Does smoking cause heart disease?

Anomalous evidence from trends in sex ratios

Basis for a possible paper

Author : P.N. Lee

Date : 27.2.86

Preface

This note is intended to summarize the work I have done so far and to assist Prof. Wald in pursuing the ideas further with a possible joint paper in prospect. It is also a note which either of us can bounce off colleagues to get additional ideas.

Introduction

Over the last 30 years or so, it is clear that women have become much closer to men in their smoking habits. Numerous epidemiological studies have shown that, especially among younger men and women, risk of coronary heart disease is related to smoking and in particular current smoking. Given that the relationship is a causal one and given that there has been no compensating trend due to factors other than smoking one would expect that women would have become closer to men in their coronary disease death rates. Superficial examination

of trends in the sex ratio of coronary disease death rates showed little evidence of much change, suggesting that there was an anomaly requiring explanation.

This document adds meat on the bones of this original idea.

Relevant epidemiological evidence

Review of the literature on smoking and coronary heart disease (see Appendix 1 for a list of references and some of the relevant evidence) indicates a number of conclusions:

(i) among those who have never smoked regularly, the risk of CHD is markedly higher in men than in women,

(ii) in both sexes the relative increase in death rate in relation to smoking cigarettes is much more marked in the young than in the old,

(iii) risk of CHD in current smokers increases with number of cigarettes smoked. In younger age-groups the increase seems reasonably linear; in older age groups there may be some flattening off (perhaps because symptomatic smokers cut down the number smoked),

(iv) for a given age and number of cigarettes smoked, the relative increase in risk over never smokers is similar for men and women,

(v) risk is somewhat elevated in ex-smokers of cigarettes but to a lesser extent than in current smokers,

(vi) pipe or cigar smoking does not materially affect risk.

Mathematical formula for estimating expected trends in CHD sex ratios

From the above, it would appear that a reasonable formula to characterise risk in a population according to smoking habits is as follows:

$$R = N(1 + \alpha X + \beta SC)$$

where N is the baseline risk in non-smokers, X is the proportion of ex-smokers, α is the excess relative risk due to ex-smoking, S is the proportion of current cigarette smokers, C is the mean number of cigarettes smoked per day per smoker and β is the excess relative risk per cigarette smoked. Since SC is the mean number of cigarettes smoked per day per adult (call this K) we can also write the formula:

$$R = N(1 + \alpha X + \beta K)$$

Thus if from epidemiology we note that, for a given age group, ex-smoking is associated with a relative risk of 1.3 and current smoking of 20 cigarettes a day with a relative risk of 3, a population consisting of 32% never smokers, 18% ex-smokers and 50% current smokers of an average of 15 per day (i.e. a per adult consumption of 7.5 per day) would be expected to have a risk which is

$$1 + 0.18(1.3 - 1) + \frac{7.5}{20}(3 - 1)$$

$$= 1 + 0.054 + 0.75$$

$$= 1.804$$

times that for a population which was 100% non-smokers.

It should be noted from this example, which is not untypical, that the contribution of ex-smoking to the total risk is minimal. Since, furthermore, most ex-smokers are ex-smokers of cigarettes, it is clear that only very small inaccuracy will be introduced by basing our calculations on ex-smokers of any product (which figures are more readily available) than on ex-smokers specifically of cigarettes.

It should also be noted that knowledge of smoking habits cannot predict the absolute risk of CHD in non-smokers or the difference between the sexes. However, provided there has been no change in the relative risk of CHD in male and female non-smokers over time, we can use the above formulae to predict the magnitude of the shift in the sex ratio of CHD over time. Thus, given estimates of α and β and knowledge of X and K for each sex for each year, we can plot the ratio

$$\frac{1 + \alpha X_m + \beta K_m}{1 + \alpha X_f + \beta K_f}$$

(the subscripts indicate sex) over time and can compare with the plot of heart disease death rates.

Data on smoking

Since the excess risk of smokers is more marked in younger age groups, since epidemiological data are not very reliable below age 35 and since data on smoking trends are conveniently available for these

age groups, it was decided to concentrate on the age groups 35-49 and 50-59. Relevant data on weekly cigarette consumption per adult and on percentages of ex-smokers are given in Table 1 and 2 for the years 1956-1984. In the case of Table 2 data for some years were missing, but it seems clear that using simple linear interpolation would be adequate to fill these gaps. Similarly, for the years 1976-1984 where the data are for age groups 35-49 and 50-64, estimates for the 50-59 age group can reasonably be calculated by the interpolation formula:

$$A_{50\text{-}59} = A_{35\text{-}49} + \frac{12.5}{15}(A_{50\text{-}64} - A_{35\text{-}49})$$

$$= \frac{1}{6}(5A_{50\text{-}64} + A_{35\text{-}49})$$

where A is the statistic being interpolated and the subscripts refer to the age range, 12.5 and 15 being the differences in years between the centres of the pairs of age ranges.

Plausible estimates for α and β

Starting with the first 15 references in Appendix 1 (i.e. choosing prospective studies), rejecting duplicates (e.g. 2 is update of 1) and studies with small numbers of deaths available and only give results by broad age groups) we have the following estimates of relative risk for current smokers to never smokers:

Study Ref	Name	35-44	45-54	55-64	65-74
2	Hammond/Garfinkel		2.81	1.84	1.45
4	Rogot and Murray	4.44	7.00	1.80	1.60
5	Hirayama		1.66	1.52	
6	Hammond and Horn			1.74	
7	Doll and Peto	9.35	2.81	1.62	1.04
8	Best			1.76	1.59
10	Weir and Dunn	6.24	2.95	1.56	
12	Cederlof		1.85	1.70	
	Geometric mean	6.37	2.82	1.69	1.40

(N.B. some estimates are calculated by averaging, combination or linear interpolation since figures for precise age group are not available.)

The consistency of the estimates for the 55-64 year age group is remarkable. The Rogot and Murray figure for the 45-49 year age group is clearly discrepant and inspection of the raw data shows that there were relatively few deaths in this age group in the Veteran's study. Omitting it gives a G.M. of 2.35.

Data for women from prospective studies are less readily available. A summary of available data is given below:

Study Ref	Name	45-54	55-64	65-74
2	Hammond/Garfinkel	2.00	1.69	1.44
5	Hirayama	1.69	1.59	
11	Bush and Comstock	<---- 1.49	---->	
12	Cederlof		1.33	
	Geometric mean	1.84	1.53	1.44

The case-control data for women show large relative risks in the youngest age groups (Rosenberg, ref.18, RR = 5.28 for age <50;

Slone, ref.19, RR = 11.53 for age <45). It seems that the relative risks for females follow a similar pattern to males, the somewhat lower estimates perhaps reflecting their lower average consumption per head.

