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ORIGINAL ARTICLE

All-Cause Mortality Following an Acute Coronary Syndrome: 12-Year Follow-Up of the Comprehensive 2002 New Zealand Acute Coronary Syndrome Audit

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Background To describe the long-term mortality of a complete national cohort of acute coronary syndrome (ACS) patients enrolled in 2002, to compare this with a national age, sex and Māori ethnicity matched population, and to assess the influence of baseline factors on the 12-year mortality.

Methods We reviewed 721 patients with a discharge diagnosis of an ACS who were enrolled in the first New Zealand ACS audit group cohort over 14 days in May 2002. We matched the cohort to the national mortality database using each patient's unique national identity number.

Results Over a median follow-up of 12.7 years of 721 patients discharged with an ACS, overall mortality was 52%: ST-elevation myocardial infarction (STEMI) (58%), non-ST-elevation myocardial infarction (NSTEMI) (61%) and unstable angina pectoris (UAP) (42%) patients, $p < 0.0001$. In an age-adjusted survival model, males had a 29% increased mortality rate compared to females with a hazard ratio of 1.29 (95% CI 1.04, 1.61, $p = 0.019$). Over 12 years there were 339 (47%) deaths, compared to 284 (39%) deaths observed in the matched population. The standardised mortality ratio for patients admitted with an ACS in New Zealand is 1.3 (95% CI 1.2, 1.5) with eight patients per 100 not surviving to 12 years compared to this matched population.

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Conclusions The high mortality rate in this ACS cohort is a stark reminder of the prognostic implications of a presentation with an ACS. It emphasises the on-going need for optimal management of these patients throughout every stage of their initial treatment and subsequent on-going care.

Keywords Acute coronary syndromes • Prognosis • Follow-up studies • Death

Introduction

The short-term risk of death after an acute coronary syndrome (ACS) has been well characterised [1–5] with the 12-month mortality of a contemporary 2012 Australia and New Zealand population being recorded as 9.8% ST-elevation myocardial infarction (STEMI patients), 6.0% non-ST-elevation myocardial infarction (NSTEMI patients) and 1.7% unstable angina pectoris (UAP patients) [6].

However, published long-term mortality data are very limited. A principle problem is that data collection methods differ and many ACS cohorts are hampered by selection and information bias. Hence comprehensive follow-up data of complete ACS cohorts are rare. Long-term data from Australia and New Zealand are particularly uncommon.

Long-term mortality data following an ACS would be of significant value to patients, clinicians and, potentially, for the design of a contemporary ACS follow-up service. In particular, it is well known that patients benefit from on-going secondary prevention medication, although up to 50% are no longer taking all of their medications some 3 years following an ACS [7]. In addition, further coronary revascularisation may significantly improve symptoms and prognosis for ACS patients during follow-up but many patients do not access these procedures [1–5,8,9]. A more intensive follow-up program may help patients who are currently not followed in a systematic way. An awareness of the actual prognostic disadvantage that ACS patients experience following their initial hospitalisation, may lead to changes in the design of their long-term management, and subsequently to an improved long-term prognosis for these high-risk survivors of an ACS.

The 2002 New Zealand ACS Audit Group carried out a comprehensive collection of data from all ACS patients admitted to a New Zealand Hospital over a 14-day period in May 2002. The objective was to better understand patient numbers, characteristics, in-hospital management and prognosis, and facilitate improved ACS management across New Zealand [10,11]. Here we report on the long-term prognosis of this entire ACS cohort of 721 patients, and compare mortality with a calculated age, sex, and Māori ethnicity-adjusted New Zealand population.

Methods

Study Population and Centres

The 2002 audit was conducted by the New Zealand ACS Audit Group, a network created for this purpose, which consisted of one or more cardiologists or general physicians from every hospital in New Zealand that admitted ACS patients (n = 36 hospitals in 2002). Most centres also co-opted one or more research nurses or registrars to assist with data collection for the study.

All hospitals contributed fully to the collection of ACS patient data. Detailed methodology of how the audit was undertaken has been previously reported [10,11]. In brief, all patients admitted to a New Zealand hospital overnight with a suspected or definite ACS during the study period of 2 weeks in mid-May of 2002, were included.

