Long-term all-cause and cardiovascular mortality following incident myocardial infarction in men and women with and without diabetes: temporal trends from 1998-2009

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Abstract:

Background: Long-term mortality following myocardial infarction (MI) is higher in diabetic than non-diabetic individuals. Early case-fatality after MI has improved but it is unclear whether trends extend to long-term mortality. We aimed to determine whether the disparity in long-term all-cause and cardiovascular disease (CVD) mortality by diabetes status has decreased.

Methods: All incident MI cases were identified from Western Australian whole-population linked data for 1998–2009. Mortality follow-up was available until 30 June 2011. Unadjusted survival was estimated using Kaplan Meier survival curves. Hazard ratios (HRs) comparing 5-year mortality in diabetic versus non-diabetic people across three periods (1998–2001, 2002–2005, 2006–2009) were estimated from multivariable Cox regression models, and adjusted trends calculated from interaction (diabetes status $\times$ period) models.

Results: There were 22, 594 30-day survivors of incident MI. There was little change across the three periods in all-cause mortality in diabetic men (27.1%, 28.2%, 25.5%) and women (34.9%, 36.8%, 36.1%), but small declines from first to last periods in non-diabetic men (14.5% to 12.1%, $p=0.03$) and women (21.0% to 19.4%, $p=0.08$). There was no temporal change in the increased all-cause mortality HRs in diabetic versus non-diabetic men and women. Multivariable-adjusted relative risk for CVD mortality remained elevated in diabetic women (2006–2009 HR 1.73, 95% CI 1.29, 2.32) but not in men (2006–2009 HR 1.08, 95% CI 0.85, 1.37).

Conclusions: The excess long-term mortality associated with diabetes and excess CVD mortality in diabetic women indicates a need for improved secondary prevention in diabetic patients, especially women.

Keywords: Diabetes; Myocardial infarction; Mortality; Trends

Introduction

Myocardial infarction (MI) is a frequent and serious complication of diabetes. Individuals with diabetes who suffer an MI are at high risk of further vascular complications.^{1,2} The elevated mortality associated with diabetes is predominantly cardiovascular-related, but up to 40% of the excess risk of death may relate to non-vascular causes.³ Although long-term mortality following MI in people with diabetes has improved in recent decades, there is limited evidence that the gap between people with diabetes and without diabetes has reduced,⁴⁻⁶ despite temporal improvements in mortality rates in the broader diabetic population.^{7,8} There is some evidence of declining CVD mortality rates in patients with diabetes within 1-year of a first acute coronary syndrome presentation,⁹ but limited data regarding CVD mortality with longer-term follow-up. Additionally, an increasing proportion of misclassified CVD-related deaths in people with diabetes¹⁰ could impact trends in CVD mortality in this patient group.

Changing patterns of comorbidities, treatment and MI severity over time can all impact long-term mortality after MI. The combined effect of these factors at a population level is of particular interest in our population due to declining MI incidence in people with diabetes since the late 1990s and concurrent reductions in 30-day case fatality in MI patients with diabetes.^{11,12} These population-level trends likely indicate improved management of cardiovascular risk factors and acute care in people with diabetes, but whether these findings extend to improvements in longer-term outcomes is unknown. The aim of this study was to estimate trends in long-term all-cause and CVD mortality following incident MI in men and women with diabetes and without diabetes, and determine whether the excess mortality associated with diabetes has reduced over time.

Methods

Data source and participants

Data for this study were obtained from the WA Data Linkage System (WADLS) which systematically links population-based administrative health datasets using probabilistic

matching.¹³ The current study used a de-identified dataset containing linked records from two core WADLS sources, the Hospital Morbidity Data System and the Mortality Register for the period 01 January 1985 to 30 June 2011. The linked dataset contained records for all hospitalisations and deaths recorded as CVD or diabetes, and all hospital and death records within the period for each person in the dataset. The statutory nature of these data collections ensures capture of all hospitalisations (public and private) and deaths in WA. Variables contained within the linked dataset included demographic data, principal and 20 secondary discharge diagnosis fields, inpatient procedures, admission and discharge dates, and date and cause of death (underlying and associated). Approval to conduct this study was obtained from the Human Research Ethics Committees of The University of Western Australia and the WA Department of Health under a waiver of consent.