From the geometric means for men one can estimate that for the age groups 35-49 and 50-59 the associated relative risks are of the order 4.5 and 2.25 respectively. If one assumes that men who smoke smoke on the average 140 cigarettes per week, this means that for the age group 35-49 a sensible estimate of β would be about 0.025 (equivalent to RR 4.5) with a plausible range around 0.015 (RR 3.1) - 0.035 (RR 5.9) while for the age group 50-59 a sensible estimate would be about 0.010 (RR 2.4) with a plausible range around 0.005 (RR 1.7) - 0.015 (RR 3.1).

Some data on relative risks of ex-smokers to never smokers for men are summarized below:

Study	Age	Consumption	
Hammond & Garfinkel	40-79	1-19	1.16
		20+	1.28
Doll and Peto	All	All	1.29
Cederlof	All	All	1.5
Kahn			

Although these figures mainly refer to the whole age range it seems that it would not be unreasonable to choose a value for α of about 0.3 with a range of say 0.1-0.6 for our purposes.

Predicted changes in the sex ratio of CHD

Based on the data of Table 1 and 2, the above formulae and the assumed estimates and ranges for α and β Tables 3 and 4 presents predicted changes in the sex ratio of CHD. The figures for Table 3 show the effect of change of risk per number of cigarettes smoked on the assumptions, while the figures for Table 4 show the effect of change of the ex-smoker risk assumed. In both cases the assumed approximate best estimate appears on the left of the table. Both tables give separate estimates for the age-group 35-49 on the first page and for the age group 50-59 on the second. Table 3 gives estimates for every year whilst Table 4 gives estimates at 5 yearly intervals.

From Table 4 it can be seen that changes in the α (ex-smoker) coefficient over the range specified had virtually no effect on the predicted sex ratio of CHD. In only one case was the difference as much as 2 units (counting male/female equality as 100 units) and in many cases it did not effect results at all, when measured to the nearest unit. There seems no point in considering the effect of ex-smokers any further - indeed one could have set $\alpha = 0$ and got much the same answers.

From Table 3 it can be seen that the smoking data taken in conjunction with the epidemiological data predict that male rates would have declined markedly over the period, mainly over the last 10 years. Female rates on the other hand should have risen fairly steadily over the first 15 years stayed static for about 10 years and then have fallen off. The sex-ratio should have declined markedly,

with males having rates over 50% higher than females at the start of the period but having only a small excess at the end of the period. If one fits a linear regression to the sex ratio values and then computes the statistic

$$100 \times \frac{\text{fitted decline 1956-1984}}{\text{fitted 1956 value}}$$

as some sort of smoothed indicator of percentage decline over the period one comes up with the following answers:

Age 35-49

$\beta = 0.025$	-37.7%
$\beta = 0.015$	-31.0%
$\beta = 0.035$	-41.5%

Age 50-59

$\beta = 0.010$	-29.2%
$\beta = 0.005$	-18.8%
$\beta = 0.015$	-36.0%

Actual changes in the sex ratio of CHD

Table 5 gives data extracted from Registrar General's statistics on population and numbers of deaths from CHD by age, year and sex. On Prof. Wald's advice we have used ICD 420 + 422.1 for years 1956-1967 and ICD 410-414 subsequently.

From these figures, death rates per milion by sex were calculated for the two age groups 35-49 and 50-59 for each year together with their ratios. Results are presented in Table 6. From

these tables a number of points stand out:

(i) The pattern of change in male rates over time is highly discrepant from that predicted from changes in smoking patterns. Thus over the period 1956-1972 rates increased substantially whereas the smoking patterns suggested some decline. The observed decline since 1972, though in the same direction as predicted, is relatively more marked than predicted in the age group 35-49.

(ii) The female rates have shown a rise over the first 15 years or so followed by a final decline, particularly in the younger age groups in the last few years, but the magnitude of the rise is much more than predicted.

(iii) The sex ratios are much larger than predicted on the basis of smoking habits - this is not surprising given one knows that male non-smokers have much higher CHD rates than female non-smokers.

(iv) There has been some decline in the sex ratios, but proportionately clearly not by as much as predicted on the basis of trends in smoking habits. computing the same statistic as above for the percentage decline over the period, we arrive at:

Age 35-49	- 16.4%
Age 50-59	- 13.0%

Clearly these are outside the range of predicted answers. If the actual decline were to be predicted by trends in smoking habits, it can be shown that one would need a β value of about 0.005 for the age group 35-49 and a β value of about 0.003 for the age group 50-59.

In other words, we have a situation where for the age group 35-49 the epidemiology suggests a relative risk for a 20 a day current cigarette smoker of the order 4.5, whereas the trends in CHD ratios suggest a relative risk of the order 1.7. For the age group 50-59 the epidemiology suggests around 2.4, while the trends in CHD ratios suggest 1.42.

What do the results mean?

From the previous paragraph, one can infer that if all other factors have not shown any relative shift for the 2 sexes, the change in CHD sex ratio observed is very much less than would have been expected from trends in smoking habits coupled with epidemiological data on the magnitude of the relative risk of CHD in smokers and non-smokers. If all other factors have not changed, in order to explain the results one would have to assume that most of the excess risk seen in smokers is not actually due to smoking at all but due to some characteristic in which smokers differ. To fit the data one would have to assume that only about 20% of the observed excess risk seen in smokers in the age group 35-49 is actually due to smoking with a corresponding figure for the age group 50-59 about 30%.

However, is it reasonable to assume that other factors have not changed? Theoretically part of the discrepancy might be explained if

there is some other CHD risk factor for which there has been a relative change in the 2 sexes over time. This relative change must have been favourable for women so that the pill cannot be an explanation - indeed taking account of it heightens the descrepancy. One might perhaps imagine that women rather than men have tended towards the healthy living - healthy diet - exercise vogue particularly recommended in women's magazines but one feels this is unlikely to be the explanation. Trends in diagnoses and cure of CHD should not be materially different for the two sexes - indeed an advantage of sex ratios is that effects of those factors on absolute rates should be cancelled out. Blood cholesterol is a major CHD risk factor - are there any good data on trends in the two sexes?

Superficially, there does not seem to be any CHD risk factor for which women, over the last 20 or 30 years, have obtained a substantial advantage over men. Clearly this needs to be considered much more by NW and his colleagues, who have a much wider view of CHD than I.

My general impression of the results is that one needs to know

(a) why male non-smokers have much higher risk of CHD than female non-smokers and

(b) why male risk of CHD rose so much between 1956 and 1972,

before one can understand the role of smoking and CHD. It seems to me that both (a) and (b) indicate the role of very important factors other than smoking, which might interact with smoking. It would also be of enormous value if one could get data on trends in CHD risk in non-smokers over time. An analysis for trends in lung cancer was carried out for the US based on the ACS million person study and the

Veteran's study. Such an analysis would be possible for CHD and might throw light on the problem.

