International Mortality and Smoking Statistics System (IMASS)

II. Relating mortality to previous smoking habits in 30 developed countries

IIA. Lung cancer

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EXECUTIVE SUMMARY

Sex- and age-specific lung cancer mortality in 30 developed countries has been related to previous smoking habits in the same birth cohort. Many of the analyses relate to smoking habits 20 years previously, but some analyses relate to average smoking habits over the period 15 to 5, 25 to 5 or 35 to 5 years previously. Three indices of smoking have been used; prevalence of cigarette smoking, consumption of cigarettes per adult unadjusted for tar and consumption of cigarettes per adult adjusted for tar. The definition of cigarette consumption includes hand-rolled as well as manufactured cigarettes.

Two types of correlation analysis have been used. One is conducted within-country and relates variations in mortality and smoking over time. The other is conducted at specific points in time and relates variations in mortality and smoking by country.

The first, within-country, analyses showed a tendency for time trends in lung cancer mortality to be positively correlated with time trends in previous smoking, more so for females than for males. However, in both sexes, there were some countries where a substantial negative correlation was seen, and there are relatively few countries where a clear positive relationship was seen for both sexes and in all age groups.

The second, between-country, analyses showed a very clear tendency in females for lung cancer rates to be positively correlated with previous smoking habits. This was evident for all ages, time periods, smoking indices and lag times studied, with the correlations nearly all statistically significant and often quite highly so. In contrast, the data for males show quite modest positive correlations which are virtually never statistically significant.

Possible explanations for the failure to find stronger relationships, particularly in men, are discussed.

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1. Introduction

The "International Mortality and Smoking Statistics System" (IMASS)[1] contains nationally-based data for 30 developed countries on mortality from major smoking-related diseases and on selected tobacco and smoking statistics. Part I of this report characterized and compared mortality trends, IA considering lung cancer, IB ischaemic heart disease (IHD) and IC chronic obstructive pulmonary disease (COPD) and respiratory diseases, non-acute (RDNA).

Part II of this report relates mortality from lung cancer, IHD and RDNA to previous smoking habits. COPD is not considered because of major changes over time in definition of the disease, as discussed in Part IC.

Two correlational approaches are used to investigate the relationship of mortality to previous smoking habits. One considers the relationship based on data over a range of time periods within a country. The other considers the relationship based on data for a set of countries at a given time. The first, within-country approach, is essentially asking the question "Can variations in mortality over a given time period within a country be explained by corresponding variations in previous smoking habits over the same period"? The second, between-country approach is asking the question "Do countries with high (or low) mortality at a given time tend to have correspondingly high (or low) previous smoking habits"?

Part IIA is concerned with lung cancer. Because it is generally considered that any effect of smoking is a fairly long-term one, attention is mainly restricted to smoking habits 20 years earlier. Thus, mortality for, say 60-64 year olds in 1991-1995 is studied in relation to the smoking habits 20 years earlier of members of the same birth cohort, i.e. of 40-44 year olds in 1971-1975. Alternative analyses relate to average consumption over the periods 15 to 5, 25 to 5 or 35 to 5 years previously.

It is recognized that the approach used is quite a simple and unsophisticated one. In view of variations in other risk factors, presence of a

statistically significant correlation does not imply a cause-and-effect relationship between smoking and lung cancer. Nor indeed does absence of a correlation imply absence of such a relationship. However, provided the smoking habit data used are accurate and relevant, some inferences can be drawn. For example, if mortality rises markedly over a period when smoking habits decline, it is reasonable to infer that factors other than smoking are responsible for the rise.

The main purpose of this report is to present the various relationships in an organized way to form a useful reference work. Some broad conclusions are reached, but detailed examination of all the various relationships presented has not been attempted.

2. Materials and methods

2.1 Countries included

The 30 countries for which data are available are listed in section 2.1 of part IA of this report, and shown in the tables of the present document. The country names relate to political boundaries as they existed pre-1990s.

2.2 Periods

Results are shown in the within-country analyses for the periods 1946-50, 1951-55 … 1996-2000. In the between-country analyses, attention is restricted to the periods 1971-75, 1981-85 and 1991-95.

2.3 Age groups

Attention is restricted to three age groups: 45-49, 60-64 and 75-79.

2.4 Definition of Lung Cancer

Section 2.3 and Appendix 1 of part I of this report gives details of when successive revisions of the International Classification of Diseases (ICD) came into use in each country and some general remarks about the problems of defining cause of death.

As noted in section 2.3 of part IA of this report, there is no real difficulty in obtaining a comparable disease definition from the data available for the various ICD revisions for lung cancer, the definition used always including cancers of the trachea, lung and bronchus.