The linked dataset was used to identify all patients aged 35 to 84 years hospitalised for MI in WA between 1998 and 2009. Incident cases of MI were identified from the principal discharge diagnosis field (ICD-9 410, ICD-10-AM I21, I22) where there was no hospitalisation for MI in the 13 years preceding the incident event. Prior hospitalisation was defined as an MI hospitalisation in any diagnosis field during the lookback period. Patients were classified with diabetes if it was recorded on the incident MI episode of care or on any hospitalisation in the 13 years prior to the incident MI (ICD-9 250, ICD-10-AM E10–E14). We have previously tested the accuracy of the recording of diabetes status in linked administrative data in WA. In a cohort of hospitalised CHD patients, sensitivity was >90% and positive predictive value was 92% using an extended lookback period.¹⁴ Patients surviving >30 days following the date of incident MI were included in the cohort.

Follow-up

Outcomes of interest were long-term all-cause and CVD mortality. CVD deaths were identified from the underlying cause of death field (ICD-9 390-459, ICD-10-AM I00-I99) for the standard definition. Sensitivity analyses were conducted using a modified CVD mortality definition to account for the potentially increasing underestimation of deaths attributed to CVD in people with

diabetes.¹⁰ Therefore in patients with diabetes, we also identified CVD deaths where uncomplicated diabetes (E10.9, E11.9, E12.9, E13.9, E14.9) or diabetes with circulatory complications (E10.5, E11.5, E12.5, E13.5, E14.5) were coded as the underlying cause of death, concurrent with a restricted range of CVD codes (I10–I25, I60–I69) in associated cause of death fields.

Follow-up was censored at the date of death or at five years' post-incident MI admission date for the first two periods, and for the third period, at date of death, five years following incident MI, or at 30 June 2011 (maximum length of dataset), whichever came first. The median follow-up time for the third period was 3.16 years. Of the patients recorded as dying during the follow-up period, seven had a missing cause of death (three with diabetes and four without diabetes) and were excluded from all CVD mortality analyses.

Comorbidities

Comorbidity variables were identified from the linked dataset. A fixed 13-year lookback period from and including the date of incident MI was used, except for prior coronary heart disease (CHD) where recording of unstable angina or other CHD codes within the same episode of care were excluded. ICD codes used to identify the comorbidities of interest were hypertension (ICD-10-AM I10–I15 and ICD-9CM equivalent), heart failure (I50), stroke (I60–I64), chronic kidney disease (CKD)¹⁵ and CHD (I20, I23–25).

Statistical analyses

All results are presented by period (1998–2001, 2002–2005, 2006–2009), gender and diabetes status. Baseline cohort characteristics are presented as mean (SD) for continuous and percentages for categorical variables. Overall comparisons and trends in continuous and categorical baseline characteristic variables were estimated from unadjusted linear and logistic regression models respectively. To determine whether the coding of underlying cause of death changed throughout

the study, the percentage of all deaths recorded as CVD was measured, and changes between periods estimated using logistic regression. Unadjusted 5-year mortality was estimated from Kaplan Meier survival curves, and log-rank p-values are presented for comparisons in unadjusted mortality between periods for each gender and diabetes status grouping. Cox proportional hazards regression models were used to estimate the effect of diabetes on the risk of all-cause and CVD mortality using time since incident MI as the time scale. Stepwise addition of variables to the model was undertaken to determine the impact of each covariate on the estimated diabetic versus non-diabetic hazard ratio (HR). Covariates included in the models were age (continuous) and age², Indigenous status, CKD, hypertension, heart failure, stroke and prior CHD. Results are presented as HR (95% CI). To test for a change in HRs over the study period, an interaction term (period × diabetes status) was added to the model. The proportional hazards assumption was tested with an interaction term for diabetes status and time, separately for each period and gender grouping. No evidence of violation of the assumption was found. Statistical significance levels are set at $p < 0.05$. All statistical analyses were undertaken using SAS v9.4 (Cary, NC).

RESULTS

There were 24,186 incident MI cases identified between 1998 and 2009. Patients dying within 30 days of MI hospitalisation ($n=1592$) were excluded from the study, leaving 22,594 people in the study cohort. The percentage of MI cases with diabetes increased from 20.4% to 24.1% in men, and from 27.7% to 31.8% in women over the study period (Table 1). Women were on average older than men at the time of incident MI in both the diabetes (3.6 years) and non-diabetic groups (6.7 years). Men with diabetes were on average 3 years older in each period than their non-diabetic counterparts ($p < 0.0001$), while there was no significant difference in women by diabetes status. People with diabetes had higher levels of all comorbidities in each period ($p < 0.0001$). Similar trends in the percentage of diabetic and non-diabetic patients with heart failure (decreasing) and hypertension (increasing) were apparent. The percentage with CKD increased over time in diabetic men and women but remained unchanged in those without diabetes.

