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Improved prognosis since 1969 of myocardial infarction treated in a coronary care unit: lack of relation with changes in severity

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Abstract

Objective—To study changes from 1969 to 1983 in the prognosis of patients with acute myocardial infarction treated in a coronary care unit.

Design—Mortality follow up of all patients with definite acute myocardial infarction.

Setting—The coronary care unit of the Royal Melbourne Hospital, a tertiary referral centre.

Subjects—4253 Patients (3366 men, 887 women) admitted from 1969 to 1983.

Main outcome measure—Mortality recorded at discharge from hospital and 12 months after admission.

Results—Details of clinical findings, history, electrocardiograms, arrhythmias, and radiological findings were recorded on admission. Mean ages were 63 for women and 57 for men, and women had haemodynamically more severe infarcts than men. In the later years patients were older and had less severe infarcts. Overall, hospital mortality in men was 16.7% in 1969-73 and 8.5% in 1979-83 and declined in all grades of the Norris and Killip infarct severity indices compared with a constant 19.2% in women. Even after adjustment for age and severity by logistic regression, hospital mortality fell in men by an average of 8% (95% confidence interval 4% to 11%) a year but remained constant in women. By 1983 male mortality was 60% that of women of similar age and comparable severity of infarction. Mortality of hospital survivors at 12 months declined by 7% (4% to 9%) a year in both sexes, even after adjustment for age and severity, with a male to female mortality ratio of about 0.8. New indices were derived to predict mortality in hospital and at 12 months.

Conclusion—The observed declines in mortality cannot be explained by changes in severity of infarction or in prognostic characteristics of patients.

Introduction

Early observational studies¹⁻⁴ noted that the prognosis of patients with acute myocardial infarction improved after the introduction of coronary care units.^{5,6} Controlled but non-randomised studies showed that such patients treated in a coronary care unit had a lower mortality than patients treated in general wards.⁹⁻¹² Two randomised studies suggested, however, that patients with acute myocardial infarction treated at home had better survival than those admitted to hospital.^{13,14} Reservations have been expressed about the effectiveness of coronary care units,¹⁵ and some

have suggested that the decline in mortality from acute myocardial infarction in the United States may have been due to a higher proportion of "milder" cases among patients admitted to these units.^{16,17}

This study was undertaken to ascertain whether the prognosis of patients with acute myocardial infarction admitted to the coronary care unit at the Royal Melbourne Hospital had changed between 1969 and 1983 and, if so, whether this change could be explained by any changes in the age distribution of patients admitted or in the severity of their infarctions. A previous report from this unit showed a significant fall in mortality in patients with Q wave myocardial infarction in mild and severe categories between 1969-70 and 1974-75 but no change among patients with cardiogenic shock.¹⁸

Methods

The Royal Melbourne Hospital is a 620 bed tertiary referral hospital affiliated to the university. Patients with suspected or definite acute myocardial infarction are admitted to the coronary care unit irrespective of age, provided beds are available. The general function and policies of the unit have been reported.¹⁹ From 1969 patient data were recorded by medical staff on questionnaire forms. This study was confined to patients with definite acute myocardial infarction.^{20,21} Characteristics recorded for each patient on admission included history; clinical, electrocardiographic, and radiological findings; and arrhythmias. Outcome was recorded later.

Patients were classified by severity according to the Killip classification¹: class I—no heart failure; class II—heart failure (appearance of third heart sound or presence of basal crepitations or pulmonary congestion on radiograph, or both); class III—severe heart failure (pulmonary oedema); and class IV—cardiogenic shock. The Norris index of severity was computed from age, heart size, radiological changes in lung fields, location of infarct, systolic blood pressure, and history of ischaemia.¹

From 1969 to 1983, 8135 patients were admitted to the coronary care unit, of whom 4340 (53%) had definite acute myocardial infarction. For 4253 of these patients (3366 men, 887 women) we had data on mortality at discharge from hospital and at 12 months after admission, and they constitute the present study population.