2.5 Smoking habits

Three indices of smoking have been used, all based on total cigarette consumption, i.e. of manufactured and hand-rolled cigarettes combined. "Prevalence" is the estimated percentage of the population who are current smokers, "Consumption" is the estimated daily number of cigarettes smoked per adult, and "Consumption (square root tar adjusted)" is the estimated daily number of cigarettes smoked per adult multiplied by a factor $\sqrt{T/35}$ where T is the sales-weighted average tar consumption at the time. The square root

adjustment is an attempt to take "compensation" into account, i.e. the tendency of smokers to increase the intensity of smoking following a reduction in the tar level of the brand smoked. Estimates of the three indices are not available for all countries in all periods studied.

For the United Kingdom, some additional results are also shown based on consumption of manufactured cigarettes only.

2.6 Correlations

Correlations always relate mortality for a given age group in a given period to the estimated smoking habits of members of the same birth cohort at a previous time or for a previous period. Standard Pearson correlation coefficients (R) are presented, together with the number of data pairs (N) used for the correlation. Correlations are not calculated where N<3. The statistical significance of correlations can be obtained from Table 1.

2.7 Individual country tables (Tables L5.1 to L5.30)

Each page relates to one of the 30 countries. On each page, the relevant data (mortality for each period from 1946-50 to 1996-2000 and three smoking indices for 20 years earlier) are shown separately for the two sexes x three age groups considered. At the end of each set of smoking data, the N and R values are shown relating mortality to smoking habits 20 years earlier. Table 5.27 (United Kingdom) is split into 2 pages, one for total cigarettes (manufactured + handrolled) and one (Table 5.27a) for manufactured cigarettes only.

2.8 Summary over countries (Tables L5.31 to L5.33)

Tables L5.31-L5.33 consist of a separate page for each smoking index summarizing the N and R values for all 30 countries shown in Tables L5.1 – L5.30 (and Table L5.27a).

Tables L5.34-L5.36 are similar to Tables L5.31-L5.33 but summarize N and R values based on smoking habits averaged from 25 to 5 years earlier than the mortality rates to which they refer.

Table L5.37 is similar to Table L5.31 but relates lung cancer mortality to prevalence of smoking 20 years earlier, of all tobacco products, rather than of total cigarettes.

2.9 Between-country correlations (Tables L6.1 to L6.30 and Figures L6.1 to L6.30)

Tables and Figures L6.1 to L6.18 relate mortality to smoking habits 20 years earlier and consist of separate pairs of pages for each combination of sex x age group (45-49, 60-64, 75-79) x period (1971-75, 1981-85, 1991-95). The left-hand page of each pair gives the relevant data for each country in a table, together with the estimated N and R values for the between-country correlations. The right-hand page presents the same data as scatter plots, one for each of the three smoking indices. The R value from the table is repeated on the figure for convenience. Note that tar is assumed constant up to 1955 for virtually all countries, so 1971-75 results for consumption and tar adjusted consumption differ little.

Tables and Figures L6.19 to L6.22 relate to smoking habits averaged from 15 to 5 years previously, while Tables and Figures L6.23 to L6.26 relate to smoking habits averaged from 25 to 5 years previously and Tables and Figures L6.27 to L6.30 relate to smoking habits averaged from 35 to 5 years previously. The format is the same as L6.1 to L6.18, but the data relate to mortality in 1991 to 1995, with the four pairs of tables and figures giving results for the two sexes x two age groups (60-64, 75-79).

3. Results

3.1 Within-country analyses (Table L5)

Looking at the summary tables (Tables L5.31-L5.37), it is evident that the completeness of the data varies markedly by country, index of smoking and period covered. Data are most complete for prevalence of smoking and least complete for tar adjusted consumption, with unadjusted consumption intermediate. They are somewhat more complete for analyses relating to smoking habits 20 years previously than for analyses relating to average smoking habits over the period 25 to 5 years before the mortality data. For prevalence of smoking 20 years earlier, the data in Table L5.31 (total cigarettes) and Table L5.37 (all tobacco products) provide estimates for 24 countries for males and for 22 countries for females.

The data for males in Table L5.31 show a variable relationship between lung cancer mortality and smoking prevalence 20 years previously. The data for Ireland, UK, Finland, Belgium and Netherlands, and, to a lesser extent for Sweden, New Zealand and Austria, show positive correlations at each age group due to a decline in mortality being matched by a corresponding decline in previous smoking habits. Often these correlations are based on data for only three or four 5-year periods. Spain also shows relatively high correlations, but here both prevalence and mortality have increased. The longest run of data is for the USA, where moderate positive correlations are seen over a period where mortality has risen then fallen. Some countries, notably France, Italy, Norway and Poland show substantial negative correlations between lung cancer mortality and prevalence 20 years previously.