There were 3780 deaths, with 26.9% of people with diabetes and 13.4% of people without diabetes dying during the follow-up period. Of all recorded deaths, the percentage where CVD was the underlying cause of death was higher in non-diabetic (50.2%) than diabetic men (46.0%, $p=0.02$), but similar in non-diabetic and diabetic women (48.0% and 49.8% respectively, $p=0.49$). The percentage of deaths recorded as CVD did not significantly change during the study period in diabetic women ($p=0.16$), but decreased for non-diabetic men and women, and men with diabetes (all $p<0.01$). When the modified definition of CVD death was applied, trends were similar to those for the standard definition across each gender/diabetes grouping.

Trends in all-cause mortality

. Unadjusted all-cause mortality remained stable over the study period for diabetic men (27.1% to 25.5%; $p=0.30$) and women (34.9% to 36.1%; $p=0.59$) (Table 2), as well as for non-diabetic women (21.0% to 19.4%, $p=0.08$), whereas it showed a small significant decrease for non-diabetic men (14.5% to 12.1%, $p=0.03$) (Table 2).

The estimated unadjusted and age-adjusted HRs for 5-year mortality were about two-fold higher in men and women with diabetes than those without diabetes (Table 3). There was no significant change in the unadjusted or multivariable-adjusted HRs throughout the study period in men or women (period x diabetes status interaction $p=0.99$ and $p=0.85$ respectively). The adjusted hazard of all-cause mortality in men and women remained, respectively, 31% (HR 1.31, 95% CI 1.13, 1.53) and 43% (HR 1.43, 95% CI 1.17, 1.74) greater in those with diabetes versus without diabetes in 2006-2009.

Trends in CVD mortality

There was a significant decrease in unadjusted CVD mortality over time for non-diabetic men and women ($p<0.0001$) and men with diabetes ($p=0.006$) (Table 2). However for women with diabetes, CVD mortality was unchanged across the three periods (20.4%, 19.2%, 20.6%, $p=0.79$). The absolute difference between women with and without diabetes increased from the first (-8.1%) to last calendar periods (-13.3%) (Table 2).

There was no significant change in the age-adjusted and multivariable-adjusted HRs for CVD mortality in diabetic versus non-diabetic men from the first to last periods (Table 3). The estimated multivariable-adjusted HR was 1.12 (95% CI 0.91, 1.38) for 1998–2001, 1.43 (1.18, 1.75) for 2002–2005 and 1.08 by 2006–2009 (95% CI 0.85, 1.37; period x diabetes status $p=0.89$). In women, the HRs remained significantly elevated (1998-2001 HR 1.38, 95% CI 1.07, 1.79; 2006-2009 HR 1.73, 95% CI 1.29, 2.32; period x diabetes status $p=0.22$).

When the modified definition of CVD mortality was used for people with diabetes, unadjusted rates were on average 1% higher than those estimated using the standard CVD mortality definition, with declining unadjusted mortality from first to last period in men ($p=0.0013$) but not in women ($p=0.75$) (data not shown).

Effect of covariates

Adding age to the unadjusted models attenuated the HRs in men for all-cause and CVD mortality, whereas for women, HRs tended to be larger (Table 3). Adjustment for CKD and heart failure attenuated the risk appreciably but adjustment for Indigenous status, hypertension, stroke and prior CHD had little additional impact. The effect of adjustment for CKD was greater in each subsequent period, with attenuation of the HR from 1.94 to 1.58 in men, and from 2.03 to 1.71 in women by the last period.

DISCUSSION

Our study demonstrates three important findings. Firstly, there has been little change in excess long-term all-cause mortality following incident MI in people with diabetes over the past decade. Secondly, people with diabetes continue to experience a 1.5-times greater relative risk of all-cause mortality. Thirdly, despite major advances in the management of cardiovascular risk in people with diabetes, the adjusted relative risk of CVD mortality remains significantly elevated

in diabetic versus non-diabetic women, whereas diabetes status is not significantly associated with CVD mortality in men.