STATISTICAL METHODS

A tendency for the mortality to change over the

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TABLE 1—Hospital mortality and 12 month mortality by age, sex, and admission period. For each sex the number of patients in each category is expressed as a percentage of total admissions for the admission period

Age	1969-73			1974-8			1979-83			Total		
	No (%)	Hospital mortality (%)	12 Month mortality (%)	No (%)	Hospital mortality (%)	12 Month mortality (%)	No (%)	Hospital mortality (%)	12 Month mortality (%)	No (%)	Hospital mortality (%)	12 Month mortality (%)
<i>Men</i>												
<40	45 (5)	2.2	4.5	57 (5)	3.5	10.9	59 (5)	1.7	6.9	161 (5)	2.5	7.6
40-49	189 (21)	12.2	6.6	219 (17)	4.6	6.8	154 (13)	2.6	3.3	562 (17)	6.6	7.6
50-59	347 (39)	12.7	12.9	438 (35)	13.0	8.9	440 (36)	5.9	8.7	1225 (36)	10.4	9.9
60-69	260 (29)	23.8	23.2	430 (34)	14.4	16.6	412 (34)	10.7	7.9	1102 (33)	15.3	14.6
≥70	52 (6)	38.5	31.3	113 (9)	24.8	20.0	151 (12)	19.2	13.9	316 (9)	24.1	18.4
Total	893	16.7	15.6	1257	12.7	12.2	1216	8.5	8.2	3366	12.2	11.6
<i>Women</i>												
<40	6 (3)		16.7	5 (2)		20.0	10 (3)			21 (3)		9.5
40-49	18 (9)		16.7	32 (10)	13.4		15 (4)	6.7	7.1	65 (7)	6.2	6.6
50-59	73 (37)	20.6	17.2	82 (25)	13.4	7.6	71 (19)	4.2	8.9	226 (26)	12.8	11.2
60-69	61 (31)	16.4	25.5	153 (47)	23.5	18.8	152 (42)	17.1	13.5	366 (41)	19.7	17.7
≥70	39 (20)	38.5	29.2	52 (16)	28.8	18.9	118 (32)	30.5	12.2	209 (24)	31.6	16.8
Total	197	20.3	21.7	324	19.7	13.8	366	18.3	11.4	887	19.2	14.5

study period was first assessed by examining crude and age-sex specific mortalities. The influence of each admission characteristic on prognosis was studied.

For each sex, multivariate logistic regression analyses²² of mortality were performed using the generalised linear interactive modelling package (GLIM),²³ adjusting for age, severity, and year of admission. Severity was represented in two ways, firstly, by using clinical characteristics shown in these data to be independent prognostic factors, and, secondly, by using the established Killip classification and Norris index. A significant effect of year of admission would indicate that an observed trend could not be explained, using these statistical methods, by changes in age or severity of infarctions.

Let p be the probability a patient does not survive a given period. Let x_1, \dots, x_n represent explanatory variables such as age, sex, an admission characteristic, or year(s) of admission. The model assumes that the expected value, E , of the logarithm of the odds, the logit, is a linear function of these variables—that is, $E[\text{logit}(p)] = E[\log(p/(1-p))] = b_0 + b_1x_1 + b_2x_2 + \dots + b_nx_n$. (1) The coefficients b_0, \dots, b_n represent the “effects” of the variables and are estimated by maximum likelihood. Modelled associations with age and clinical characteristics form the bases of the new Royal Melbourne Hospital indices of severity that we derived from these data.

If p_i is the probability of dying if $x_i = j$, $j = 0$ or 1 , and if $x_i = 1$ if the factor is present, else 0 , then

$$e^{b_i} = p_i(1-p_0)/(1-p_1)p_0 \quad (2)$$

If p_0 is small the mortality when factor i is present is approximately e^{b_i} times greater than in the absence of the factor. The baseline coefficient b_0 corresponds to an individual with 0 on all variables. For the continuous variate year of admission b_i estimates an average change over the study period, which when p is close to 0.5 is about one quarter of the linear change in p per year, while if p is small it is approximately the percentage change in p per year. A negative estimate means that p is less in the later years.

Changes in mean age and in mean Norris index were analysed by linear regression. Throughout means and parameter estimates are presented with their standard errors in parentheses.