The data for females in Table L5.31 show a more consistent tendency towards a positive correlation than do the data for males. This may reflect the general tendency for both lung cancer rates and prevalance of smoking to rise. Thus, of the 22 countries with data, the correlations for all 3 age groups are quite strongly positive (>0.5) for France, Germany, Hungary, Italy, Norway, Poland, Romania, Sweden and the UK and are all positive, but, on some occasions at a lower level, for Netherlands and the USA. However, there are

some countries which show consistent negative correlations (Austria, Belgium, Israel) or marked negative correlations in one or two age groups (Canada, Denmark, Greece, Ireland, New Zealand, Spain).

The data relating mortality to consumption 20 years earlier (Table L5.32) or to tar adjusted consumption 20 years earlier (Table L5.33) also do not show a consistent pattern of correlations for the countries where data are available. Quite a number of negative correlations are seen, some relatively large, and there are only a few countries where a consistent positive correlation is seen for both sexes and at all 3 age groups (Canada, Hungary and USA in Table L5.32 and Sweden in Table L5.33).

The general pattern of results for Tables L5.34 to L5.36, which relate mortality to average consumption from 25 to 5 years previously, is quite similar to that for Tables L5.31 to L5.33. Again, although positive correlations are more frequent than negative ones, negative ones are quite common, and even in one table there are relatively few cases where positive correlations are seen for all age groups and both sexes.

3.2 Between-country analyses (Table I6 and Figure I6)

Between-country correlations have been estimated for each combination of sex, age (45-49, 60-64, 75-79) and period (1971-75, 1981-85, 1991-95) for smoking habits 20 years previously. Earlier periods were not chosen due to the relatively small number of countries providing data, and even for 1971-75 numbers of countries are small, particularly for consumption. Between-country correlations have also been estimated for the period 1991-95 for each combination of sex, age (60-64, 75-79) and period of smoking habits (15 to 5, 25 to 5, 35 to 5 years previously). The correlations are summarized in Table 2.

As can be seen from Table 2, all the correlations for females are positive and relatively large, the lowest being 0.40 (age 45-49, 1991-95, consumption 20 years previous), many >0.80, the great majority statistically significant at $p<0.05$ and many significant at $p<0.001$. The correlation in

females is evident for all ages, time periods and smoking indices and lag times studied.

In contrast, the data for males typically show quite modest positive correlations which, with one exception, are never significant at $p<0.05$. A few of the correlations are non-significantly negative.

3.3 Comments

It is not surprising that the correlations of mortality with smoking habits are more clearly seen for females than for males. In the first place, women tend to smoke manufactured cigarettes only, whereas men also smoke handrolled cigarettes, pipes and cigars. In the second place, smoking by women has occurred predominantly in the second half of the 20th century whereas smoking by men was common before the Second World War. Both these observations would make it difficult to observe a close relationship between smoking and mortality for men using, as we are doing here, a fairly simple correlational approach based on relatively recent data.

It is also not surprising that correlations are not very close, especially within-country, when there are relatively few data points which may derive in some countries from disparate surveys. In any case, the approach used, which assumes a simple linear relationship between mortality and either prevalence of smoking or consumption of cigarettes is unlikely to be as precise as a more complex algorithm, taking into account a combination of prevalence, daily consumption, frequency of past smoking, duration of smoking and type of product. This is beyond the scope of the IMASS approach.

Nevertheless, the findings may be of interest in that they may highlight possible anomalies deserving further attention. For example, extensive recent work by us has brought to attention an unexplained recent rise in US lung cancer rates relative to those in the UK[2]. Further detailed work might help to understand lung cancer mortality trends in some countries where our relatively simplistic work here indicated an apparent negative association over time between mortality and previous smoking habits.

4. Summary and conclusions

Sex- and age-specific lung cancer mortality in 30 developed countries has been related to previous smoking habits in the same birth cohort. Many of the analyses relate to smoking habits 20 years previously, but some analyses relate to average smoking habits over the period 15 to 5, 25 to 5 or 35 to 5 years previously. Three indices of smoking have been used; prevalence of cigarette smoking, consumption of cigarettes per adult unadjusted for tar and consumption of cigarettes per adult adjusted for tar. The definition of cigarette consumption includes hand-rolled as well as manufactured cigarettes.

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The second, between-country, analyses showed a very clear tendency in females for lung cancer rates to be positively correlated with previous smoking habits. This was evident for all ages, time periods, smoking indices and lag times studied, with the correlations nearly all statistically significant and often quite highly so. In contrast, the data for males show quite modest positive correlations which are virtually never statistically significant.