A number of studies have reported a temporal decrease in excess all-cause mortality in the broader diabetic population.^{7, 8, 16, 17} However studies confined to MI patients have shown limited improvement in the excess long-term mortality associated with diabetes.^{4-6, 9} Even where the decline in long-term mortality in people with diabetes has been substantial, for example, ~30% decline from 1985-2004 in a MI cohort from the Netherlands,⁴ the mortality differential between individuals with and without diabetes has not reduced. In contrast, a Swedish study using a whole-population MI registry reported a narrowing of this disparity out to 8 years following MI.¹⁸ This result could be partly due to more marked declines in 30-day deaths in people with diabetes in that population. Exclusion of these patients from the present study provides a clearer picture of long-term mortality trends.

Favourable trends in MI incidence and subsequent 30-day case fatality in people with diabetes have been observed in the WA population during the current study period.^{11, 12} However, substantial improvements in long-term mortality in people with diabetes after a first MI were not evident. The disparity between diabetic and non-diabetic patients in the use of evidence-based drugs and revascularisation in the acute phase following an MI is likely to have reduced in recent years^{12, 18} contributing to observed short-term mortality improvements. Despite strong evidence of the effect of control of LDL-C and blood pressure in the secondary prevention setting,^{19, 20} the EUROASPIRE III survey showed that diabetic patients with established CHD continue to receive lower levels of combination therapy for management of cardiovascular risk factors.²¹

The limited change in all-cause mortality in people with diabetes may reflect the increasingly higher prevalence of CKD, hypertension and prior CHD hospitalisations in these patients.¹¹ Renal impairment imparts a high risk of mortality in diabetic patients²² and the multivariable

modelling in our study showed that CKD was increasingly associated with excess all-cause mortality. The Emerging Risk Factors Collaboration reported that diabetes is associated with substantial premature death from cancer, renal disease, pneumonia and infectious diseases,³ and an increasing percentage of deaths are attributed to non-vascular causes in people with diabetes.^{16,17} This may reflect changes in disease aetiology and comorbidity profile in this patient group.

Changes in coding practices may have influenced trends in cause-specific mortality in people with diabetes in Australia.^{10,23} However, our study showed that the percentage of deaths with CVD as the underlying cause decreased in non-diabetics and in men with diabetes, perhaps indicating a real shift in cause of death. This pattern was not observed in women with diabetes for the standard or modified definition of CVD death, supporting the current trends, as artefactual coding changes are likely to impact men and women equally.

In one of few studies reporting trends in CVD mortality after MI, rates fell similarly in diabetic and non-diabetic patients out to 1 year after first acute coronary syndrome presentation, with no gender differences observed.⁹ Our results out to 5-years demonstrate that these favourable trends continued in men with diabetes, but not in women, despite adjustment for differences in baseline risk characteristics, consistent with other studies where further confounders, including dyslipidaemia and weight, were adjusted for.²⁴ Absolute all-cause and CVD mortality rates remained 8–10% higher in women than men in the diabetic group in our study. The higher comorbidity burden and older age in diabetic women is likely to contribute to the elevated mortality risk post-MI.²⁵ Vascular mortality rates have shown less temporal improvement in women who are overweight or obese compared with lean women,²⁶ pertinent given the greater relative increases in obesity in Australian women than men.²⁷

The strength of this study lies in its use of high quality administrative health data, with capture of all incident MI cases and mortality status. We included patients aged up to 84 years, increasing the generalisability of results, but imposed the upper age limit because of decreasing reliability of MI recording with increasing age.²⁸ A limitation of our study is that comorbidity status is

only ascertained from hospitalisation data, which may underestimate the prevalence of some conditions. Because the coding of underlying cause of death may be influenced by changing standards, we also identified CVD death if coded in any cause of death field. This produced trends in CVD mortality in diabetic and non-diabetic patients similar to those seen for our standard and modified definitions. This, along with the modified definition analysis, demonstrates that any changes in cause of death coding are unlikely to have influenced our trend results.

Conclusions

Our study shows that there has been no significant improvement in long-term all-cause mortality in people with and without diabetes following an incident MI in this whole-population setting, resulting in continued excess long-term mortality associated with diabetes. Encouragingly, there is some improvement over time in CVD mortality in men with diabetes, however a lack of improvement in CVD mortality in women with diabetes means that the gap for women may be widening. These results highlight an urgent need for addressing both cardiovascular and non-vascular risk in post-MI patients with diabetes, particularly in women, as improvements in MI incidence and short-term outcomes in people with diabetes are not reflected in current long-term outcomes.