Results

From 1969-73 to 1979-83 the median delay from onset of symptoms to admission to the coronary care unit decreased from 5.5 to 3.8 hours. The proportion of delays between onset of symptoms and admission to

the emergency department of more than 24 hours fell from 15% (167/1090) to 8% (123/1582). From the emergency department to the coronary care unit the proportion of delays of less than one hour fell from 43% (474/1090) to 22% (349/1582) and the proportion of delays of more than four hours from 24% (261/1090) to 11% (167/1582).

ANALYSIS OF ADMISSION CHARACTERISTICS AND SEVERITY OF INFARCT

A logistic regression analysis of the characteristics recorded on admission²⁴ showed that almost all characteristics were less common in the later years, irrespective of adjustments for age and sex. Characteristics were more common in older patients. Men were more likely to have had a previous acute myocardial infarction, a Q wave infarct, atrial arrhythmias, ventricular premature beats, and ventricular tachycardia. Women were more likely to have had hypertension, diabetes, cardiogenic shock, ventricular standstill, and third degree atrioventricular block and to have never smoked.

The mean Norris index was lower in men (5.72 (0.05)) than in women (6.44 (0.12)) and increased with age. In later years patients had on average less severe infarcts. After adjusting for age the mean index fell with year of admission by 0.12 (0.01) a year, independent of sex, and was on average 0.25 (0.12) lower in men. The proportion of admissions without failure or shock (Killip class I) averaged 0.49 (men 0.50, women 0.46). By multiple logistic regression, after adjustment for an increase with age that was independent of sex, this proportion increased with year of admission by about 0.015 (0.002) a year.

ANALYSIS OF MORTALITY BY AGE, SEX, AND YEAR OF ADMISSION

Mortality in hospital and mortality after 12 months in those who survived to leave hospital are shown by sex, age, and year of admission in table I. Men comprised 79% (3366/4253) of those admissions throughout. The proportions of patients in the older age groups increased with admission period. The mean age (57.1 men, 63.2 women) increased by 0.3 years per year. Both mortalities tended to decrease across the admission periods, especially in the older age groups. Univariate logistic regression analyses showed that both mortalities increased with age and were higher in women. For men mortality in hospital declined with year of admission, while for women it was constant. The 12 month mortality of survivors fell with year of admission in both sexes at a similar rate.

ANALYSIS OF MORTALITY BY ADMISSION CHARACTERISTICS

The odds ratios given by equation 2 and presented in table II show that for all characteristics except hypertension the presence of that characteristic was associated with a significantly increased hospital mortality, independent of sex and adjustment for age and year of admission. A similar conclusion applied to the 12 month mortality of hospital survivors, except that some characteristics were not significant risk factors for one or both sexes. The odds ratios for most of the major risk factors decreased with age.

Major risk factors for hospital mortality were cardiogenic shock and ventricular standstill, each associated with over 80% mortality (298/356 and 259/317 respectively). Other high risk factors were third degree atrioventricular and bundle branch blocks, ventricular fibrillation, and tachycardia. Major risk factors for 12 month mortality of survivors were bundle branch block, pulmonary oedema, enlarged heart, and a history of previous acute myocardial infarction.

ANALYSIS OF MORTALITY BY AGE, SEX, PROGNOSTIC VARIABLES, AND YEAR OF ADMISSION

Tables III and IV present the results of logistic regression analyses of hospital mortality and 12 month mortality respectively, listing the logistic regression coefficients (b_0, b_1, \dots, b_n of equation 1) and their standard errors for age, sex, and the characteristics found to be independently predictive of mortality. None of the coefficients for these independent factors showed variation with age or sex.

For hospital mortality nine independent prognostic factors were identified. After adjustment for these there was a decline in mortality with year of admission ($p < 0.001$) for men, corresponding to an average fall of about 8% a year. For women the trend was not significant, and it was different from that for men ($p < 0.05$). When we compared men and women of the same age and prognostic profile the model predicted that in 1969 women had about 70% of the mortality of men, whereas by 1983 the relation had reversed and men had about 60% of the mortality of women.

