PAPERS AND ORIGINALS

Myocardial Infarction in Young Women with Special Reference to Oral Contraceptive Practice

J. I. MANN, M. P. VESSEY, MARGARET THOROGOOD, Sir RICHARD DOLL

British Medical Journal, 1975, 2, 241-245

Summary

Sixty-three women discharged from hospital with a diagnosis of myocardial infarction and 189 control patients were studied. All were under 45 years of age at the time of admission. Current oral contraceptive use, heavy cigarette smoking, treated hypertension and diabetes, pre-eclamptic toxaemia, and obesity were all reported by, and type II hyperlipoproteinaemia was found more often in, patients with myocardial infarction than their controls. The relationship between myocardial infarction and oral contraceptives could not be explained in terms of an association between the use of these preparations and the other factors. The combined effect of the risk factors was clearly synergistic.

Introduction

Oral contraceptives are apt to produce arterial as well as venous thrombosis.[1 2] Evidence about their role in myocardial infarction is, however, conflicting.[3] Myocardial infarction is uncommon in young women,[4] and little relevant information may be expected from any of the large prospective studies of this disease now in progress.[5 6] We therefore undertook a retrospective study of women under 45 years of age who survived a myocardial infarction as this method offered the possibility of obtaining information direct from enough patients to enable a definite conclusion to be reached. Several other factors are known to cause the disease, or are suspected of doing so, and we studied them also to see whether oral contraceptives acted independently or synergistically.

University of Oxford
J. I. MANN, M.B., PH.D., Lecturer in Social and Community Medicine
M. P. VESSEY, M.A., M.D., Professor of Social and Community Medicine
MARGARET THOROGOOD, B.SC., Research Assistant
SIR RICHARD DOLL, M.D., F.R.C.P., F.R.S., Regius Professor of Medicine

Patients and Methods

Married women under 45 years of age who had been treated for myocardial infarction during 1968-72 were identified in the discharge records of hospitals in two of the 15 hospital regions of England and Wales. All hospitals which treated general medical and surgical patients and had more than 300 beds were included in the study provided that a satisfactory diagnostic index had been maintained. Altogether 84 patients were identified from the records of 24 hospitals. Patients were included only when the diagnosis satisfied the criteria of the World Health Organization.[7] Sixteen of the patients had died in hospital and five had died subsequently. Only limited information could be obtained about these 21 patients and they were therefore excluded from the study. The ages of the remaining 63 patients ranged from 25 to 44 years, with a mean of 40·1 years. Fifty were classified according to the World Health Organization as having had "definite myocardial infarction," and 13 as having had "probable myocardial infarction." Nine had been admitted on a previous occasion for definite or suspected infarction.

Three other patients were taken as controls for each patient with infarction. They were selected at random from women who had been discharged after treatment for certain acute medical or surgical conditions or after certain elective surgical procedures, and matched each patient with infarction in respect of marital status, five-year age group, and year of admission. The conditions from which the control patients suffered are listed in table I.

TABLE I—*Medical and Surgical Conditions in Control Group*

	No. of Controls	
Acute medical conditions		44
Lobar pneumonia	14	
Infectious hepatitis	4	
Pyrexia of unknown origin	5	
Urinary tract infection	12	
Other	9	
Acute surgical conditions		96
Appendicitis	41	
Undiagnosed abdominal pain	13	
Acute cholecystitis	18	
Trauma	20	
Foreign body	2	
Renal colic	2	
Elective surgery		49
Excision of lipoma	22	
Excision of other benign tumours	8	
Dental extraction	12	
Haemorrhoidectomy	4	
Herniorrhaphy	3	
Total		189

Permission was obtained from hospital consultants and general practitioners to interview the patients in their homes. All the patients with infarction and 174 of the 189 control patients (92·1%) were traced. Those who had moved to inaccessible areas or who refused to see the interviewer were sent a postal questionnaire. In a few instances the general practitioner thought that the patient should not be interviewed. When this occurred, and also when a patient refused to be interviewed or to complete a postal questionnaire, the general practitioner gave the desired information. The numbers of patients investigated by each of these methods are shown in table II.