Data Collection

Demographics, past history, presentation, investigations, treatments and discharge diagnoses were prospectively recorded for each patient's acute care episode including hospital transfers. Discharge diagnosis was used to describe the patient groups. Here we review the ACS patients: ST-segment elevation myocardial infarction (STEMI), Non-STEMI (NSTEMI) and unstable angina pectoris (UAP) patients. All 36 hospitals had the facilities for assessing troponin levels, with one of five different troponin analysers being used. NSTEMI and UAP ACS patients were separated by means of a 'positive' troponin at the local centre, using the (then) standard 'cut-off' level for a 'positive' test, for patients with an ACS [10].

Hypertension and dyslipidaemia were defined as patients on treatment, or with a previous clinical diagnosis. Patients with diabetes mellitus were those on diet control, oral or insulin treatment. We calculated a Global Registry of Acute Coronary Events (GRACE) risk score for in-hospital mortality, for each patient, using the Grainger method [12].

A 2-week audit period was accepted as a compromise between the need to collect sufficient patient numbers to obtain an accurate representative cohort versus the ability of unfunded clinicians and nurses to collect the consecutive, comprehensive patient data. We collected data from 00.00 on Monday 13 May to 24.00 on Sunday 26 May 2002.

National health index (NHI) numbers for all patients were matched for date of death with the New Zealand Ministry of Health national mortality index database. The national mortality index also records the cause of death (primary International classification of diseases (ICD)-10 code), which we have characterised as cardiovascular system (CVS) death (ICD-10 I00 to I99 Inclusive) and non-CVS death at follow-up. Cause of death for deaths which occurred after 2015 (36/374 (10%)) were not available as the national mortality cause of death data are not distributed until all coronial or other investigations have been completed.

Ethical approval was obtained using the 2002 New Zealand ethics process from the 'Northern' Health Ethics

Committee after input from all 14 local ethics committees across New Zealand. As an audit of current practice, individual patient consent was not required.

Data Analyses

General

Mean (standard deviation) or median (interquartile range) were used to present continuous variables as indicated, and frequency (percentage) for categorical variables. Wilcoxon/Kruskal Wallis test and Fisher's exact or chi-squared test (exact methods) as appropriate were used for between group comparisons for continuous and categorical variables. Confidence intervals for rates were calculated using a mid P method (www.openepi.com accessed 4/05/2017) SAS (v 9.4, SAS Institute Inc, Cary, NC, USA) was used to perform statistical analyses.

Life table and Cox proportional hazards models were calculated using the lifetest and phreg procedures of SAS. Analysis of variance was used to compare normally distributed mean differences between treatment arms and Tukey's post hoc test was employed to identify the nature of any differences between the groups. All tests were two tailed and $p < 0.05$ was considered significant.

Matched Population Specific

The 12.5 year all-cause mortality was calculated for a theoretical New Zealand population matched on age (per year), sex and Māori or Non-Māori ethnicity using the 2005-2007 life table (http://www.stats.govt.nz/browse_for_stats/health/life_expectancy/new-zealand-life-tables-2005-07.aspx, accessed 4/05/2017), all ages over 99 years are treated as 99-year-olds. The individual year percentages were used to calculate the overall probability of a person living to 12.5 years from their start age. The standardised mortality ratio and confidence interval were calculated using OpenEpi (http://www.openepi.com/Menu/OE_Menu.htm, accessed 14 July2016). This matched patient population was of the whole population, including people who subsequently died from an ACS, rather than an 'ACS-free' population (which cannot be calculated).

Mortality Curves by ACS Type

An age and sex-adjusted Cox proportional hazard model was fitted, however the proportionality assumption was not met for those patients with a STEMI discharge diagnosis and so an interaction term was created for death during the first 5 years of follow-up and then 5 years and beyond. The proportionality assumption was then satisfied for each time band.

Results

Over 14 days, 721 patients with a medium age of 70 years were admitted to a New Zealand Hospital with an ACS [STEMI (14%), NSTEMI (40%), or UAP (46%)]. Female patients were 42% of the cohort, and were 4 years older than male patients (72 vs 68 years, $p < 0.0001$) (Table 1). Most patients (81%) were of European ethnicity; 37% patients had experienced a previous myocardial infarction (MI); 12% previous peripheral arterial disease (PAD); and 13% a prior transient ischaemic attack (TIA) or stroke.