Possible explanations for the failure to find stronger relationships, particularly in men, are discussed.

5. References

1. Forey BA, Hamling J, Lee PN. *International mortality and smoking statistics system. A brief description and user's guide*. Sutton, Surrey: P N Lee Statistics and Computing Ltd; 2002. www.pnlee.co.uk

2. Lee PN, Forey BA. Why are lung cancer rate trends so different in the United States and United Kingdom? *Inhal Toxicol* 2003;**15**:909-49.

TABLE 1 : Critical values of the correlation coefficient for statistical significance at $p<0.05$, $p<0.01$ and $p<0.001$

Number of pairs considered	Critical value of correlation coefficient*		
	$p<0.05$	$p<0.01$	$p<0.001$
3	0.997	0.9999	1.000
4	0.950	0.990	0.999
5	0.878	0.959	0.991
6	0.811	0.917	0.974
7	0.754	0.875	0.951
8	0.707	0.834	0.925
9	0.666	0.798	0.898
10	0.632	0.765	0.872
11	0.602	0.735	0.847
12	0.576	0.708	0.823
13	0.553	0.684	0.801
14	0.532	0.661	0.780
15	0.514	0.641	0.760
16	0.497	0.623	0.742
17	0.482	0.606	0.725
18	0.468	0.590	0.708
19	0.456	0.575	0.693
20	0.444	0.561	0.679
21	0.433	0.549	0.665
22	0.423	0.537	0.652
23	0.381	0.487	0.597
28	0.349	0.449	0.554

* Values on or above the given value or on or below minus the given value are statistically significant at the level stated.

TABLE 2 : Summary of between-country correlation coefficients

Sex	Age	Period	Time of smoking habits	Prevalence R(N)	Consumption per adult (unadjusted) R(N)	Consumption per adult (tar adjusted) R(N)
Male	45-49	1971-75	20 years earlier	0.03 (8)	0.76 (3)	0.76 (3)
		1981-85		0.31 (20)	0.08 (15)	-0.03 (10)
		1991-95		0.14 (25)	0.26 (21)	0.17 (14)
	60-64	1971-75		-0.32 (8)	0.43 (3)	0.44 (3)
		1981-85		0.16 (21)	0.04 (16)	0.02 (10)
		1991-95		0.30 (25)	0.39 (21)	0.29 (14)
	75-79	1971-75		-0.09 (8)	-0.15 (3)	-0.14 (3)
		1981-85		0.20 (22)	0.22 (17)	0.36 (11)
		1991-95		0.41 (25) *	0.38 (21)	0.44 (14)
Female	45-49	1971-75		0.59 (9)	0.95 (3)	0.95 (3)
		1981-85		0.57 (14) *	0.70 (11) *	0.68 (8)
		1991-95		0.49 (25) **	0.40 (19)	0.61 (14) *
	60-64	1971-75		0.84 (9) **	1.00 (3) **	1.00 (3) **
		1981-85		0.81 (14) ***	0.81 (11) **	0.84 (8) **
		1991-95		0.77 (25) ***	0.74 (19) ***	0.85 (14) ***
	75-79	1971-75		0.79 (9) *	0.92 (3)	0.91 (3)
		1981-85		0.80 (14) ***	0.68 (11) *	0.76 (8) *
		1991-95		0.81 (25) ***	0.87 (19) ***	0.91 (14) ***
Male	60-64	1991-95	15-5 years earlier	0.28 (23)	0.29 (19)	-0.45 (8)
Female				0.86 (23) ***	0.86 (19) ***	0.95 (8) ***
Male	75-79			0.08 (23)	0.26 (19)	-0.10 (8)
Female				0.84 (23) ***	0.86 (19) ***	0.96 (8) ***
Male	60-64		25-5 years earlier	0.25 (21)	0.30 (14)	-0.53 (6)
Female				0.83 (20) ***	0.78 (11) **	0.97 (5) **
Male	75-79			0.20 (21)	0.35 (15)	-0.31 (6)
Female				0.86 (20) ***	0.91 (11) ***	0.98 (5) **
Male	60-64		35-5 years earlier	0.10 (12)	0.43 (16)	0.65 (3)
Female				0.85 (10) **	0.85 (5)	0.94 (3)
Male	75-79			-0.03 (13)	-0.24 (8)	-0.72 (5)
Female				0.87 (10) **	0.90 (5) *	1.00 (3) **

* $p<0.05$ ** $p<0.01$ *** $p<0.001$

R correlation coefficient

N number of countries with data on mortality and smoking that R is based on

See Tables L6.1 to L6.30 for the data these correlations are based on