Mortality in light smokers

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1. <u>Overall mortality</u>

In 1979, in a major review of the evidence then available, the US Surgeon-General [1] summarized data relating overall age-adjusted mortality in males to number of cigarettes currently smoked from seven very large prospective studies, four conducted in the US and one each in Britain, Canada and Sweden. These data (reproduced in <u>Table 1</u>) consistently showed that though mortality was higher in current smokers than in nonsmokers, the proportional increase in risk was lowest in the lightest smoking group. On average, the excess mortality in the lightest smoking group was about half that for smokers as a whole. In most studies, this lightest smoking group smoked about 1-9 cigarettes per day. In view of the nature of the dose-response relationship it can be assumed that the risk would be even less for the group smoking less than five cigarettes a day, though data are not usually reported in this form.

In that report, data from only one major prospective study were presented for females. These data, reproduced in <u>Table 2</u>, showed that though there was a clear excess mortality in smokers of 20-39 cigarettes a day and to a lesser extent in smokers of 10-19 cigarettes a day, there was not clear evidence of an excess mortality in smokers of 1-9 cigarettes a day.

More recent evidence from large prospective studies on the relationship between amount smoked and overall mortality appears to be rather thin on the ground. However, that which is available clearly suggests that lighter smoking is associated with a lesser risk on average, than for smokers as a whole. For example, in their recently reported 40 year follow-up of male British doctors, Doll and Peto [2] presented age-adjusted mortality rates per 100,000 of 1706, 2542, 3004, 3928 and 3038 for, respectively, never smokers, current smokers of 1-14, 15-24 and 25+ cigarettes a day and all current cigarette smokers. Here excess mortality in smokers of 1-14 cigarettes a day was 63% of that of all smokers.

2. Coronary heart disease

A recent report [3] from a Swedish prospective study claimed that very light cigarette smoking considerably increased the risk of coronary heart disease [CHD] and that there was no dose-response relationship. However this was based on a very small number of CHD deaths indeed. My general impression of the literature (some examples shown in <u>Table 3</u>) is that the majority of studies <u>do</u> show an increasing dose response relationship and that a number of other studies show little or no increase at low consumption levels.

3. <u>Lung cancer</u>

Numerous prospective and case-control studies have shown a very clear dose-response relationship with amount smoked. Based on 20 year follow-up in the British doctors prospective study, Doll and Peto [4] found that, among cigarette smokers who started smoking at ages 16-25 and who smoked 40 or less per day, the annual lung cancer incidence in the age range 40-79 was well described by the formula:

$$0.273 \times 10^{-12} \text{ (cigarettes/day + 6)}^2 \text{ (age - 22.5)}^{4.5}$$

This formula implies that, compared to an average smoker, of 20 cigarettes a day, the excess lung cancer risk of a light smoker is given by:

Cigarettes/day	Excess risk
0	0%
2	4%
5	13%
10	38%
20	100%

Although the literature is unclear as to whether the dose-response relationship is linear or has a quadratic component, as Doll and Peto claim, the larger studies are all very consistent in reporting a very clear dose-response relationship. This is illustrated by <u>Figure 1</u> which is taken from a very large recently published US prospective study ("MRFIT") and by <u>Table 4</u> which gives some examples from the literature. For lung cancer, it seems that the excess risk is, at most, proportional to the number of cigarettes smoked, so that, for example, someone who smokes two cigarettes a day would be

expected to have at most 2/20th = 10% of the excess risk of a typical smoker, of 20 cigarettes a day.

4. <u>Overall conclusion</u>

Although data specifically relating to smokers of very small numbers of cigarettes a day are sparse, it is abundantly clear from the evidence presented that mortality in light smokers is far less increased than in smokers overall.

5. <u>References</u>

- U.S. Surgeon General. Smoking and health, a report of the Surgeon General. US
 Department of Health, Education and Welfare, Public Health Service. Office on
 Smoking and Health, 1979.
- 2. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. *BMJ* 1994;**309**:901-11.
- 3. Rosengren A, Wilhelmsen L, Wedel H. Coronary heart disease, cancer and mortality in male middle-aged light smokers. *J Intern Med* 1992;**231**:357-62.
- 4. Doll R, Peto R. Cigarette smoking and bronchial carcinoma: dose and time relationship among regular smokers and lifelong nonsmokers. *J Epidemiol Community Health* 1978;**32**:303-13.