ACS Type

STEMI and NSTEMI patients were older than UAP patients (72, 73 and 67 years, $p < 0.0001$) (Table 2). Fewer STEMI patients had a history of a previous MI compared to NSTEMI or UAP patients (24%, 45% and 33%, $p < 0.0001$). STEMI and NSTEMI patients had a higher GRACE score than UAP patients (140, 138 and 107, $p < 0.0001$).

All-Cause Mortality

For all ACS patients, 26 (3.6%) patients died in hospital, 38 (5.3%) by 30 days, 83 (12%) by 1 year, and 374 (52%) patients by a median of 12.7 (IQR, 4.6-13.3, maximum 13.5) years of follow-up (Table 3). Significantly more STEMI patients died in hospital compared to NSTEMI and UAP patients (14%, 3.5% and 0.6%, $p < 0.0001$). However, after 6 months of follow-up, there was then no difference in the mortality of STEMI and NSTEMI patients. However, UAP patients had a consistently lower mortality throughout the follow-up.

Mortality Curves by ACS Type

All-cause, unadjusted 12-year mortality from an ACS admission by ACS type was worse for STEMI patients (54%) and NSTEMI patients (57%), compared to UAP patients (37%), ($p < 0.001$) (Figure 1a). Compared to patients discharged with unstable angina, the age/sex adjusted hazard of death to 5 years, was 1.09 (95% CI 0.78, 1.54) for patients discharged with a NSTEMI, and 2.63 (95% CI 1.68, 4.12) for patients discharged with a STEMI (Figure 1b). However, the age and sex adjusted hazard of death *after* 5 years following discharge was similar: 1.45 (1.05, 2.00), NSTEMI patients, and 1.28 (95% CI 0.81, 2.01) for STEMI patients, respectively, compared to UAP patients *after* 5 years (Figure 1b).

Mortality Curves by Sex

For all ACS patients, all-cause unadjusted mortality from an ACS admission by sex was the same ($p = 0.81$) (Figure 2a). However, an age-adjusted Cox proportional hazard mortality curve over the median 12.7 years follow-up demonstrated a 29% worse survival in males, with a hazard ratio of 1.29 (95% CI 1.04, 1.61, $p = 0.019$) compared to female patients (Figure 2b).

Kaplan-Meier All-Cause ACS Mortality vs a 'Matched' Population

The age, sex and Māori-ethnicity adjusted 'matched' population had an overall mortality of 39% after 12 years. This compared to patients presenting with an ACS who after 12 years had a 47% death rate, with a 50% median survival at

Table 1 **ACS Patient demographics (n = 721).**

	Male	Female	p	All
n	418	303		721
Median Age (IQR)	68 (55, 77)	72 (63, 80)	**<0.0001**	70 (58, 78)
Ethnicity				
European	337 (81%)	249 (82%)	0.63	586 (81%)
Māori	24 (5.7%)	20 (6.6%)	0.64	44 (6.1%)
Other	57 (14%)	34 (11%)	0.36	91 (13%)
Smoker				
Current	99 (24%)	39 (13%)	**0.0003**	138 (19%)
Previous	205 (49%)	94 (31%)	**<0.0001**	299 (41%)
Never	104 (25%)	159 (52%)	**0.0009**	263 (36%)
Not reported	10 (2.4%)	11 (3.6%)	0.37	21 (2.9%)
Major Risk Factors				
Hypertension	172 (43%)	181 (60%)	**<0.0001**	353 (50%)
Diabetes Mellitus	69 (17%)	58 (20%)	0.32	127 (18%)
Dyslipidaemia	145 (36%)	111 (39%)	0.58	256 (37%)
CVS History				
Prior MI	152 (38%)	104 (35%)	0.58	256 (37%)
Prior PAD	48 (12%)	33 (11%)	0.81	81 (12%)
Prior TIA/Stroke	54 (13%)	40 (13%)	0.99	94 (13%)
Prior AF	55 (13%)	33 (11%)	0.42	88 (13%)
Prior Angiogram	123 (30%)	75 (25%)	0.15	198 (28%)
Prior PCI	53 (62%)	32 (11%)	0.48	85 (12%)
Prior CABG	49 (12%)	24 (8%)	0.10	73 (10%)
GRACE Score				
GRACE Score	124 (44)	123 (44)	0.75	124 (44)
GRACE Score ≥ 140	145 (57%)	237 (58%)	0.99	253 (58%)

Abbreviations: IQR: interquartile range, MI: Myocardial infarction, PAD: Peripheral arterial disease, TIA: Transient ischaemic attack, PCI: Percutaneous coronary intervention. CABG: Coronary artery bypass graft, AF: Atrial fibrillation, GRACE: Global registry of acute coronary events, STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST-elevation myocardial infarction, UAP: Unstable angina pectoris.