Overall the analyses done to date point to substantial anomalies that need explanation but no obvious solution. Certainly the conclusion that smoking is the all important risk factor for CHD in young age groups seems open to question.

TABLE 1

Weekly number of manufactured cigarettes per adult - UK

Year	Men		Women	
	35-49	50-59	35-49	50-59
1956	94	79	39	27
1957	94	79	41	28
1958	95	84	44	30
1959	90	89	47	32
1960	97	89	44	30
1961	91	85	46	34
1962	86	84	46	36
1963	86	77	54	37
1964	87	77	51	35
1965	80	74	49	41
1966	80	71	53	38
1967	85	72	50	44
1968	85	75	51	42
1969	82	77	52	44
1970	86	74	53	46
1971	84	70	57	46
1972	88	72	59	44
1973	88	75	63	56
1974	87	76	66	57
1975	77	83	61	50
	35-49	50-64	35-49	50-64
1975	77	81	61	46
1976	75	75	61	53
1977	70	64	61	54
1978	73	63	62	45
1979	70	61	58	46
1980	73	67	55	55
1981	55	50	60	44
1982	58	48	51	46
1983	56	51	50	44
1984	55	49	47	40

TABLE 2

Percentages of ex-smokers - UK

Year	Men		Women	
	35-49	50-59	35-49	50-59
1956	11	14	9	7
1957				
1958	14	15	9	7
1959				
1960				
1961	14	18	7	8
1962				
1963	16	18	9	6
1964				
1965	16	19	9	9
1966				
1967				
1968	14	18	10	12
1969				
1970				
1971	17	23	12	14
1972	14	19	10	13
1973	16	21	9	17
1974	15	20	9	15
1975	19	21	11	15
	35-49	50-64	35-49	50-64
1975	19	22	11	15
1976	18	23	12	18
1977	19	27	13	18
1978	20	25	12	19
1979	19	27	14	18
1980	19	25	14	17
1981	21	31	16	21
1982	22	33	16	22
1983	23	31	18	23
1984	22	29	16	20

TABLE 3

Predicted change in risk of CHD (relative to a population of 100% non-smokers = 100) showing effects of variation in β

Age : 35-49

	α = 0.3, β = 0.025			α = 0.3, β = 0.015			α = 0.3, β = 0.035		
	M	F	M/F (x100)	M	F	M/F (x100)	M	F	M/F (x100)
1956	338.3	200.2	169	244.3	161.2	152	432.3	239.2	181
1957	338.8	205.2	165	244.8	164.2	149	432.8	246.2	176
1958	341.7	212.7	161	246.7	168.7	146	436.7	256.7	170
1959	329.2	220.0	150	239.2	173.0	138	419.2	267.0	157
1960	346.7	212.3	163	249.7	168.3	148	443.7	256.3	173
1961	331.7	217.1	153	240.7	169.1	142	422.7	263.1	161
1962	319.5	217.4	147	233.5	169.4	138	405.5	263.4	154
1963	319.8	237.7	135	233.8	183.7	127	405.8	291.7	139
1964	322.3	230.2	140	235.3	179.2	131	409.3	281.2	146
1965	304.8	225.2	135	224.8	176.2	128	384.8	274.2	140
1966	304.6	235.3	129	224.6	182.3	123	384.6	288.3	133
1967	316.9	227.9	139	231.9	177.9	130	401.9	277.9	145
1968	316.7	230.5	137	231.7	179.5	129	401.7	281.5	143
1969	309.5	233.2	133	227.5	181.2	126	391.5	285.2	137
1970	319.8	235.9	136	233.8	182.9	128	405.8	288.9	140
1971	315.1	246.1	128	231.1	189.1	122	399.1	303.1	132
1972	324.2	250.5	129	236.2	191.5	123	412.2	309.5	133
1973	324.8	260.2	125	236.8	197.2	120	412.8	323.2	128
1974	322.0	267.7	120	235.0	201.7	117	409.0	333.7	123
1975	298.2	255.8	117	221.2	194.8	114	375.2	316.8	118
1976	292.9	256.1	114	217.9	195.1	112	367.9	317.1	116
1977	280.7	256.4	109	210.7	195.4	108	350.7	317.4	110
1978	288.5	258.6	112	215.5	196.6	110	361.5	320.6	113
1979	280.7	249.2	113	210.7	190.2	111	350.7	307.2	114
1980	288.2	241.7	119	215.2	186.7	115	361.2	296.7	122
1981	243.8	254.8	96	188.8	194.8	97	298.8	314.8	95
1982	251.6	232.3	108	195.6	181.3	108	309.6	283.3	109
1983	246.9	230.4	107	190.9	180.4	106	302.9	280.4	108
1984	244.1	222.3	110	189.1	175.3	108	299.1	269.3	111

TABLE 3 (continued)

Predicted change in risk of CHD (relative to a population of 100% non-smokers = 100) showing effects of variation in β

Age : 50-59

	α = 0.3 β = 0.010			α = 0.3 β = 0.005			α = 0.3 β = 0.015		
	M	F	M/F (x100)	M	F	M/F (x100)	M	F	M/F (x100)
1956	183.2	129.1	142	143.7	115.6	124	222.7	142.6	156
1957	183.4	130.1	141	143.9	116.1	124	222.9	144.1	155
1958	188.5	132.1	143	146.5	117.1	125	230.5	147.1	157
1959	193.8	134.2	144	149.3	118.2	126	238.3	150.2	159
1960	194.1	132.3	147	149.6	117.3	128	238.6	147.3	162
1961	190.4	136.4	140	147.9	119.4	124	232.9	153.4	152
1962	189.4	138.1	137	147.4	120.1	123	231.4	156.1	148
1963	182.4	138.8	131	143.9	120.3	120	220.9	157.3	140
1964	182.6	137.3	133	144.1	119.8	120	221.1	154.8	143
1965	179.7	143.7	125	142.7	123.2	116	216.7	164.2	132
1966	176.6	141.0	125	141.1	122.0	116	212.1	160.0	133
1967	177.5	147.3	121	141.5	125.3	113	213.5	169.3	126
1968	180.4	145.6	124	142.9	124.6	115	217.9	166.6	131
1969	182.9	147.8	124	144.4	125.8	115	221.4	169.8	130
1970	180.4	150.0	120	143.4	127.0	113	217.4	173.0	126
1971	176.9	150.2	118	141.9	127.2	112	211.9	173.2	122
1972	177.7	148.3	120	141.7	125.9	113	213.7	169.9	126
1973	181.3	161.1	113	143.8	133.1	108	218.8	189.1	116
1974	182.0	161.5	113	144.0	133.0	108	220.0	190.0	116
1975	189.3	154.5	123	147.8	129.5	114	230.8	179.5	129
1976	181.7	159.4	114	144.2	132.3	109	219.2	186.6	117
1977	172.7	160.4	108	140.2	132.8	106	205.2	188.0	109
1978	172.0	153.2	112	139.6	129.3	108	204.3	177.1	115
1979	170.2	153.2	111	139.0	129.2	108	201.5	177.2	114
1980	175.2	160.0	110	141.2	132.5	107	209.2	187.5	112
1981	159.6	152.8	104	134.2	129.4	104	185.0	176.1	105
1982	159.1	153.1	104	134.2	129.7	103	183.9	176.5	104
1983	160.7	151.7	106	134.8	129.2	104	186.6	174.2	107
1984	158.4	147.0	108	133.4	126.4	106	183.4	167.6	109