TABLE 1

Overall mortality in males in relation to number of cigarettes currently smoked

Data from Seven Large Prospective Studies

Age adjusted mortality ratios by smoking habits

<u>Author</u>	Study	Non- smokers	<u>1-9</u> /day	<u>10-20</u> /day	21-39 /day	<u>40+</u> /day	All smokers	1-9 day as % total*
Doll	British Doctors**	1.00	1.41	1.57	2.16		1.63	65%
Hammond	25 US States	1.00	1.45	1.75	1.90	2.20	1.83	54%
Rogot	US Veterans	1.00	1.25	1.51	1.69	1.89	1.55	45%
Best	Canadian Pensioners [†]	1.00	1.41	1.56	1.65		1.54	76%
Hammond & Horn	9 US States	1.00	1.34	1.70	1.96	2.23	1.74	46%
Weir & Dunn	California	1.00	1.44	1.79	2.27	1.83	1.78	56%
Cederlof	Sweden ^{††}	1.00	1.20	1.40	1.80		1.58	34%

^{*} Excess risk for lowest smoking group as percentage of excess risk for all smokers, e.g. Doll (1.41-1.00)/(1.63-1.00) = 65%.

Adapted from Table 4, p2-17, of 1979 US Surgeon-General's Report.

^{**} Smoking groups were 1-15, 16-25, >25 cigs/day.

[†] Last smoking group is >20 cigs/day.

^{††} Smoking groups were 1-7, 8-15, >15 cigs/day.

TABLE 2

Overall mortality in females in relation to number of cigarettes currently smoked

Data from the US 25 State Study of Hammond

<u>Age</u>	<u>Nonsmoker</u>	<u>1-9/day</u>	<u>10-19/day</u>	20-39/day
35-44	1.00	0.90	0.97	1.35
45-54	1.00	0.95	1.22	1.54
55-64	1.00	0.99	1.31	1.46
65-74	1.00	1.09	1.18	1.51
75-84	1.00	1.07	1.21	-

Adapted from Table 25, p2-26, of 1979 US Surgeon-General's Report.

TABLE 3

CHD dose-response relationships in males
Some examples from the literature

1. British Male Doctors (Doll and Peto, 1976, BMJ, 2, 1525-1536)

Age standardized CHD death rates (number of deaths)

Current cigarettes only smokers

<u>Age</u>	Nonsn	<u>nokers</u>	1-14/	<u>'day</u>	<u>15-24</u>	<u>/day</u>	<u>≥25/</u>	<u>day</u>
<45	7	(3)	46	(12)	61	(22)	104	(18)
45-54	118	(32)	220	(38)	368	(90)	393	(69)
55-64	531	(79)	742	(91)	819	(123)	1025	(125)
65-74	1190	(82)	1866	(134)	1511	(101)	1731	(81)
≥75	2432	(92)	2719	(13)	2466	(50)	3247	(27)

2. ACS "Million Person" Study (Hammond and Garfinkel, 1969, Archives of Environmental Health, 19, 167-182)

CHD mortality ratios

Current cigarette smokers

<u>Age</u>	<u>Nonsmokers</u>	<u>1-9/day</u>	<u>10-19/day</u>	20-39/day	40+/day
45-54	1.00	2.35	3.09	3.11	3.35
55-64	1.00	1.54	1.92	2.04	2.13
65-74	1.00	1.26	1.61	1.56	-
75-84	1.00	1.17	1.39	1.11	-

TABLE 3 (continued 1)

CHD dose-response relationships in males Some examples from the literature

3. <u>National Cooperative Pooling Project (Pooling Project Research Group 1978, Journal of Chronic Diseases, 31, 204-306</u>

Average annual CHD risk per 1000 man years (cases)

Current cigarette smokers

<u>Age</u>	Nonsn	nokers_	About ½ pa	ack/day	About 1	pack/day	<1 pa	ck/day
40-44	1.5	(1)	3.1	(3)	3.9	(14)	4.9	(10)
45-49	3.0	(11)	5.0	(7)	8.4	(49)	12.2	(36)
50-54	3.6	(10)	6.2	(9)	10.3	(64)	17.4	(56)
55-59	7.3	(13)	15.5	(19)	13.8	(61)	22.5	(48)
60-64	15.5	(18)	24.3	(15)	22.0	(42)	26.8	(22)

4. <u>Japanese Doctors (Kono et al, 1985, Journal of Cancer Research and Clinical Oncology, 110, 161-164)</u>

Age-adjusted CHD relative risks (95% confidence intervals)