12.8 years (Figure 3). This equates to a difference of eight ACS patients per 100 not surviving to 12 years following an ACS, compared to this matched population.

Univariate Analysis of All-Cause Death

We used a univariate analysis of variables thought likely to be associated with all-cause death over the maximum 13.5 years of follow-up. We found that significant factors which more than doubled the mortality risk were age: >75 years (HR 8.3, 95% CI 6.0, 11.4); age 60–75 years (HR 2.6, 95% CI 1.9, 3.7); and the presence of previous vascular disease in other arterial territories; history of PAD (HR 2.4, 95% CI 1.8, 3.1); and a history of previous TIA or stroke (HR 2.1, 95% CI 1.6, 2.7) (Figure 4a).

Multivariate Analysis of All-Cause Death

All variables from the univariate analysis were included in a fully saturated multivariate analysis model of all-cause death over the maximum 13.5 years of follow-up. We found that the significant factors which more than doubled the risk were now only age: >75 years (HR 7.1, 95% CI 4.7, 10.7) and age 60–75 years (HR 2.4, 95% CI 1.6, 3.6) (Figure 4b). Other factors which significantly increased the risk were: a presentation with a NSTEMI (HR 1.5); a history of MI (HR 1.3); TIA or stroke (HR 1.5) or hypertension (HR 1.3).

Kaplan-Meier Mortality by Age Group

All-cause, unadjusted 12-year death from an ACS admission by age group emphasised the importance of age on all-cause patient mortality: 19% (<60 years), 41% (60–75 years) and 81% (>75 years), ($p < 0.001$) (Figure 5).

Cause of Death

Cause of death was available for 90% of deaths after discharge from the index admission. Numerically, slightly more deaths were primarily related to the cardiovascular system in the first 5 years post discharge (98 [58%]) compared with

Table 2 Baseline demographics by STEMI, NSTEMI or UAP.

	STEMI	NSTEMI	UAP	p*	p**
n	**101 (14%)**	**287 (40%)**	**333 (46%)**		
Median Age (IQR)	72 (58, 81)	73 (62, 80)	67 (55, 76)	<**0.0001**	0.57
Gender (male)	60 (59%)	178 (62%)	180 (54%)	0.13	0.64
Ethnicity					
European	80 (79%)	236 (82%)	270 (81%)	0.79	0.55
Māori	8 (7.9%)	12 (4.2%)	24 (7.2%)	0.21	0.19
Other	13 (13%)	39 (14%)	39 (12%)	0.78	0.99
Smoker					
Current	29 (29%)	52 (18%)	57 (17%)	**0.037**	**0.03**
Previous	35 (35%)	126 (44%)	138 (41%)	0.27	0.13
Never	33 (33%)	100 (35%)	130 (39%)	0.39	0.72
Not reported	4 (4.0%)	9 (3.1%)	8 (2.4%)	0.69	0.74
Major Risk Factors					
Hypertension	41 (41%)	145 (51%)	167 (52%)	0.15	0.10
Diabetes Mellitus	10 (10%)	64 (23%)	53 (26%)	**0.014**	**0.005**
Dyslipidaemia	20 (21%)	93 (34%)	143 (45%)	<**0.0001**	**0.016**
CVS History					
Prior MI	24 (24%)	128 (45%)	104 (33%)	<**0.0001**	**0.0002**
Prior PAD	9 (9.3%)	37 (13%)	35 (43%)	0.49	0.37
Prior TIA/Stroke	14 (14%)	37 (13%)	43 (12%0	0.95	0.86
Prior AF	7 (7.1%)	42 (15%)	39 (12%)	0.13	0.055
Prior Angiogram	12 (12%)	69 (25%)	117 (36%)	<**0.0001**	**0.01**
Prior PCI	4 (4.1%)	23 (8.3%)	58 (18%)	<**0.0001**	0.25
Prior CABG Surgery	4 (4.1%)	28 (9.8%)	41 (13%)	0.054	0.09
GRACE Score					
GRACE Score	140 (46)	138 (42)	107 (38)	<**0.0001**	0.86
GRACE Score > 140	47 (53%)	139 (52%)	67 (22%)	<**0.0001**	0.82

Abbreviations: IQR: interquartile range, MI: Myocardial infarction, PAD: Peripheral arterial disease, TIA: Transient ischaemic attack, PCI: Percutaneous coronary intervention. CABG: Coronary artery bypass graft, AF: Atrial fibrillation, GRACE: Global registry of acute coronary events, STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST-elevation myocardial infarction, UAP: Unstable angina pectoris.