TABLE 4

Predicted change in risk of CHD (relative to a population of 100% non-smokers = 100) showing effects of variation in α

Age : 35-49

	α = 0.3, β = 0.025			α = 0.1, β = 0.025			α = 0.6, β = 0.025		
	M	F	M/F (x100)	M	F	M/F (x100)	M	F	M/F (x100)
1956	338.3	200.2	169	336.1	198.4	169	341.6	202.9	168
1960	346.7	212.3	163	343.9	210.8	163	350.9	214.6	164
1965	304.8	225.2	135	301.6	223.4	135	309.6	227.9	136
1970	319.8	235.9	136	316.6	233.6	136	324.6	239.3	136
1975	298.2	255.8	117	294.4	253.6	116	303.9	259.1	117
1980	288.2	241.7	119	284.4	238.9	119	293.9	245.9	120
1984	244.1	222.3	110	239.7	219.1	109	250.7	227.1	110

TABLE 4 (continued)

Predicted change in risk of CHD (relative to a population of 100% non-smokers = 100) showing effects of variation in α

Age : 50-59

	α = 0.3, β = 0.010			α = 0.1, β = 0.010			α = 0.6, β = 0.010		
	M	F	M/F (x100)	M	F	M/F (x100)	M	F	M/F (x100)
1956	183.2	129.1	142	180.4	127.7	141	187.4	131.2	143
1960	194.1	132.3	147	190.7	130.8	146	199.2	134.6	148
1965	179.7	143.7	125	175.9	141.9	124	185.5	146.4	127
1970	180.4	150.0	120	176.1	147.3	120	186.8	154.0	121
1975	189.3	154.5	123	185.1	151.5	122	195.6	159.0	123
1980	175.2	160.0	110	170.8	156.7	109	182.4	165.0	111
1984	158.4	147.0	108	152.8	143.1	107	166.8	152.8	109

TABLE 5

Population (thousands) and numbers of deaths from CHD by age, sex and year - England and Wales

		35-39		40-44		45-49		50-54		55-59	
		M	F	M	F	M	F	M	F	M	F
1956	p	1516	1561	1603	1655	1626	1670	1503	1593	1225	1436
	420	346	40	838	118	1918	274	3574	642	5069	1300
	422.1	3	-	8	3	15	9	47	22	138	87
1957	p	1570	1615	1554	1612	1623	1666	1524	1607	1271	1457
	420	340	38	865	114	1944	303	3667	622	5384	1307
	422.1	2	-	3	2	17	6	44	26	110	72
1958	p	1636	1681	1474	1531	1618	1662	1543	1622	1314	1479
	420	409	46	912	135	2056	346	3947	705	6016	1461
	422.1	3	-	8	2	13	3	43	17	115	75
1959	p	1705	1752	1390	1443	1617	1665	1554	1630	1354	1503
	420	476	50	853	126	2017	310	3921	706	6087	1509
	422.1	2	-	2	-	7	7	40	21	89	55
1960	p	1639	1680	1446	1499	1613	1665	1565	1636	1387	1525
	420	523	59	965	134	2214	321	4067	739	6465	1597
	422.1	-	1	3	3	11	5	38	18	94	65
1961	p	1597	1621	1518	1554	1594	1641	1571	1639	1415	1547
	420	490	57	1001	150	2273	337	4178	739	6694	1596
	422.1	-	-	6	-	10	7	23	16	89	52
1962	p	1570	1578	1587	1604	1562	1605	1570	1635	1434	1562
	420	538	73	1176	157	2341	349	4339	811	7183	1703
	422.1	1	1	7	5	8	6	31	18	83	48
1963	p	1558	1536	1664	1667	1467	1523	1552	1639	1443	1565
	420	502	78	1312	179	2347	363	4634	773	7502	1811
	422.1	4	-	5	-	12	8	29	25	87	50
1964	p	1542	1507	1707	1706	1416	1459	1553	1642	1456	1574
	420	563	65	1374	203	2339	376	4637	766	7466	1775
	422.1	6	-	5	-	13	8	30	9	69	45
1965	p	1528	1487	1669	1661	1445	1477	1550	1639	1464	1582
	420	596	68	1486	226	2445	369	4857	856	7608	1875
	422.1	-	1	1	2	11	4	24	18	64	44
1966	p	1524	1473	1613	1598	1510	1535	1524	1610	1469	1589
	420	540	77	1409	184	2555	401	4707	870	7689	1884
	422.1	-	-	8	3	14	4	26	9	56	31

TABLE 5 (continued)

Population (thousands) and numbers of deaths from CHD by age, sex and year - England and Wales