For 12 month mortality there were eight independent prognostic factors. After adjusting for these the decline in mortality with year of admission ($p < 0.001$ men; $p < 0.05$ women) was independent of sex and equal to an average fall of about 7% per year. Men had average mortality about 80% of that of women of similar age and prognostic profile ($p = 0.06$, two sided).

TABLE III—Hospital mortality logistic regression coefficients and standard errors for independent prognostic factors, age, sex, and year of admission. Coefficients were used to construct the Royal Melbourne Hospital index for hospital mortality following equation 3

Characteristic	Hospital mortality	
	RMH index coefficient	Standard error
Baseline	-7.027	0.600
Cardiogenic shock	3.060	0.182
Ventricular standstill	2.656	0.196
Third degree atrioventricular block	0.090	0.181
Ventricular fibrillation	0.893	0.167
Angina	0.714	0.134
Pulmonary oedema	0.625	0.160
Never smoked	0.556	0.142
Bundle branch block	0.607	0.153
Anterior infarct	0.507	0.133
Age (years)	0.0477	0.0076
Sex (1 if man, 0 if woman)	0.662	0.312
Year of admission from 1969 (men)	-0.0765	0.0186
Year of admission from 1969 (women)	0.0036	0.0300

TABLE IV—12 Month mortality of hospital survivors. Logistic regression coefficients and standard errors for independent prognostic factors, age, sex, and year of admission. Coefficients were used to construct the Royal Melbourne Hospital index for 12 month mortality of hospital survivors following equation 3

Characteristic	12 Month mortality	
	RMH index coefficient	Standard error
Baseline	-3.638	0.450
Bundle branch block	0.816	0.139
Enlarged heart	0.554	0.112
Previous acute myocardial infarction	0.515	0.115
Atrial arrhythmias	0.326	0.131
Pulmonary oedema	0.497	0.146
Sinus tachycardia	0.402	0.110
Ventricular premature beats	0.235	0.109
Angina	0.340	0.114
Age (years)	0.0210	0.0062
Sex (1 if man, 0 if woman)	-0.250	0.130
Year of admission from 1969	-0.0673*	0.0136

*-0.0633 (SD 0.0154) for men, -0.0808 (0.0275) for women.

There was no evidence that the rates of decline in mortality with year of admission depended on age or that there were any significant interactions between these trends and the prognostic factors, with one exception. For hospital mortality, once age and the other prognostic factors were in the model, the coefficient for ventricular fibrillation was $b = 1.52 - 0.012 \times (\text{year} - 1969)$, suggesting that by 1983 there was no independent increased risk associated with ven-

TABLE II—Hospital mortality and 12 month mortality for men and women by characteristic and mortality odds ratio for the characteristic (equation 2) and its 95% confidence interval, after adjustment for age, sex, and year of admission by sex

Characteristic	Hospital mortality				12 Months mortality			
	Men	Women	Characteristic odds ratio	95% CI	Men	Women	Characteristic odds ratio	95% CI
Previous acute myocardial infarction	18.4	28.3	1.96	1.62- 2.36	18.1	22.7	2.10	1.70-2.58
Angina	16.9	23.6	1.89	1.57- 2.27	15.4	18.7	1.80	1.46-2.21
Hypertension	11.7	17.5	1.13	0.93- 1.37	12.2	15.1	1.12	0.90-1.38
Diabetes	17.7	29.1	1.57	1.19- 2.07	14.7	27.0	1.70*	1.24-2.32
Never smoked	19.5	23.8	1.67	1.37- 2.04	11.0	18.4	1.02	0.80-1.30
Crepitations	18.7	27.1	2.82	2.31- 3.45	16.0	16.1	1.69	1.37-2.08
Cardiogenic shock	80.8	81.2	54.0	39.8- 73.3	21.9	22.7	1.93†	1.07-3.51
Enlarged heart	17.1	26.5	1.60	1.33- 1.92	18.9	21.6	2.26	1.84-2.79
Pulmonary venous congestion	15.3	25.8	1.53	1.27- 1.83	16.7	19.8	2.13	1.73-2.63
Pulmonary oedema	31.0	42.1	3.64	2.95- 4.50	24.7	27.3	2.52	1.93-3.29
Anterior (v inferior)	16.1	24.4	1.72	1.44- 2.07	13.4	15.6	1.25	1.02-1.54
Q wave (v non-Q wave)	13.3	25.4	1.42	1.12- 1.79	11.9	15.5	1.32	1.03-1.67
Sinus tachycardia	17.9	26.7	2.17	1.81- 2.60	16.0	19.2	1.80	1.47-2.21
Atrial arrhythmias	20.5	27.1	1.49	1.20- 1.84	15.2	17.5	1.60	1.25-2.04
Ventricular premature beats	14.3	21.0	1.17	0.97- 1.40	15.1	17.1	1.48	1.21-1.67
Ventricular tachycardia	26.5	36.4	3.27	2.67- 4.00	16.9	21.9	1.66	1.28-2.14
Ventricular fibrillation	38.7	42.6	5.56‡	4.43- 6.98	20.6	20.4	1.99	1.44-2.75
Ventricular standstill	81.7	81.8	48.1	35.0- 66.1	29.1	18.8	1.72	0.91-3.25
Bundle branch block	34.0	49.2	4.68	3.80- 5.76	26.1	35.9	2.87	2.21-3.73
Third degree atrioventricular block	44.4	47.7	5.97	4.74- 7.50	12.4	20.6	1.04	0.70-1.54