*To assess significant differences between all three groups.

**STEMI v NSTEMI.

deaths after 5 years follow-up (86 [48%]), although this was a non-significant finding (p = 0.083).

Discussion

This study has several important findings. We have shown that, from a comprehensive New Zealand cohort of ACS patients, by 12 years, there was an overall mortality of nearly half (47%) of these patients. STEMI (54%) and NSTEMI (57%) patients had a higher mortality compared to UAP (37%) patients. Furthermore, we have calculated that there are eight more deaths per 100 people than would be expected from a matched age, sex and Māori-ethnicity population. These data suggest there is a need to improve the long-term management of ACS patients.

It is remarkable that accurate mortality data from a complete ACS cohort are so uncommon.

There have been three broad categories of studies used to assess mortality following an ACS. The first category originates from large-scale randomised controlled trials with numerous inclusion and exclusion criteria. These provide the most secure evidence for the impact of a specific treatment, and help to understand predictors of early mortality but, the trial population is selected, and not a representative cohort. A trial will often exclude individuals who are at higher risk who may be older, with additional co-morbidities such as renal dysfunction, and those at higher risk of complications of the drug or treatment. Trials may also under-represent females or certain ethnicities, hence even short-term prognostic data from these sources are of limited value [13,14].

Table 3 Cumulative all-cause mortality: by type of myocardial infarction.

	STEMI	NSTEMI	p*	UAP	p**	All
n	101	287		333		721
Died in Hospital	14 (14%)	10 (3.5%)	**0.0005**	2 (0.6%)	**0.011**	26 (3.6%)
Dead by 30 days	16 (16%)	20 (7.0%)	**0.015**	2 (0.6%)	<**0.0001**	38 (5.3%)
Dead 30 days–6 months	21 (21%)	34 (12%)	**0.032**	10 (3.0%)	<**0.0001**	65 (9.0%)
Dead 6 months–1 year	23 (23%)	47 (16%)	0.18	13 (4.2%0	<**0.0001**	83 (12%)
Dead 1 year–18 months	24 (24%)	53 (18%)	0.25	19 (5.7%)	<**0.0001**	96 (13%)
Dead 18 months–5 years	34 (34%)	96 (33%)	0.99	60 (18%0	<**0.0001**	190 (26%)
Dead 5 years–10 years	48 (48%)	146 (51%)	0.64	107 (32%)	<**0.0001**	301 (42%)
Dead 10 years–13.5 years	59 (58%)	174 (61%)	0.72	141 (42%)	<**0.0001**	374 (52%)
Years FU Median (IQR)	11.2 (1.8, 13.3)	9.4 (2.6, 13.3)	0.84	13.3 (7.9, 13.3)	<**0.0001**	12.7 (4.6, 13.3)

Abbreviations: STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST-elevation myocardial infarction, UAP: Unstable angina pectoris.

*To assess significant differences between STEMI and NSTEMI.

**NSTEMI v UAP.

The second category of studies come from registries based on voluntarily reported cases. Prognostic data from these large registries, may be hampered by selection and information bias. However, there are certainly notable international cohorts which have enrolled populations widely acknowledged to be relatively representative of the entire cohort, from which much of our current knowledge on prognosis after an ACS is based [15,16].

The third category of studies rely on the use of electronically collected disease coding data. However, these tend to supply a limited in-depth knowledge of each ACS case. Nonetheless, identifying all ACS patients from data which is routinely collected is intuitively correct, and has great promise for understanding ACS patient management [17]. Subsequent data matching for patient outcomes, particularly readmission rates and mortality can then be undertaken [18,19], although there will always be an inability to collect in-depth patient treatment and management, from this approach.