TABLE II—*Method of Data Collection from Whole Series of 63 Myocardial Infarction (M.I.) and 174 Control Patients*

	No. (%) of M.I. Patients	No. (%) of Controls
Interview with patient	53 (84·1)	134 (77·0)
Postal questionnaire completed by patient	4 (6·4)	23 (13·2)
Postal questionnaire completed by general practitioner	6 (9·5)	17 (9·8)
Total	63 (100·0)	174 (100·0)

The interviews and questionnaires were designed to obtain information on the patients' medical, obstetric, social, family, and contraceptive histories before the relevant admission to hospital. Physical examination was not carried out, but fasting blood samples were obtained for lipid analysis whenever possible. In all cases the sample was obtained more than six months after the infarction had occurred.

The statistical significance of the results was tested, when appropriate, by the method of Pike and Morrow[8] for the analysis of individually matched case-control studies. When the number of exposed patients was less than five Fisher's exact test was used instead. Standardized relative-risk estimates and summary χ^2 values were calculated by an exact maximum-likelihood method.[9]

Results

Information was sought from each patient about all the items included in this study but the response was not always complete. A general practitioner, for example, might have known whether his patient had been treated for hypertension without knowing the occupation of her husband or whether she smoked. The results for the different items, therefore, relate to different totals. With the exception of the blood lipid analyses all the totals varied between 84% and 95% of the patients with infarction and between 77% and 99% of the control patients.

The proportion of patients who had used oral contraceptives during the month before admission was significantly higher among the patients with infarction than among the controls ($P<0·001$) (table III), as was the proportion of those who had used oral contraceptives at any time ($P<0·01$). There was no appreciable difference between the two groups, however, in the proportions who had used oral contraceptives only at some time in the past (10·3% compared with 12·0%). The relative risk of admission for myocardial infarction in women who had been using oral contraceptives in the previous month compared with that in women who had never used them is estimated from these figures to be 4·5 to 1. None of the nine women who had had a previous myocardial infarction had ever used oral contraceptives, but two or more of the other risk factors mentioned below were present in all of them. The 17 patients with infarction who had been using oral contraceptives during the month before admission (table III) had been using them longer on average than the corresponding control patients, but the numbers were small and the difference could easily have been due to chance (88% of the patients with infarction and 76% of the controls had used these preparations for over 12 months).

TABLE III—*Oral Contraceptive Practice of Myocardial Infarction and Control Patients*

	No. (%) of M.I. Patients	No. (%) of Controls
Never used	35 (60·3)	132 (79·5)
Used during month before admission	17 (29·3)*	14 (8·4)*
Used only more than one month before admission	6 (10·3)	20 (12·0)
Total	58 (100·0)	166 (100·0)

*M.I. patients *v.* controls: χ^2 (1) = 13·58; $P<0·001$.

TABLE IV—*Cigarette-smoking Habits of Myocardial Infarction and Control Patients*

	No. (%) of M.I. Patients	No. (%) of Controls
Never smoked	12 (20·3)	60 (38·2)
Ex-smokers	2 (3·4)	14 (8·9)
1-14 cigarettes a day	12 (20·3)	50 (31·8)
15-19 cigarettes a day	7 (11·9)	11 (7·0)
20-24 cigarettes a day	17 (28·8)	18 (11·5)
25 or more cigarettes a day	9 (15·3)	4 (2·6)
Total	59 (100·0)	157 (100·0)

Test for linear trend among all smoking categories: χ^2 (1) = 20·63; $P<0·001$.

Cigarette smoking was reported more often by the patients with infarction than by the controls, which was due almost entirely to the inclusion of a large excess of moderate and heavy smokers (table IV). In comparison with non-smokers, the relative risk increased from 1·2 to 1 in women smoking fewer than 15 cigarettes a day to 4·1 to 1 in women smoking 15 to 24 a day and 11·3 to 1 in women smoking 25 or more a day.

