)

where the age categories are as follows: \(35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, \) and \(70–74 \text{ years}. \)

\[ S_j = \sum_{i=1}^{3} r_i p_{ij} \] (step 3)

\[ h_j = \text{the age-specific incidence rate.} \] (step 4)
\[ f_j = h_j(S_1 + \ldots + S_j). \]  
(step 5)

\[ a_{ij} \] is the absolute rate in the \((i,j)\)th cell, and \[ a_{ij} = \frac{f_j* r_i}{R_j}. \]  
(step 6)

\[ C_i \] is the cumulative rate, and \[ C_i = \Sigma_j R_j a_{ij}. \]  
(step 7)

where \( R_j \) is the width of the \(j\)th age category in years.

Cumulative risk (percent) = 100 \times (1 - \exp(-C_i)).  
(step 8)

Briefly, to estimate the cumulative risk, we need first to calculate the relative risks in the various smoking categories (step 1). In our study, the relative risks of lung cancer were estimated by means of the odds ratios using unconditional logistic regression, and lifelong nonsmokers formed the reference category.

The next step was to calculate the percentage of controls in each smoking category and for each age group (step 2) using the assumption that, within each country, the smoking distribution of the population was represented by the smoking distribution observed among the study controls.

The third step was the estimation of common factors combining the relative risk (step 1) for the different smoking categories with the age-specific prevalence of such smoking habits among study controls (step 2), thus obtaining the quantities denoted (step 3).

Combining the age-specific cancer incidence rates of each country (step 4) with the common factors (step 3), we obtained the proportions given (step 5). Multiplying these proportions with the relative risks for the different smoking categories produced the age-specific absolute risks in the different smoking categories (step 6).

Next, we calculated the cumulative rates (step 7) for the different categories of smoker by adding age-specific absolute rates, and then finally the cumulative risks by age 75 years were estimated using the standard formula (step 8). The cumulative risk may be interpreted as the probability that an individual will develop lung cancer before age 75 years in the absence of competing causes of death.