International ACS Long-Term Follow-Up Studies

The Global Registry of Acute Coronary Events (GRACE) study is widely acknowledged to have significantly increased our understanding of ACS populations [15]. In 2010, Fox and colleagues reported the GRACE 'long-term' study and emphasised how few long-term follow-up studies of ACS cohorts were available in the literature, and stated that the late consequences of an ACS were therefore poorly defined [20]. Their 'long-term' follow-up was over 5 years of 3721 GRACE ACS patients recruited from the United Kingdom and Belgium. They found that less than a fifth of all deaths occurred during the initial hospitalisation, with a subsequent ''under-estimated and under-recognized'' ongoing patient mortality, which at 5 years they reported as 19% (STEMI), 22% (NSTEMI) and 11% (UAP) patients [20].

In comparison with the 2002 New Zealand cohort patients, the GRACE long-term study patients were younger: STEMI 65 vs 72 years, NSTEMI 67 vs 73 years, UAP 66 vs 67 years, and their mortality was less at 5 years: STEMI 19% vs 34%, NSTEMI 22% vs 33%, UAP 11% vs 18%. It is possible that the patients' age difference was the result of some selection bias of the GRACE patients, compared to the complete national cohort obtained from the New Zealand cohort.

An increasingly recognised aspect of ACS patient management and outcomes is the influence of sex [21]. We have found that in a complete population of ACS patients, the mortality at 12 years was the same for male and female patients. However, female patients were older than male patients (72 vs 68 years, $p < 0.001$), and with an adjustment for age, there was a 29% increased mortality risk for male patients.

In other studies of long-term outcomes, the evidence for a difference in mortality between female and male patients following ACS is conflicting. Bucholz and colleagues undertook a major systematic review to evaluate the existing literature on sex differences in long-term mortality after ACS, with follow-up periods of >5 years [22]. They assessed 39 studies, although most studies included less than one-third women. Not surprisingly there was significant heterogeneity between these study populations, but of 26 studies reporting mortality at 5 to 9 years after an MI, 13 (50%) reported significantly higher unadjusted mortality for women compared with men, two (8%) reported higher mortality for men, and seven (27%) found non-significant differences in mortality between men and women. However, many of the differences in mortality became attenuated after adjustment for age. Further, although multivariate models varied between studies, most reported a further reduction in sex differences after covariates other than age were examined.

Hence, our finding that females have a *better* long-term outcome, when adjustment for age is made, is of interest. Again, it is possible that most previous cohorts were not of