		35-39		40-44		45-49		50-54		55-59	
		M	F	M	F	M	F	M	F	M	F
1967	p	1520	1455	1574	1552	1567	1584	1485	1567	1466	1589
	420	494	67	1414	206	2722	397	4434	784	7667	1790
	422.1	2	-	1	-	15	10	17	12	58	29
1968	p	1509	1443	1541	1522	1626	1645	1412	1489	1458	1585
	410-414	470	77	1463	240	2883	443	4563	870	8074	1816
1969	p	1496	1425	1519	1492	1667	1681	1360	1425	1457	1588
	410-414	457	85	1356	232	3255	479	4464	889	7891	1896
1970	p	1488	1411	1502	1468	1630	1637	1387	1442	1452	1584
	410-414	528	84	1378	208	3086	446	4729	845	8127	1912
1971	p	1412	1380	1465	1464	1539	1570	1418	1486	1427	1534
	410-414	497	65	1436	201	3153	467	4900	933	7850	1890
1972	p	1418	1378	1454	1446	1505	1525	1475	1546	1385	1489
	410-414	523	75	1381	211	3232	509	5408	1032	8011	2034
1973	p	1431	1387	1438	1424	1485	1498	1547	1616	1315	1419
	410-414	503	64	1340	234	3120	546	5567	1069	7553	1876
1974	p	1447	1401	1421	1397	1464	1474	1605	1668	1244	1344
	410-414	488	79	1367	229	2967	505	5916	1105	7134	1883
1975	p	1458	1408	1405	1375	1448	1456	1543	1595	1291	1391
	410-414	446	89	1290	202	2914	473	5783	1072	7218	1902
1976	p	1437	1394	1394	1360	1433	1440	1497	1540	1344	1446
	410-414	472	72	1192	230	2701	491	5275	1027	7749	1936
1977	p	1432	1394	1397	1354	1421	1422	1458	1496	1397	1500
	410-414	451	73	1233	193	2665	462	5176	993	7889	1990
1978	p	1454	1420	1412	1369	1406	1404	1429	1462	1461	1563
	410-414	521	84	1243	203	2667	445	5249	1045	8462	2163
1979	p	1494	1461	1427	1387	1390	1379	1410	1441	1513	1612
	410-414	456	64	1153	192	2628	445	5106	1052	8804	2217
1980	p	1527	1499	1438	1397	1377	1358	1394	1426	1452	1542
	410-414	455	67	1154	178	2425	368	4849	906	8382	2177
1981	p	1614	1590	1427	1405	1379	1360	1408	1431	1433	1508
	410-414	463	74	1083	181	2352	372	4601	915	7802	2027

TABLE 5 (continued)

Population (thousands) and numbers of deaths from CHD by age, sex and year - England and Wales

		35-39		40-44		45-49		50-54		55-59	
		M	F	M	F	M	F	M	F	M	F
1982	p	1735	1710	1417	1397	1369	1352	1381	1398	1382	1446
	410-414	428	72	1018	152	2152	330	4353	872	7404	1896
1983	p	1798	1784	1445	1421	1384	1366	1368	1380	1363	1417
	410-414	453	78	985	145	2263	353	4148	859	7237	1961
1984	p	1830	1817	1488	1462	1401	1385	1351	1358	1347	1397
	410-414	404	61	928	140	2110	340	3877	805	7030	1874

Key : p = population (thousands)

420,422.1,410-414 = number of deaths from relevant ICD codes.

TABLE 6

CHD death rates per million and sex ratios - England and Wales

	35-49			50-59		
	Male Rate	Female Rate	Ratio	Male Rate	Female Rate	Ratio
1956	659.2	90.0	7.25	3236	677.1	4.78
1957	668.0	94.6	7.06	3293	661.6	4.97
1958	719.3	109.2	6.59	3543	728.2	4.87
1959	712.4	101.4	7.02	3486	731.2	4.77
1960	791.0	108.0	7.33	3613	765.3	4.72
1961	802.7	114.4	7.02	3679	754.2	4.88
1962	862.7	123.5	6.99	3874	807.0	4.80
1963	891.9	132.9	6.71	4091	829.9	4.93
1964	921.8	139.6	6.61	4055	806.9	5.03
1965	977.8	144.9	6.75	4165	867.1	4.80
1966	974.0	145.2	6.71	4169	873.4	4.77
1967	997.2	148.1	6.73	4126	828.6	4.98
1968	1029.9	164.9	6.25	4403	873.8	5.04
1969	1082.4	173.1	6.25	4386	924.3	4.74
1970	1080.5	163.4	6.61	4528	911.1	4.97
1971	1151.7	166.1	6.94	4482	934.8	4.79
1972	1173.4	182.8	6.42	4692	1010.2	4.64
1973	1139.9	195.9	5.82	4584	970.3	4.72
1974	1113.1	190.3	5.85	4581	992.0	4.62
1975	1078.6	180.2	5.98	4588	996.0	4.61
1976	1023.7	189.1	5.41	4584	992.3	4.62
1977	1023.3	174.6	5.86	4576	995.7	4.60
1978	1037.2	174.6	5.94	4744	1060.5	4.47
1979	982.8	165.8	5.93	4756	1071.1	4.44
1980	929.1	144.1	6.45	4649	1038.7	4.48
1981	881.9	144.0	6.13	4366	1001.0	4.36
1982	795.8	124.2	6.41	4255	973.3	4.37
1983	799.9	126.0	6.35	4169	1008.2	4.13
1984	729.4	116.0	6.29	4043	972.4	4.16

N.B. Line marks change in cause of death classification

Coronary heart disease mortality ratios and rates by age and smoking habit

Study (ref no)		Mortality ratio and (rate)[1] by age				
ACS 25-State (1,2)		35-44	45-54	55-64	65-74	75-84
male	NS	1.00(---)	1.00(150)	1.00(542)	1.00(1400)	1.00(3132)
	SM	--- (148)	2.81(422)	1.84(996)	1.45(2025)	1.24(3871)
female	NS	1.00	1.00(33)	1.00(163)	1.00(653)	1.00(1973)
	SM	---	2.00(66)	1.69(275)	1.44(941)	1.19(2349)
US Veterans (3,4)		35-44	45-54	55-64	65-74	75-84
male	NS	1.00(18)	1.00(50)	1.00(501)	1.00(1015)	1.00(2216)
	SM	4.44(80)	7.00(353)	1.80(880)	1.60(1659)	1.20(2683)
Japanese (5)		40-49	50-59	60-69	>70	
male	NS	1.00(8.0)	1.00(48.3)	1.00(105.5)	1.00(189.6)	
	SM	3.09(24.7)	1.42(68.8)	1.62(170.7)	1.71(323.8)	
female	NS	1.00(6.1)	1.00(23.6)	1.00(79.5)	1.00(109.4)	
	SM	1.46(8.9)	1.75(41.2)	1.54(122.5)	1.44(157.9)	
ACS 9 State (6)		50-54	55-59	60-64	65-69	
male	NS	1.00(271)	1.00(431)	1.00(733)	1.00(1247)	
	SM	1.92(521)	1.85(801)	1.66(1219)	1.41(1759)	
Brit Physicians (7)		<45	45-54	55-64	65-74	>75
male	NS	1.00(7.0)	1.00(118)	1.00(531)	1.00(1634)	1.00(2432)
	SM	9.35(65)	2.81(332)	1.62(859)	1.04(1704)	2.39(5800)
Can Veterans (8)		55-59	60-64	65-69	70-74	75-79
male	NS	1.00	1.00	1.00	1.00	1.00
	SM	1.90	1.61	1.38	1.79	1.45
Swiss Doctors (9)		35-54	55-65	66-74	>75	
male	NS	1.00	1.00	1.00	1.00	
	SM	2.30	2.20	1.90	1.00	