*Odds ratio in women, 3.00, was higher than in men, 1.35; $p < 0.05$.

†Odds ratio decreased with year of admission by about 20% (8%) a year.

‡Odds ratio decreased with year of admission to about 6% (3%) a year.

tricular fibrillation once the other factors had been considered ($p < 0.01$).

ROYAL MELBOURNE HOSPITAL INDICES

For a patient with any set of given characteristics the predicted probability of death at a given time point (the Royal Melbourne Hospital index) could be calculated from the coefficients in tables III or IV and equation 1 to be

$$\text{RMH index} = e^c / (1 + e^c), \text{ where } c = b_0 + b_1x_1 + \dots + b_nx_n. \quad (3)$$

For example, a 53 year old non-smoking man with angina, admitted in 1979 with acute myocardial infarction and found to have an anterior infarct but no other complications would have a probability of dying in hospital of $e^c / (1 + e^c) = 0.056$, where $c = -7.027 + 0.714 + 0.556 + 0.507 + 0.0477 \times 53 + 0.662 - 0.0765 \times (1979 - 1969)$.

The 320 patients who had an Royal Melbourne Hospital index for hospital mortality of 0.10 to 0.25 (of whom 80% (256) had a history of previous acute myocardial infarction and 82% (262) were aged over 60, while none had cardiogenic shock or ventricular standstill) showed a significantly greater fall in mortality than did patients in other severity ranges based on the Royal Melbourne Hospital index. The observed mortality of this group was over 30% in 1969-73, yet less than 10% in 1979-83.

ANALYSIS OF HOSPITAL MORTALITY BY THE NORRIS INDEX AND KILLIP SCALE

Analysis of hospital mortality by the four Killip classes, age, and year of admission showed a decline of mortality with year of admission in men ($p < 0.001$) and to a lesser extent in women ($p < 0.05$). Mortality increased with age in every class. In men in class IV mortality was above 80% (average 87% (136/156)) from 1969 to 1979 but was successively 82% (18/22), 73% (11/15), 67% (8/12), 64% (14/22), and 58% (7/12) in the