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Table 1. Characteristics of men and women aged 35–84 years with an incident myocardial infarction, stratified by diabetes status.

	Diabetes			No diabetes		
	1998–2001 (n=949; 20.4%)	2002–2005 (n=1186; 23.0%)	2006–2009 (n=1500; 24.1%)	1998–2001 (n=3699; 79.6%)	2002–2005 (n=3965; 77.0%)	2006–2009 (n=4714; 75.9%)
Men						
Mean age, years (SD)	64.38 (11.2)	64.06 (11.36)	64.75 (11.62)	61.45 (12.12)	61.79 (12.19)	61.36 (11.94)
Indigenous, %	6.7	9.6	8.9	2.7	2.6	2.6
Comorbidities, %						
Hypertension	58.4	67.5	79.7**	37.6	39.3	47.6**
Chronic kidney disease	19.6	21.2	23.4*	8.0	6.1	5.2**
Heart failure	27.0	25.4	22.6*	12.3	11.2	8.4**
Stroke	6.7	6.7	5.4	3.2	2.5	2.1*
Prior coronary heart disease	28.3	28.0	32.0*	15.4	14.6	14.3
Women						
Mean age, years (SD)	67.67 (11.42)	68.15 (11.87)	68.14 (11.67)	68.81 (11.65)	68.45 (11.82)	67.51 (12.12)*
Indigenous, %	13.0	12.8	14.4	2.6	2.6	3.0
Comorbidities, %						
Hypertension	71.5	79.6	88.7**	53.2	55.8	57.4*
Chronic kidney disease	19.8	25.4	28.3*	8.4	8.4	6.2*
Heart failure	41.3	36.8	35.2*	20.6	17.4	12.7**
Stroke	7.9	8.4	7.7	4.2	4.2	3.3
Prior coronary heart disease	30.0	31.4	33.2	19.0	17.2	17.1

*P<0.05, **P<0.0001, for trend in each baseline characteristic over the three periods, separately within each diabetes and gender grouping.

Table 2. Trends in 5-year mortality following incident myocardial infarction in men and women aged 35–84 years, stratified by diabetes status.

			All-cause mortality				Cardiovascular disease mortality			
			Deaths, n	Mortality, % [†]	Log-rank p-value	Absolute difference, % [*]	Deaths, n	Mortality, % [†]	Log-rank p-value	Absolute difference, % [*]
Men										
Diabetes	1998–2001	257	27.1	0.30	–12.6	130	14.6	0.006	–6.4	
	2002–2005	334	28.2			160	14.5			
	2006–2009	291	25.5			116	10.5			
No diabetes	1998–2001	536	14.5	0.03	–13.4	294	8.2	<0.0001	–7.6	
	2002–2005	526	13.3			264	6.9			
	2006–2009	410	12.1			181	5.5			
Women										
Diabetes	1998–2001	185	34.9	0.59	–13.9	99	20.4	0.79	–8.1	
	2002–2005	238	36.8			111	19.2			
	2006–2009	201	36.1			101	20.6			
No diabetes	1998–2001	291	21.0	0.08	–16.7	163	12.3	<0.0001	–10.0	
	2002–2005	290	19.2			132	9.2			
	2006–2009	221	19.4			90	7.3			

[†]Unadjusted 5-year mortality from Kaplan Meier survival curves.

*Absolute 5-year mortality difference between diabetic and non-diabetic patients.

Table 3. Unadjusted hazard ratios (95% confidence interval), and adjusted hazard ratios after stepwise addition of covariates, for 5-year all-cause and cardiovascular mortality in people with and without diabetes, stratified by gender and period.[†]