Calif 9 Occup (10)		35-44	45-54	55-64	65-69
male	NS	1.00	1.00	1.00	1.00
	SM	6.24	2.95	1.56	1.24
White Females (11)		25-44	45-64	65-74	
	NS	1.00(2.1)[2]	1.00(36.2)	1.00(163.1)	
	SM	2.21(6.9)	1.49(53.8)	0.17(135.3)	
Swedish (12)		40-49	50-59	60-69	
male	NS	1.00(5.8)[3]	1.00(29.7)	1.00(97.9)	
	SM	2.60	1.70	1.70	
female	NS	1.00(0.5)	1.00(10.0)	1.00(55.8)	
	SM	---------	2.60	1.10	
Framingham (13)		41-55	>55		
male	NS	1.00(119)[3]	1.00(269)		
	SM	1.90(208)	1.07(261)		
Former College Students (14)		30-44	45-54	55-69	
male	NS	1.00	1.00	1.00	
	SM	1.80(88)	1.60(163)	1.20(134)[5]	
Albany + Fram. (15)		40-49			
male	NS	1.00(209)[2]			
	SM	4.3 (723)			
Middle-Aged Smokers(16)		35-54	person years studied (whites only)		
male	NS	1.00(1.13)[4]	2571		
	SM	4.58(5.48)	5129		
female	NS	1.00(0.31)	6000		
	SM	4.90(1.68)	5845		

[1]Mortality rate per 100,000 unless otherwise stated

[2]Mortality rate per 10,000

[3]Mortality rate per 1000

[4]Mortality rate per 1000 person years

[5]Actual number of deaths

CORONARY HEART DISEASE MORBIDITY RATIOS AND RATES BY AGE

PROSPECTIVE STUDIES

REF NO	STUDY AND AUTHOR	SEX	MORBIDITY RATIO AND (RATE) BY AGE	
			<55	>55
	Framingham	male NS	1.00(59)[1]	1.00(147)
		SM	1.87(248)	1.12(326)
13	Castelli et al			
			39-49	50-59
	Western Collaborative Group Study	male NS	1.00(2.9)[2]	1.00(11.0)
		SM	3.09(8.9)	1.88(20.5)
17	Jenkins et al~			

CASE CONTROL STUDIES

REF NO	STUDY AND AUTHOR	SEX	MORBIDITY RATIO BY AGE		
			<50		
	Myocardial Infarction in Women Under 50	female	5.28	255 women with MI; 802 controls	
18	Rosenberg et al				
			<45	45-49	55 women with MI; 220 controls
	Smoking and MI in Young Women	female	11.53	6.87	
19	Slone et al				
			30-44	45-54	502 men with MI; 835 controls
	Risk of MI in Young Men	male	5.54	1.75	
20	Kaufman et al				

[1]MI rate per 1000

[2]Annual rate CHD per 1000 men at risk

Coronary heart disease and smoking: outline of major prospective studies and selected case contol studies

AUTHOR (Reference)	SUBJECTS	POPULATION SIZE (female)	AGE RANGE	YEAR OF ENROLLMENT	YEARS OF FOLLOW-UP REPORTED	NUMBER OF DEATHS *CHD M/F	EXPERIENCE: PERSON YEARS	SMOKERS	NON-SMOKERS
Hammond (1)	males and females 25 states	1,003,229 (562,671)	20-85+	1959-60	4	25,895	1,639,211(men) 2,125,360(wom)	current regular cigarette	never smoked regularly
Hammond and Garfinkel (2)	males and females 25 states	804,409 (445,875)	40-79	1959-60	6	*10771/4048		as above	
Kahn (3) Rogot and Murray (4)	U S Veterans	293,658 (<1%)	35-84	1954,1957	13,10	87,000 *34,874	8,000,000	current cigarette smoker	never or occasional smoker
Hirayama (5)	Japanese in 25 health districts	265,000 (142,857)	40+	1966	13	21,000 *3351/2653	2,000,000		
Hammond and Horn (6)	white males in 9 states	187,783	50-69	1952	4	11870 *5297	667,753	cigarettes only	never smoked regularly
Doll and Peto (7)	British doctors	34,400	20-85+	1951	20	10,072 *3191	600,000	regular cigarette smoker	non-smoker or never > 1/da for > 1 yr
Best (8)	Canadian veterans	78,000	30-90	1955	6	11,000 *3405		cigarettes only	never smoked
Gsell et al (9)	Swiss Physicians	3749	35-75+	1955	18	*280			
Weir and Dunn (10)	California males in 9 occupations	68,153	35-64	1954	5-8	4706 *1718	482,658	current & ex cig. smoker	never reg. cigarettes includes pipe & cigar
Bush and Comstock (11)	white female Washington County	(23,572)	25-74	1963	12	2609 */852		current cigarette	never smoked
Cederlof et al (12)	Swedish probability sample	52,786 (27,342)	18-69	1963	10	5655 *1792/427	550,000	current cigarette	never smoked
Castelli et al (13)	selected males: Framingham	1605	41-74	1963	14	*115		cigarette smoker	non-smoker
Paffenbarger and Wing (14)	former male university students	50,000	30-69	1939-1950	17-51	1146			
Doyle et al (15)	Albany and Framingham cohorts	4120	30-62	1949 (F) 1952 (A)	10 (F) 8 (A)	249 *223		cigarette smoker	never smoked
Freidman et al (16)	health insurance group members	1129 white men 2328 " women	35-54	1964	11	88/62 * 36/14	men NS 2571[1] SM 5129 wo NS 6000 SM 5845	cigarettes	never smokers of cigarettes no tobacco now

Morbidity Studies

Jenkins et al (17)	employed men	3182	39-59	1960-61	4.5			current cigarette smoker	never smoked
Rosenberg et al (18)	women with myocardial infarction	255 women 802 controls	25-49	1976-1979	2			current cigarette	never smoked
Slone et al (19)	women with myocardial infarction	55 women 220 controls	< 49	1976	1.5			current cigarette	never or ex smoker
Kaufman et al (20)	men with 1st myocardial infarction	502 cases 835 controls	30-54	1980	1981			current cigarette	never smoked

[1]Figures selected for whites only as no sex differentiation in figures given for total study population

References: Smoking and Coronary Heart Disease

1. HAMMOND, E.C. Smoking in relation to the death rates of one million men and women. In: Haenzel W. (Editor). Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases. National Cancer Institute Monograph No. 19. U S Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, National Cancer Institute, January 1966, pp.127-204.

2. HAMMOND, E.C., GARFINKEL, L. Coronary heart disease, stroke, and aortic aneurysm. Factors in etiology. Archives of Environmental Health 19(2):167-182, August 1969.