Tables V and VI give the numbers of patients who had been treated for certain medical conditions which might in some way have predisposed to the development of the disease. More of the patients with infarction than the controls had been treated for hypertension, diabetes, pre-eclampsia, and obesity. Blood pressure and blood glucose were not measured in individual patients, and our figures are likely to underestimate the prevalence of hypertension and diabetes in both groups.

Fourteen of the patients with infarction (23·3%) gave a clear history of seeking advice because of obesity compared with 17 (9·9%) of the control patients. Weight and height at the time of admission, known for 50 of the patients with infarction and 119 of the controls, were used to calculate Quetelet's index of obesity (weight/height^2; ref.[10]). The mean values of this index did not differ significantly

TABLE V—*Proportions of Myocardial Infarction and Control Patients Treated for Hypertension and Diabetes*

	No. (%) of M.I. Patients	No. (%) of Controls
Hypertension		
No treatment	49 (81·7)	165 (96·5)
Regular drug therapy for less than 3 years	2 (3·3)	1 (0·6)
Regular drug therapy for more than 3 years	2 (3·3) *	2 (1·2) *
Intermittent therapy	7 (11·7)	3 (1·8)
Total	60 (100·0)	171 (100·0)
Diabetes		
No treatment	56 (93·3)	171 (100·0)
Diet only	1 (1·7)	0
Oral hypoglycaemic agent and diet	2 (3·3) †	0 †
Insulin	1 (1·7)	0
Total	60 (100·0)	171 (100·0)

*M.I. patients *v.* controls: χ^2 (1) = 12·21; $P<0·001$.
†M.I. patients *v.* controls: $P = 0·004$ (Fisher's exact probability test).

TABLE VI—*Proportions of Myocardial Infarction and Control Patients with Obesity and Pre-eclamptic Toxaemia*

	No. (%) of M.I. Patients	No. (%) of Controls
Obesity		
Never been overweight	33 (55·0)	132 (77·2)
Clear history of obesity	14 (23·3)*	17 (9·9)*
Uncertain history of obesity	13 (21·7)	22 (12·9)
Total	60 (100·0)	171 (100·0)
Pre-eclamptic Toxaemia		
No pre-eclamptic toxaemia	39 (65·0)	135 (79·4)
Clear history of pre-eclamptic toxaemia in one or more pregnancies	18 (30·0)†	19 (11·2)†
Uncertain history of pre-eclamptic toxaemia	3 (5·0)	16 (9·4)
Total	60 (100·0)	170 (100·0)

*M.I. patients *v.* controls: χ^2 (1) = 6·58; $P<0·02$.
†M.I. patients *v.* controls: χ^2 (1) = 9·36; $P<0·01$.

between the two groups (2·46 and 2·30 respectively), but significantly more of the patients with infarction (8;16%) than the controls (6; 5%) had an index greater than 3·0 ($P<0·05$). The increased frequency of pre-eclampsia (30·0% compared with 11·2%) was not due to an increased number of pregnancies (see table VII).

No appreciable difference was recorded between the groups in the frequency of previous renal or thyroid disease. Information on previous psychiatric history was difficult to interpret and will be reported separately.

Table VII shows the distribution of the patients by social class, country of origin, parity, and menopausal state at the time of admission. No statistically significant differences were found between the two groups with respect to any of these factors. The patients with infarction, however, tended to belong to the higher socioeconomic groups and to have had fewer pregnancies. The proportion of women who were postmenopausal on admission was closely similar in both groups. An artificial menopause under 40 years of age had been induced in only one patient, a control.