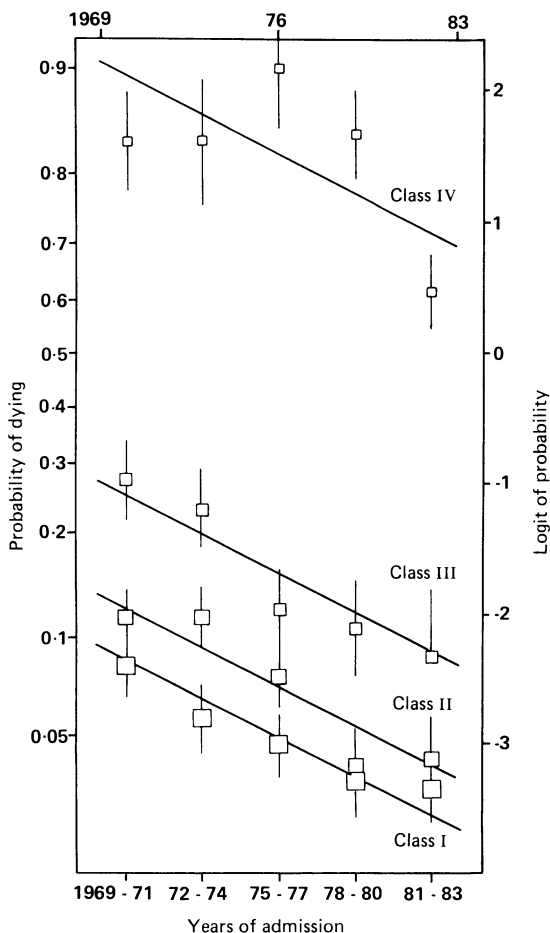


FIG 1—Hospital mortality for men for Killip classifications by year of admission, with best fitting linear logistic model (trend with year of admission = -0.100 ± 0.017). Size of square suggests number of patients in category; length of vertical line from point equals one standard error.
Class I □; class II □; class III □; class IV □

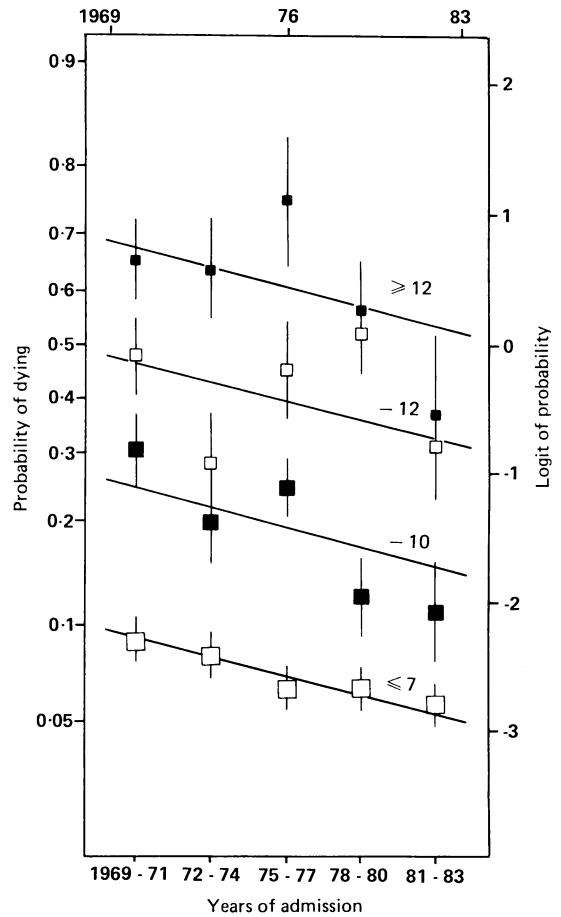


FIG 2—Hospital mortality for men for Norris index groupings by year of admission with best fitting linear logistic model (trend with year of admission = -0.049 ± 0.014). Size of square suggests number of patients in category; length of vertical line from point equals one standard error.
Norris index ≤ 7 □; -10 ■; -12 □; ≥ 12 ■

next five years. In contrast, for women in class IV mortality averaged 77% (89/116) and was never less than 66% across the study period.

A similar analysis, using groupings of the Norris index instead, showed a decline with year of admission in men ($p < 0.001$) but a non-significant decline in women. In men and in all age groups the most rapid decline with year of admission occurred in patients with a Norris index of 8 to 10.

Figs 1 and 2 show hospital mortality for men by year of admission and by Killip class and Norris index groupings respectively. On the logistic scale the trends for mortalities to decrease with year of admission in each grouping were linear and parallel. As more recent patients were older, statistically these trends would be even greater in absolute terms if they were adjusted for age.