<u>Age</u>	Nonsmokers Nonsmokers	<u>≤9/day</u>	10-19/day	<u>≥20/day</u>
All	1.00	1.51 (0.68-3.36)	2.12 (1.13-3.97)	3.01 (1.61-5.65)

5. US Veterans (Rogot and Murray, 1980, Public Health Reports, 95, 213-228)

Age-adjusted mortality ratios

Current cigarette smokers

<u>Age</u>	<u>Nonsmokers</u>	<10/day	<u>10-20/day</u>	21-39/day	40+/day
All	1.00	1.24	1.56	1.76	1.94

TABLE 3 (continued 2)

<u>CHD dose-response relationships in males</u> <u>Some examples from the literature</u>

6. <u>Swedish Men (Carstensen et al, 1987, Journal of Epidemiology and Community Health, 41, 166-172</u>

Age-adjusted mortality ratios

Current smokers, any tobacco

<u>Age</u>	Never smokers	<u>1-7g/day</u>	8-15g/day	>15g/day
All	1.00 (744)	1.31 (316)	1.44 (607)	1.66 (333)

TABLE 4

<u>Lung cancer relative risk dose-response relationships</u> <u>Some examples from the literature</u>

1. American Cancer Society 25 state study (Ref 1, Table 2 p5-13, Table 11 p5-22)

	Nonsmokers	<u>1-9/day</u>	10-19/day	<u>20-39/day</u>	40+/day
Males	1.00	4.62	8.62	14.69	18.77
Females	1.00	< 1.06	>	< 4.76	>

2. Swedish males (Ref 1, Table 2, p5-13)

	Nonsmokers	<u>1-14/day</u>	15-24/day	25+/day
Males	1.00	2.30	8.80	13.90

3. Japanese males (Ref 1, Table 2, p5-13)

	Nonsmokers	<u>1-9/day</u>	<u>10-14/day</u>	<u>15-24/day</u>	25-49/day	50+/day
Males	1.00	1.90	3.52	4.11	4.57	5.78

4. <u>American Cancer Society CPS-II (Garfinkel and Stellman, 1988, Cancer Research, 48, 6951-6955)</u>

	Nonsmokers	<u>1-10/day</u>	11-19/day	<u>20/day</u>	21-30/day	31+/day
Females	1.0	5.5	11.2	14.2	20.4	22.0

5. British Doctors 40 year follow-up (Ref 2)

	Nonsmokers Nonsmokers	<u>1-14/day</u>	<u>15-24/day</u>	25+/day
Males	1.00	7.50	14.86	25.36

TABLE 4 (continued)

<u>Lung cancer relative risk dose-response relationships</u> <u>Some examples from the literature</u>

6. <u>Eight case-control studies in China (Liu, 1992, International Journal of Epidemiology, 21, 197-201</u>

	Nonsmokers	<10/day	<u>10-19/day</u>	<u>20+/day</u>
Males + Females	1.00	1.03	2.04	3.33

7. US case-control study (Wynder and Kabat, 1988, Cancer, 62, 1223-1230)

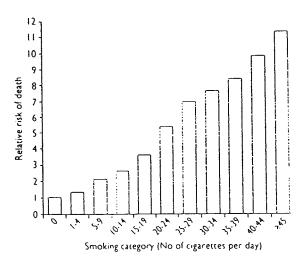
	Nonsmokers	<u>1-10/day</u>	11-20/day	21-30/day	31-40/day	41+/day
Kreyberg I lung cancer						
Males	1.00	13.25	15.84	29.56	37.65	64.05
Females	1.00	6.56	18.16	26.53	95.17	88.69
Kreyberg II lung cancer						
Males	1.00	2.44	8.42	15.39	11.08	28.35
Females	1.00	3.06	4.50	9.40	13.79	20.68

8. European 7 centre case-control study (Lubin and Blot, 1984, JNCI, 73, 383-389

	<u>1-9/day</u>	<u>10-19/day</u>	20-29/day	30+/day
Squamous cell				
Males	1.0	1.5	2.1	3.1
Females	1.0	2.4	5.3	4.2
Adenocarcinoma				
Males	1.0	1.9	2.5	3.5
Females	1.0	2.0	1.1	2.3

(NB. Base for comparison is 1-9 cigs/day in this study whereas it is nonsmokers in all other studies.)

FIGURE 1



Relative risk of death from lung cancer according to number of cigarettes smoked per day

Source : Davey Smith G and Phillips AN (1996) BMJ, $\underline{313}$, 929-932.

Study: "MRFIT" - Multiple Risk Factor Intervention Trial