TABLE VII—*Social Class, Country of Origin, Parity, and Menopausal State of Myocardial Infarction and Control Patients at Time of Admission*

	No. (%) of M.I. Patients	No. (%) of Controls
Social Class		
I-II	22 (41·5)	51 (38·1)
III	22 (41·5)	46 (34·3)
IV-V	5 (9·4)	24 (17·9)
Widowed or divorced	4 (7·5)	13 (9·7)
Total	53 (100·0)	134 (100·0)
Country of Origin		
United Kingdom	45 (83·3)	114 (85·1)
Commonwealth countries	4 (7·4)	6 (4·5)
European countries	4 (7·4)	12 (9·0)
Asian countries	1 (1·9)	2 (1·5)
Total	54 (100·0)	134 (100·0)
Parity		
Nulliparous	6 (10·0)	16 (9·5)
1-3 pregnancies	44 (73·3)	101 (60·1)
More than 3 pregnancies	10 (16·7)	51 (30·4)
Total	60 (100·0)	168 (100·0)
Menopausal State		
Still menstruating	53 (89·8)	146 (90·7)
Postmenopausal	6 (10·2)	15 (9·3)
Total	59 (100·0)	161 (100·0)

Blood lipids were examined in 44 (70%) of the patients with infarction and 84 (48%) of the controls. The results, which are reported in detail elsewhere,[11] showed that the mean levels of both serum cholesterol and serum triglyceride were substantially higher in the patients with infarction. Type IIa hyperlipoproteinaemia (cholesterol 6·9 mmol/l (267 mg/100 ml) or more)* or IIb (cholesterol 6·9 mmol/l or more and triglyceride 2·3 mmol/l (207 mg/100 ml) or more) was present in 18 (41%) of the patients with infarction but in none of the controls. In contrast, hyperlipoproteinaemia of type IV occurred with almost equal frequency in both groups (6·8% and 8·3% respectively).

With the finding of so many associations it is necessary to consider whether any of them are secondary, arising because the risk factors are themselves interrelated. For example, in Britain oral contraceptive use is associated with cigarette smoking,[12 13] and cigarette smoking is associated with myocardial infarction. It is therefore necessary to examine the data separately for different smoking categories. This is done in table VIII. The data confirm that heavy smokers tend to use oral contraceptives more often than light or non-smokers and show that the relationship between oral contraceptive use and myocardial infarction is present in each category. The numbers of observations in each category are, however, small and the differences between patients with infarction and controls are significant only when all the smoking categories are considered together ($P<0·01$). The relationship appears more pronounced in smokers than in non-smokers.

Table IX gives estimates of the relative risk associated with the use of oral contraceptives after allowing for the effect of four other factors associated with myocardial infarction. Of the four factors only cigarette smoking has any material effect on the estimate of risk, reducing the ratio from 4·5 to 1 to 3·2 to 1. When cigarette smoking is allowed for, the other three factors show no effect at all. Diabetes is not considered since there were only four patients known to have this disease and none were using oral contraceptives.

*Lipid abnormalities were classified as recommended by the World Health Organization (a modification of the Fredrickson classification).[26] The upper limits of normal for both cholesterol and triglyceride were set at twice the standard deviation above the mean for our control population, and the lipoprotein pattern of each patient was examined after serum electrophoresis.

TABLE VIII—*Oral Contraceptive Practice of Myocardial Infarction and Control Patients in Different Smoking Categories*

No. of Cigarettes Smoked Daily at Onset of Episode	No. (%) of Patients Using Oral Contraceptives at Onset of Episode		Total	
	M.I. Patients	Controls	M I. Patients	Controls
None	3 (18·8)	8 (10·3)	16 (100·0)	78 (100·0)
1-14	2 (25·0)	2 (4·5)	8 (100·0)	44 (100·0)
15 or more	11 (33·3)	4 (12·5)	33 (100·0)	32 (100·0)
Total	16	14	57	154

TABLE IX—*Estimated Relative Risk of Myocardial Infarction in Patients Currently Using Oral Contraceptive Preparations after Standardization for Possible Confounding Variables*

Variable Standardized	Relative Risk Estimate	χ^2	Significance Level
Cigarette smoking	3·2	6·83	$P<0·01$
Hypertension	4·1	10·75	$P=0·001$
Pre-eclamptic toxaemia	3·9	10·16	$P<0·01$
Obesity	4·4	12·72	$P<0·001$
All above variables simultaneously	3·1	5·93	$P<0·02$