		Unadjusted	Adjusted for:						
			+ age	+ Indigenous status	+ chronic kidney disease	+ hypertension	+ heart failure	+ stroke	+ prior coronary heart disease
All-cause mortality									
Men	1998–2001	2.03 (1.75, 2.36)	1.76 (1.52, 2.04)	1.69 (1.46, 1.97)	1.55 (1.34, 1.80)	1.50 (1.29, 1.75)	1.35 (1.16, 1.56)	1.33 (1.14, 1.54)	1.31 (1.13, 1.52)
	2002–2005	2.35 (2.05, 2.70)	2.22 (1.93, 2.54)	2.09 (1.82, 2.40)	1.85 (1.61, 2.12)	1.75 (1.52, 2.01)	1.62 (1.41, 1.86)	1.60 (1.39, 1.84)	1.59 (1.38, 1.83)
	2006–2009	2.37 (2.04, 2.75)	1.96 (1.69, 2.28)	1.86 (1.60, 2.16)	1.53 (1.31, 1.79)	1.46 (1.25, 1.70)	1.34 (1.14, 1.56)	1.34 (1.14, 1.56)	1.31 (1.13, 1.53)
	Trend p-value [‡]	0.16	0.31	0.40	0.89	0.75	0.93	0.96	0.99
Women	1998–2001	1.80 (1.50, 2.17)	2.04 (1.69, 2.45)	1.93 (1.60, 2.32)	1.77 (1.47, 2.13)	1.76 (1.46, 2.12)	1.50 (1.24, 1.82)	1.47 (1.22, 1.78)	1.46 (1.21, 1.77)
	2002–2005	2.15 (1.81, 2.56)	2.27 (1.91, 2.69)	2.16 (1.81, 2.56)	1.89 (1.59, 2.25)	1.88 (1.58, 2.24)	1.64 (1.38, 1.96)	1.62 (1.36, 1.94)	1.61 (1.35, 1.92)
	2006–2009	2.09 (1.73, 2.53)	2.16 (1.78, 2.61)	2.02 (1.67, 2.45)	1.70 (1.40, 2.06)	1.69 (1.39, 2.05)	1.45 (1.19, 1.77)	1.45 (1.19, 1.77)	1.43 (1.17, 1.74)
	Trend p-value [‡]	0.28	0.66	0.73	0.77	0.76	0.79	0.89	0.85
Cardiovascular disease mortality [~]									
Men	1998–2001	1.87 (1.52, 2.29)	1.61 (1.31, 1.98)	1.56 (1.27, 1.92)	1.40 (1.13, 1.72)	1.34 (1.09, 1.65)	1.15 (0.94, 1.42)	1.13 (0.92, 1.40)	1.12 (0.91, 1.38)
	2002–2005	2.24 (1.84, 2.72)	2.13 (1.75, 2.59)	2.02 (1.66, 2.47)	1.73 (1.42, 2.12)	1.61 (1.32, 1.97)	1.46 (1.19, 1.78)	1.44 (1.18, 1.76)	1.43 (1.17, 1.75)
	2006–2009	2.13 (1.69, 2.69)	1.74 (1.38, 2.20)	1.67 (1.32, 2.11)	1.32 (1.04, 1.67)	1.24 (0.98, 1.57)	1.10 (0.87, 1.40)	1.10 (0.86, 1.39)	1.08 (0.85, 1.37)
	Trend p-value [‡]	0.39	0.55	0.62	0.77	0.20	0.82	0.90	0.89
Women	1998–2001	1.72 (1.34, 2.21)	1.99 (1.55, 2.55)	1.87 (1.46, 2.41)	1.74 (1.35, 2.24)	1.72 (1.33, 2.21)	1.43 (1.11, 1.86)	1.39 (1.08, 1.80)	1.38 (1.07, 1.79)
	2002–2005	2.19 (1.70, 2.82)	2.33 (1.81, 3.00)	2.21 (1.71, 2.85)	1.95 (1.51, 2.52)	1.93 (1.49, 2.50)	1.64 (1.27, 2.13)	1.61 (1.24, 2.09)	1.60 (1.23, 2.07)
	2006–2009	2.57 (1.93, 3.42)	2.69 (2.02, 3.57)	2.50 (1.88, 3.33)	2.13 (1.60, 2.85)	2.10 (1.57, 2.81)	1.75 (1.31, 2.35)	1.76 (1.31, 2.37)	1.73 (1.29, 2.32)
	Trend p-value [‡]	0.03	0.11	0.12	0.25	0.57	0.27	0.20	0.22

[†] Derived from Cox regression models. Adjustment for age includes age (continuous) and age², Indigenous status, hypertension, chronic kidney disease, heart failure, stroke and prior coronary heart disease.

[‡] Derived from Cox regression models, with stepwise adjustment for all covariates, and the addition of an interaction term for period X diabetes status.

[~]Based on standard definition of cardiovascular mortality.

Figure legend:

Figure 1. Kaplan Meier survival curves for all-cause mortality following incident myocardial infarction in men from 1998–2001 (A), 2002–2005 (B), and 2006–2009 (C); and in women from 1998–2001 (D), 2002–2005 (E) and 2006–2009 (F). People with diabetes = solid lines; people without diabetes = dashed lines. Log-rank $p < 0.0001$ for all comparisons.