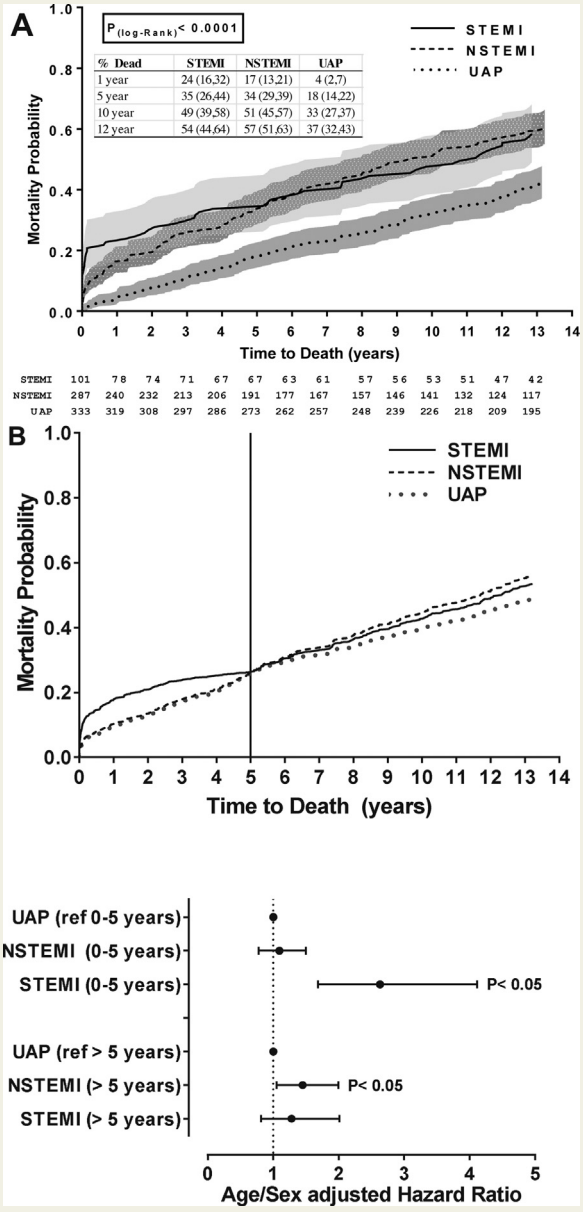

Figure 1 (a) Kaplan-Meier All Cause unadjusted mortality from an ACS admission, by ACS type. Number of patients at risk at each time point is shown below the figure. (b) Cox Proportional Hazard mortality from an ACS admission, by ACS. Adjusted for age and sex.

complete ACS populations, and our finding may be reproduced by others if complete ACS cohorts are studied in future.

Australia and New Zealand ACS Follow-Up Studies

No previous Australian or New Zealand study has described a comprehensive ACS cohort with long-term survival data. Previous studies have been of short or medium-term duration and have described registry patient data or patient data from disease coding.

Registry Studies

The local GRACE cohort was from nine centres from Australia and two from New Zealand [20]. Management and outcomes from 5615 ACS patients over 8 years (2000 to 2007) has been published. This paper described short-term mortality at 6 months, which, in four consecutive 2-year groups, was 8.9% to 12.2% (STEMI patients) and 4.2% to 7.6% (NSTEACS patients) [23].

In comparison, the 2002 New Zealand cohort had worse mortality at 6 months of 21% (STEMI patients) and 12% (NSTEMI patients). The comparison is limited by the different definitions of UAP and NSTEMI patients [24] in the New Zealand ACS cohort [10,11] and the GRACE cohort [23], but the GRACE cohort was younger: 63 vs 72 years for STEMI patients and 64 vs 73/67 years for NSTEACS vs NSTEMI/UAP patients, which might suggest an incomplete ACS population was described by the GRACE study.

The Australian Acute Coronary Syndrome Prospective Audit (ACA-CIA) was conducted between November 2005 and May 2006 and was a registry which included 3402 patients from 39 hospitals across all states and territories of Australia [25]. Patients enrolled were younger than the 2002 New Zealand cohort: 62 vs 73 years (STEMI patients), 68 vs 73 years (NSTEACS-High Risk vs NSTEMI patients) and 61 vs 67 years (NSTEACS Intermediate Risk vs UAP patients).

A comparison of the 2002 New Zealand data with the ACA-CIA 12-month overall mortality [26], again with some limitations due to a difference in definition of the patient groups, demonstrates a worse prognosis in the New Zealand cohort: 23% vs 8.0% (STEMI patients), 16% vs 10.5% (NSTEMI patients), 4.2% vs 3.3% (UAP patients). This might again suggest that an incomplete ACS population was described by the ACA-CIA study.

It might be considered that there is an actual difference in outcomes for Australian ACS patients, compared to New Zealand ACS patients, for a variety of social and health care related issues. This has been previously reported from the Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) study [27,28], which enrolled 5949 Australians and 2784 New Zealanders with a history of myocardial infarction or hospitalisation with unstable angina within the previous 3 months to 3 years. During a median follow-up period of 7.8 years, cardiovascular mortality was higher in New Zealand patients compared to Australian patients (HR 1.42, 95% CI: 1.25–1.61). Possible causes included fewer percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) revascularisation procedures in New Zealand patients, and a higher average serum total to high density lipoprotein (HDL) cholesterol ratio in New Zealand patients, from a relative lack of statin medication availability in the New Zealand health care environment at the time.

However, an in-depth comparison of the more recent SNAPSHOT 2012 cohort found virtually identical in-hospital