3. KAHN, H.A. The Dorn study of smoking and mortality among U.S. veterans: report on eight and one-half years of observation. In: Haenzel, W. (Editor). Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases. National Cancer Institute Monograph No. 19. U.S. Department of Health, Education and Welfare, Public Health Service, National Institute of Health, National Cancer Institute, January 1966, pp.1-125

4. ROGOT, E., MURRAY, J.L. Smoking and causes of death among U.S. Veterans:16 years of observation. Public Health Reports 95(3): 213-222, May-June 1980.

5. HIRAYAMA, T. Kitsuen to domyaku koka to no kanei ni kansuru ekigakuteki kenkyu. [An epidemiological study on smoking and drinking and chronic diseases.] Special Issue- Alcohol, Tobacco and Adult Diseases 12(2):11-19, 1981.

6. HAMMOND, E.C., Horn, D. Smoking and death rates- Report on 44 months of follow-up of 187,783 men: II. Death rates by cause. Journal of the American Medical Association 166(11): 1294-1308, March 15, 1958.

7. DOLL, R., PETO, R. Mortality in relation to smoking:20 years observations' on male British doctors. British Medical Journal 2(6051): 1525-1536, December 25, 1976.

8. BEST, E.W.R. A Canadian Study of Smoking and Health. Ottawa, Department of National Health and Welfare, Epidemiology Division, Health Services Branch, Biostatistics Division, Research and Statistics Directorate, 1966, 137pp.

9. GSELL, O., ABELIN, T., WIELTCHNIG, E. Rauchen und Mortalitat der Schweizer Arzte: Resultata nach 18 Jahriger Beobachtung. [Smoking and mortality of Swiss physicians: Results after 18 years of observation.] Bulletin der Schweizerischen Akademie der Medizinischen Wissenschaften 35(1-3): 71-82, March 1979.

10. WEIR,J.M., DUNN,J.E.,Jr. Smoking and mortality: A prospective study. Cancer 25(1):105-112,January 1970.

11. BUSH,T.L., COMSTOCK,G.W. Smoking and cardiovascular mortality in women.American Journal of Epidemiology 118(4):480-488,1983.

12. CEDERLOF,R.,FRIBERG,L.,HRUBEC,Z.LORICH,U.The Relationship of Smoking and Some Social Covariables to Mortality and Cancer Morbidity. A ten-year follow-up in a probability sample of 55,000 Swedish subjects, age 18-69,Part 1 and Part 2. Stockholm,Sweden, Department of Environmental Hygiene,The Karolinska Institute, 1975,91 pp.

13. CASTELLI,W.P.,GARRISON,R.J.,DAWBER,T.R.,McNAMARA,P.M.,FEINLEIB,M., KANNEL,W.B.The filter cigarette and coronary heart disease: The Framingham study.Lancet 2(8238):109-113,July 18,1981.

14. PAFFENBARGER,R.S.,WING,A.L.Chronic disease in former college students.American Journal of Epidemiology(90):527-535,1969.

15. DOYLE,J.T.,DAWBER,T.R.KANNEL,W.B.HESLIN,A.S.KAHN,H.A.The relationship of cigarette smoking to coronary heart disease. The second report of the combined experience of the Albany,NY, and Framingham,Mass.,studies. Journal of the American Medical Association 190(10):108-112,December7,1964.

16. FRIEDMAN,G.D.,DALES,L.G.,URY,H.K.Mortality in middle-aged smokers and nonsmokers.New England Journal of Medicine 300(5):213-217, February 1,1979.

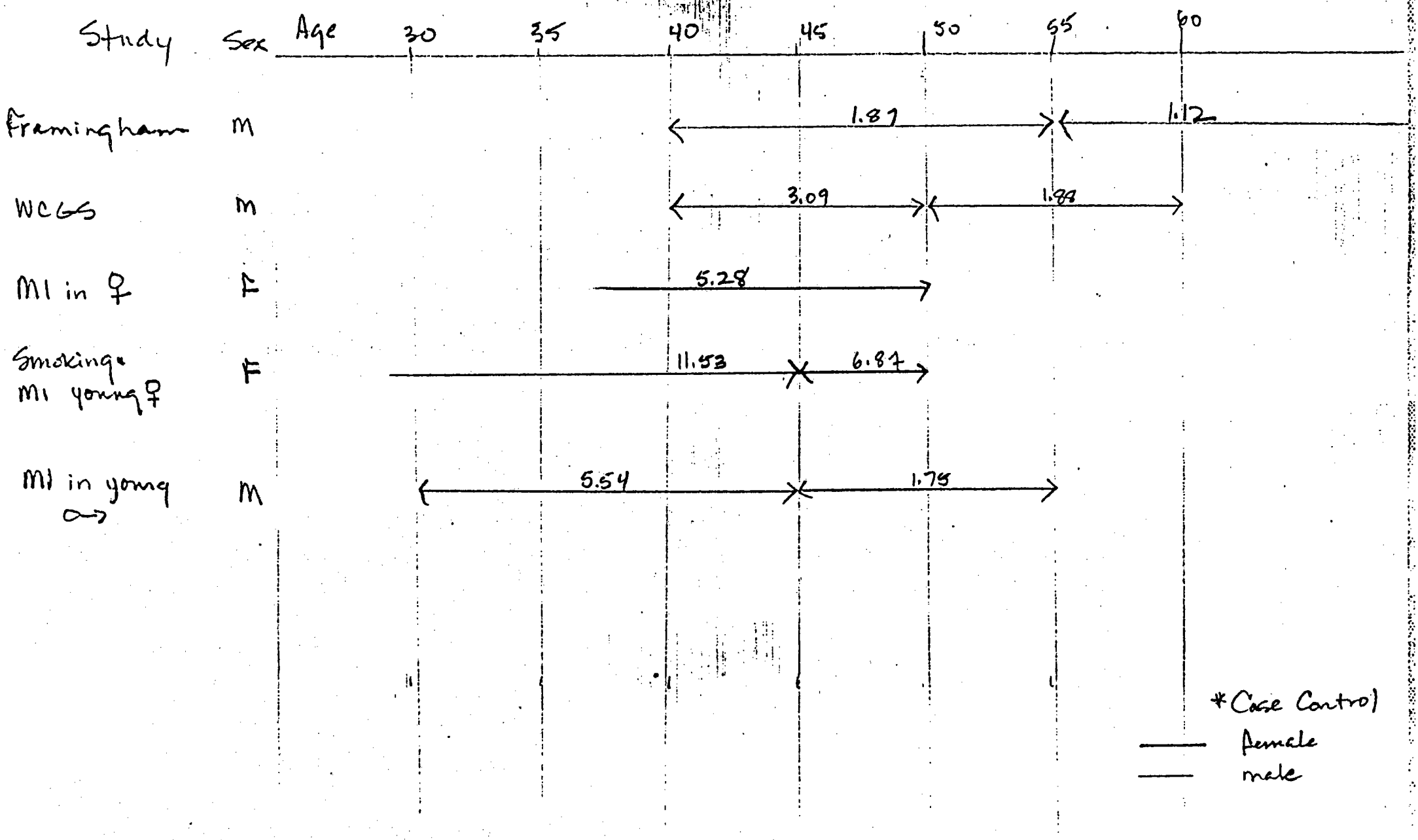
17. JENKINS,C.D.,ROSENMAN,R.H.,ZYZANSKI,S.J. Cigarette smoking. Its relationship to coronary heart disease and related risk factors in the Western Collaborative Group Study. Circulation 38(6):1140-1155,December 1968.