Blood lipid levels were known for only 44 (70%) of the patients with infarction, and the above calculations do not take account of any possible association with blood cholesterol. It is difficult to see why high values should be associated with the use of oral contraceptives except in so far as the contraceptives may themselves cause an increase in blood cholesterol.[14] Indeed, patients who are known to have hypercholesterolaemia are likely to be advised to use some other form of contraception. That this may have been so is suggested by the observation that only three of the 18 patients with infarction known to have type II hypercholesterolaemia were using oral contraceptives compared with eight of the 26 patients with infarction in whom the blood levels were considered to be normal according to our criteria.[11]

INTERACTION OF FACTORS

It would need very large numbers indeed to establish the quantitative effect of each combination of risk factors. In an attempt to disentangle the relationships, we show in table X the proportions of patients known to have had various numbers of risk factors, subdividing those who had only one factor according to its nature. Information on the presence of one or more factors was not obtained for a few patients, and lipid analyses were carried out on only 70% of the patients with infarction, so that the number who were exposed to one risk factor or to none at all is likely to be even smaller than appears from the table. It should be recalled also that hypertension and diabetes were recorded only when the patient had been treated for these conditions before the infarction occurred. The risk estimates derived from the data in table X, however, strongly suggest that the combined effect of the factors is synergistic. In comparison with patients not known

TABLE X—*Risk Factors in Myocardial Infarction and Control Patients*

	No. (%) of M.I. Patients	No. (%) of Controls
No risk factor	11 (18·3)	115 (66·5)
One risk factor:		
Type II hyperlipoproteinaemia	4 (6·7)	0
Hypertension	0	1 (0·6)
Cigarette smoking (15 or more daily)	7 (11·7)	21 (12·1)
Diabetes	0	0
Current oral contraceptive use	1 (1·7)	7 (4·1)
Obesity	3 (5·0)	8 (4·6)
Two risk factors	19 (31·7)	19 (11·0)
Three or more risk factors	15 (25·0)	2 (1·2)
Total	60 (100·0)	173 (100·0)

to have any risk factors, the relative risk increased from 4·2 to 1 in women with one factor to 10·5 to 1 in women with two factors and 78·4 to 1 in women with three or more factors.†

Discussion

RISK FACTORS

Previous studies of myocardial infarction have, with one exception, included few observations on women under 45 years of age.[15-18] Oliver [17 18] alone has reported on an appreciable number of cases. His series consisted of 81 patients who attended the Royal Infirmary, Edinburgh, during 1953-70 and is of particular value because all the patients were seen and investigated by him. Unfortunately a control series was not investigated in the same way, and comparisons could be made only with data from other surveys, some of which were carried out independently in different areas and at different times. Despite this, Oliver showed that an abnormally high proportion of patients (79%) were exposed to one or other of the three major risk factors known to be associated with the development of myocardial infarction in men and older women[19]; 48% of his patients had hypercholesterolaemia (serum cholesterol 7 mmol/l (270 mg/100 ml) or more), 39% had hypertension (diastolic pressure 100 mm Hg or more), and 43% smoked 20 cigarettes or more a day. The importance of these factors is confirmed in our study. One or more of them was present in a modified form in 80% of the 44 patients for whom blood lipid levels were known compared with 22% of the 84 control patients.

Oliver's data are less conclusive in regard to four other factors that were less prevalent—premature menopause, obesity, diabetes mellitus, and use of oral contraceptives. The last two factors were found to be clearly related to the disease in our study and in a concomitant study by Mann and Inman.[20] Obesity also emerged as a risk factor in our study, but not premature menopause.