Discussion

From 1969 to 1983 the crude hospital mortality for men, the crude 12 month mortality of hospital survivors of both sexes, and the severity of acute myocardial infarction among patients of both sexes treated in the coronary care unit at the Royal Melbourne Hospital declined, while the average ages of the patients increased. Multivariate analyses, using as measures of severity either clinical characteristics (tables III and IV) or the Killip classification and Norris index (figs 1 and 2), showed that the falls in crude mortalities were greater than could be explained by the decline in the severity of acute myocardial infarction.

Improvement in hospital mortality among men occurred at all levels of age and severity. Mortality fell

by about 8% a year in low risk men of similar age and severity. Hospital mortality among women remained constant. Improvement in 12 month mortality of hospital survivors was seen at all levels of age and severity in both men and women; this was equivalent to a reduction of about 7% a year, controlling for age and severity. Men showed an overall reduction in 12 month mortality of 15% a year.

Women were older than men and had more severe infarcts. Greater proportions of women had the severest prognostic factors of cardiogenic shock, ventricular standstill, and third degree atrioventricular block, and on average women had higher scores on the Norris index and Killip scale. Nevertheless, a higher overall mortality in women than in men, more so in the later years, was still evident after adjusting for these factors. Statistical modelling predicted that, although the hospital mortality of men was nearly twice that of women of similar age and clinical characteristics in 1969, by 1983 it was less than two thirds. For 12 month mortality of hospital survivors the ratio of male to female mortality was constant at about 0.8. Therefore a higher mortality rate in women with acute myocardial infarction^{25,26} cannot be explained by sex differences in the age or in the severity measures considered in this study.

Two predictors of mortality, the Royal Melbourne Hospital indices, were derived using the measured patient characteristics shown to be independently predictive of mortality in this study. These indices might prove to be useful because they are derived from large samples and give direct estimates of mortality. They suggest that ventricular fibrillation has become a less important predictor of mortality in recent years.

Patients who had never smoked were over 50% more likely to die in hospital than patients who had ever smoked, taking account of their ages and their having had more severe infarcts,²⁷ but the reasons for this are not clear.

There was a decrease of about 30% in the median time between onset of symptoms and admission to the coronary care unit over the study period, with at least a halving of long delays but no improvement in short delays. The decline in the severity of acute myocardial infarction over the study period was consistent, except that cardiogenic shock and ventricular tachycardia showed only a marginal decline in prevalence.

In recent years mortality from coronary heart disease has fallen in Australia,^{28,29} while that from acute ischaemic heart disease has fallen in the United States.³⁰ If the epidemic of clinical coronary heart disease is waning then the residual cases would be expected to occur among older people and might be less severe, as we have observed. Our data are, however, hospital based, and there are other possible explanations such as confounding by variables other than age or sex, a tendency for younger patients with acute myocardial infarction to seek treatment outside public hospitals, or a change in admissions policy within the hospital. Nevertheless, the time trends we have found are consistent with a waning of the epidemic of clinical coronary heart disease in the community.

Our analyses have shown that, despite the fact that more recently admitted patients have included a higher proportion of people with milder infarctions, their better prognosis was greater than could be explained by the lower severity of their infarction. This was particularly true among men, who constituted 80% of patients with acute myocardial infarction.

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Correction

Influence of maternal diet during lactation and use of formula feeds on development of atopic eczema in high risk infants

Two editorial errors occurred in this paper by Ranjit Kumar Chandra and others (22 July, pp 228-30). The conclusions in the abstract should read, "In families with a history of atopic disease [not eczema, as stated] mothers who breast feed should avoid common allergenic foods during lactation." The first sentence in the subjects and methods section should read, "In cases in which either of the baby's parents had a history [not a family history] of atopic disease mothers were asked whether they planned to breast feed exclusively."

Case-control study of infections with *Salmonella enteritidis* phage type 4 in England

Two authors' errors occurred in this paper by Dr John M Cowden and others (23 September, pp 771-3). In the last sentence of the first paragraph on p 772 "the first three" was omitted, and later in the sentence a percentage of 0.02% was given. The sentence should read, "Of 137 patients, 26 (19%) ate at least one of the first three products specified in the table compared with only four (2%) of the 196 controls."