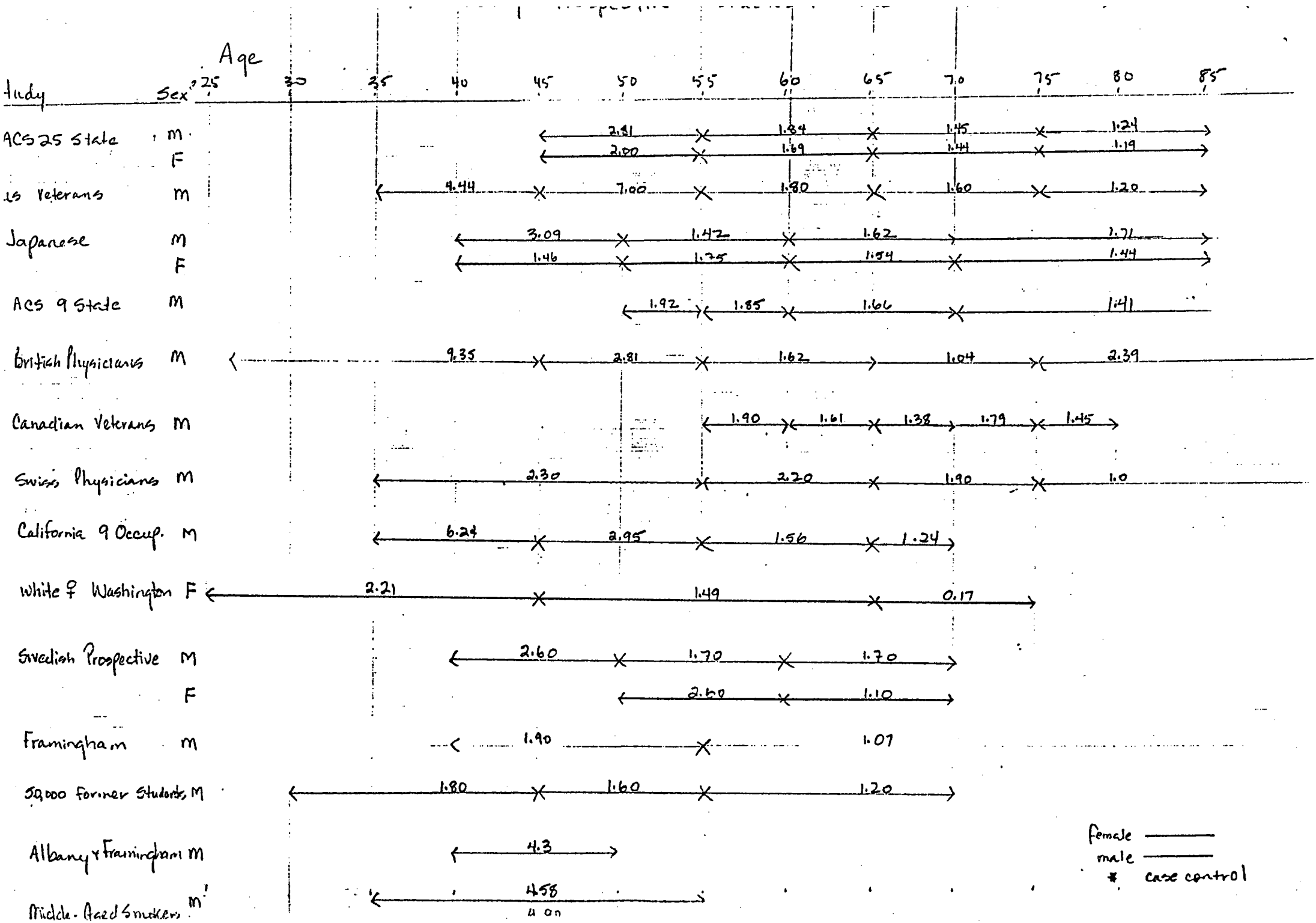
18. ROSENBERG,L.,MILLER,D.R.,KAUFMAN,D.W.,HELMRICH,S.P.,VAN DE CARR,M.D.,STOLLEY,P.D.,SHAPIRO,M.B. Myocardial Infarction in women under 50 years of age. Journal of the American Medical Association 250(20):2801-2806,November 25,1983.

19. SLONE,D.,SHAPIRO,S.,ROSENBERG,L.,KAUFMAN,D.W.,HARTZ,S.C.,ROSSI,A.C., STOLLEY,P.D.,MIETTINEN,O.S.Relation of cigarette smoking to myocardial infarction in young women. New England Journal of Medicine 298(23):1273-1276,June 8,1978.

20. KAUFMAN,D.W.,HELMRICH,S.P.,ROSENBERG,L.,MIETTINEN,O.S.,SHAPIRO,S. Nicotine and carbon monoxide content of cigarette smoke and the risk of myocardial infarction in young men. New England Journal of Medicine 308(8):409-413,February 24,2983.

Morbidity Prospective & Case Control Studies




Age
Study
Sex
25
30
35
40
45
50
55
60
65
70
75
80
85
ACS 25 State
M
2.91
1.84
1.45
1.24
F
2.00
1.69
1.44
1.19
US Veterans
M
4.44
7.00
1.80
1.60
1.20
Japanese
M
3.09
1.42
1.62
1.71
F
1.46
1.75
1.84
1.44
ACS 9 State
M
1.92
1.85
1.66
1.41
British Physicians
M
9.35
2.81
1.62
1.04
2.39
Canadian Veterans
M
1.90
1.61
1.38
1.79
1.45
Swiss Physicians
M
2.30
2.20
1.90
1.0
California 9 Occup.
M
6.24
2.95
1.56
1.24
White of Washington
F
2.21
1.49
0.17
Swedish Prospective
M
2.60
1.70
1.70
F
2.60
1.10
Framingham
M
1.90
1.07
50,000 former Students
M
1.80
1.60
1.20
Albany + Framingham
M
4.3
Middle-Aged Smokers
M
458
u on
female
male
* case control