ORAL CONTRACEPTIVES

The association between myocardial infarction and oral contraceptives shown by these two studies is unlikely to be due to bias. There was no selection in the choice of cases (other than the necessity for survival), which was determined by strict diagnostic criteria and the area of hospitalization. The method of selecting the controls ensured that the patients in both groups were comparable for age, marital status, and year and hospital of admission, and they were found to be comparable in country of origin and social class. Some patients admitted to hospital for elective surgical procedures are advised to stop using oral contraceptives before admission, but none of our control patients had stopped using them in the three months before admission. Moreover, the frequency of oral contraceptive use by the control patients was the same as that found in a survey of contraceptive practice among women in England and Wales in 1970.[21 22] In both studies the proportion of women aged 30-39 years who reported using oral contraceptives was 13·5%.

Whether the association is causal or reflects the association of oral contraceptive use with some other factor is more difficult to decide. Nevertheless, the significant relative-risk estimate, even when allowing for the other associated variables, and the relationship between the frequency of cases reported to the Committee on Safety of Medicines and the dose of oestrogen[23] all argue in favour of a causal relationship. The finding that women on oral contraceptives who developed myocardial infarction tended to have been using them longer than control patients with other, unrelated diseases[20] may go some way to explaining why earlier case-control studies based on fewer cases failed to show a clear relationship.[24 25] If, however, as these findings suggest, the risk increases with prolonged use we might have expected to find an appreciable though somewhat smaller risk in women who had used oral contraceptives in the past but had stopped using them before the infarction occurred. The numbers are too small to exclude such a possibility, but neither this study nor that of Mann and Inman provides any evidence to support it.

The strong suggestion that the combined effect of risk factors is synergistic may have important practical implications for the use of oral contraceptives. The appreciable increase in relative risk in women with more than one risk factor for myocardial infarction suggests that other methods of contraception should be considered in such cases.

INCIDENCE OF MYOCARDIAL INFARCTION

We can make a rough estimate of the incidence of myocardial infarction (as determined by admission to hospital) both in the general population and in users of oral contraceptives from the data collected in the North-West Metropolitan Region, where the proportion of hospitals included in the study was greater than in the Oxford Region. The hospitals participating in the study contained about 57% of the female acute general medical beds in the North-West Metropolitan Region. An estimate for the Region of the number of married women aged 30-44 years admitted to hospital with non-fatal myocardial infarction during 1968-72 can therefore be made by multiplying the observed number of patients by 1·75, on the assumption that the beds covered in the study served 57% of the Region's population and that the admissions to these beds were representative of the whole Region. Similarly, an estimate can be made of the corresponding number of patients admitted in the Region who were currently taking oral contraceptives. If the data acquired from the controls are assumed to be representative of the general married population in the Region, an estimate can be made of the number of women taking oral contraceptives at any point in time. On this basis the yearly hospital admission rate for non-fatal myocardial infarction is 2·1 per 100 000 in married women aged 30-39 years who do not use oral contraceptives and 5·6 per 100 000 in married women who do. In the 40-44-year age group the rates are 9·9 and 56·9 per 100 000 respectively. The increased risk of hospital admission for myocardial infarction in women currently using oral contraceptives (2·7 times in the 30-39-year age group and 5·7 times in the 40-44-year age group) is similar to the increased risk of death from the condition estimated by Mann and Inman.[20]

We are most grateful to the consultants and general practitioners who allowed us to study patients under their care and provided information, to the medical records officers of the hospitals and their staff who gave willing help in many ways, and to the patients who gave up their time to answer our questions. The McAlpine Foundation kindly loaned us a motor car, without which so many patients could not have been interviewed, and financial support was received from the D.H.S.S. Gale Mead provided invaluable secretarial help and Dr. A. J. Honour gave much advice and encouragement.

J.M. was supported by an I.C.I. Fellowship and by the Cecil John Adams Memorial Fellowship during the period of this study.

†The fact that blood lipids were examined in only 84 (48%) of the control patients is unlikely to have influenced these estimates to any appreciable extent, as type II hyperlipoproteinaemia is normally uncommon in young women. In our series no case was found in any of the control patients from whom blood samples were obtained.

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Oral Contraceptives and Death from Myocardial Infarction

J. I. MANN, W. H. W. INMAN

British Medical Journal, 1975, **2**, 245-248

Summary

We investigated 219 deaths from myocardial infarction in women under the age of 50. Their histories were compared with those of living age-matched controls selected from the same general practices. The frequency of use of oral contraceptives during the month before death was significantly greater in the group with infarction than during the corresponding month in the control group and the average duration of use was longer. No information on cigarette smoking was available but the proportion of women being treated for hypertension or diabetes was greater among those who died than among the controls. This did not alter the overall conclusion that the risk of fatal myocardial infarction was greater in the women using oral contraceptives, particularly in the older age groups.

Introduction

Inman and Vessey's report to the Committee on Safety of Drugs on deaths from pulmonary embolism and coronary and cerebral thrombosis in women of childbearing age was published in 1968.[1] In the cases of pulmonary embolism and cerebral thrombosis a strong relationship was found with the use of oral contraceptives when these disorders occurred in the absence of predisposing conditions. More of the women who died from coronary thrombosis in the absence of predisposing conditions had also been using oral contraceptives than would have been expected from the experience of the control group, but for this condition the difference was not quite significant and a definite association was considered not proved. Later studies[2,3] were not conclusive and we thought it desirable to undertake a further investigation of deaths from myocardial infarction in 1973.

Selection of Cases

Transcripts of all death certificates relating to women under the age of 50 years who died in England and Wales during 1973 and which had been coded to rubric 410 according to the eighth revision of the International Classification of Diseases (myocardial infarction and synonymous terms) were obtained from the Registrar General. A total of 726 were received. All deaths in women under the age of 40 years, every second death in the 40-44-year age group, and every fifth death in the 45-49-year age group were selected for the study, giving a total of 277 cases (table I). Selection was made consecutively as batches of certificates were received.

TABLE I—*Numbers of Death Certificates Received, Selected for Study, Investigated, and Included in Present Analysis*

Age group (years):	<40	40-44	45-49	Total
No. of death certificates received	86	192	448	726
No. selected for study	86	100	91	277
No. investigated	73	79	67	219
No. included in analysis*	51 (81)	54 (56)	48 (59)	153 (196)

*Numbers of control patients are given in parentheses.

Efforts were made to interview the general practitioners who had cared for the patients. In 15 cases either the women were not registered with any doctor or the coroner, hospital, or local executive council could not identify him, and the medical records of nine women had been lost and no other data source was available. A further 34 deaths were not investigated because the general practitioner could not be interviewed. Thus 58 (21%) of the 277 deaths could not be studied.

The remaining 219 deaths were investigated by the committee's medical field officers, as a result of which a further 66 cases were excluded. In 37 cases evidence for the diagnosis of myocardial infarction was thought to be inadequate. Deaths were included in the final analysis only when the diagnosis was substantiated by necropsy findings or a history of typical chest pain together with electrocardiographic or enzymatic confirmation as defined by the World Health Organization.[4] In 23 cases (10·5%) a necropsy carried out after the death certificate had been completed or (less often) other evidence suggested that death was attributable to a different cause. A further six cases were excluded because the wrong sex, age, or year of death had been given on the certificate. The remaining 153 deaths provide the basis for this report. In 104 cases the diagnosis was substantiated at necropsy.

Procedure

Forty-eight members of the committee's staff of medical officers took part in the field work. During the investigation of each death one of them completed a questionnaire as fully as possible with the aid of the general practitioner and any other doctors who had attended the patient during her terminal illness. Since the general practitioner's records had usually been returned to the local executive council after the patient's death he was asked to retrieve them before being interviewed. These major sources of information were often supplemented by hospital case notes, family planning clinic records, necropsy reports, and court records supplied by a coroner.

University of Oxford, OX1 3QN
J. I. MANN, M.B., PH.D., Lecturer in Social and Community Medicine

Committee on Safety of Medicines, London EC2A 1PP
W. H. W. INMAN, M.R.C.P., M.F.C.M., Principal Medical Officer