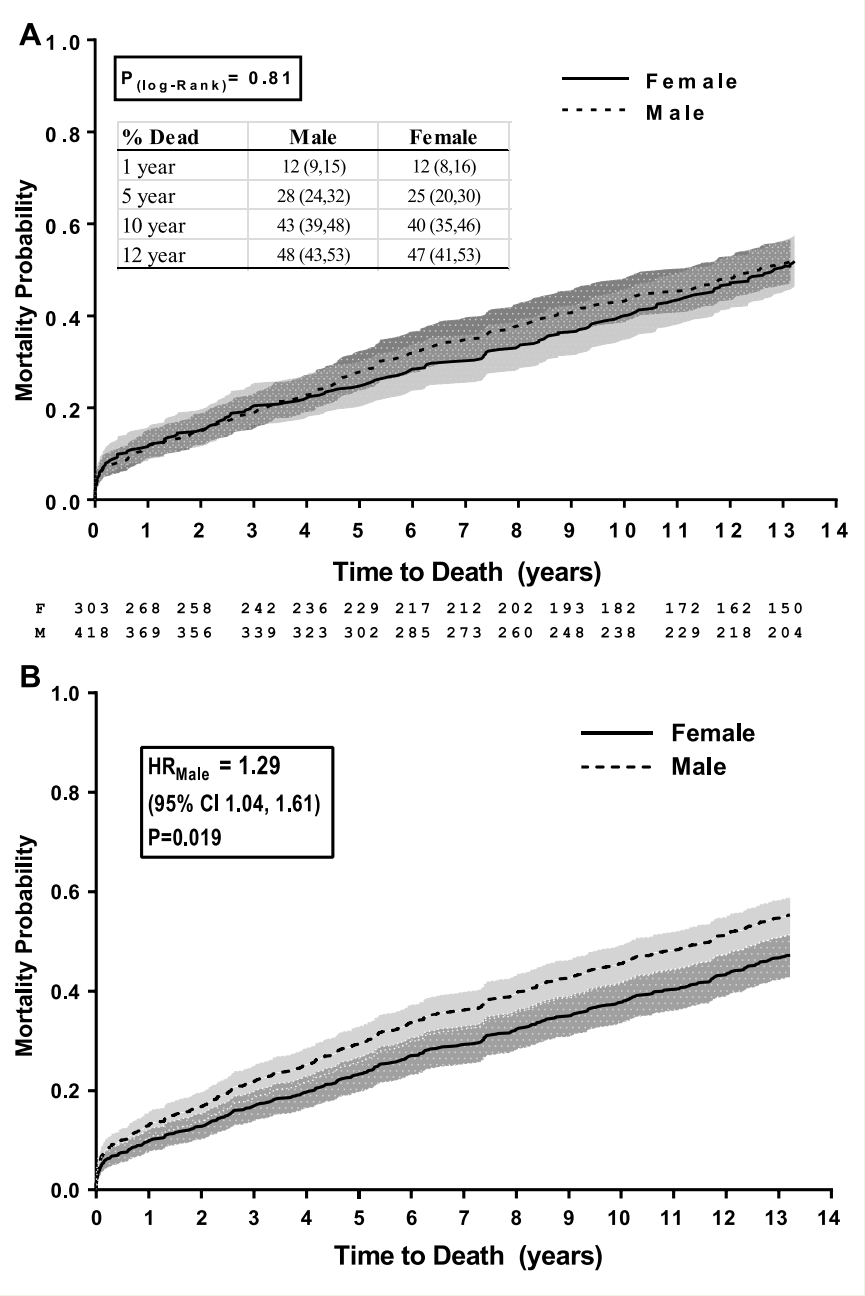

Figure 2 (a) Kaplan-Meier All Cause unadjusted mortality from an ACS admission, by sex. Number of patients at risk at each time point is shown below the figure. (b) Cox Proportional Hazard All-Cause mortality from an ACS admission, by sex: adjustedfor age.

management and mortality between Australia and New Zealand ACS patients [29]. It seems more likely that the mortality differences seen between the ACA-CIA cohort and the 2002 New Zealand cohort are due to a more selected ACS population in ACA-CIA being compared to a more complete, older 2002 New Zealand ACS population.

The Otago-Southland Registry has published several reports from two centres in New Zealand (Dunedin and Invercargill) from 2000 to 2002. This cohort is a more pertinent group to compare to our national cohort. With a follow-up of 1143 consecutive ACS patients (STEMI: 39%, NSTEMI: 39%, UAP: 22%), with a mean age of 65 years, the Otago-Southland patients had an overall mortality of 15% at 1 year, and 39% at 4 years of follow-up [30]. This is much closer to the findings from the National 2002 New Zealand cohort mortality of 12% at 1 year, and 30% at 4 years of follow-up, although there is a difference in the percentages of ACS patient type, with more STEMI (39% vs 14%) and fewer UAP (22% vs 46%) patients in the Otago-Southland group, in comparison to the national group.

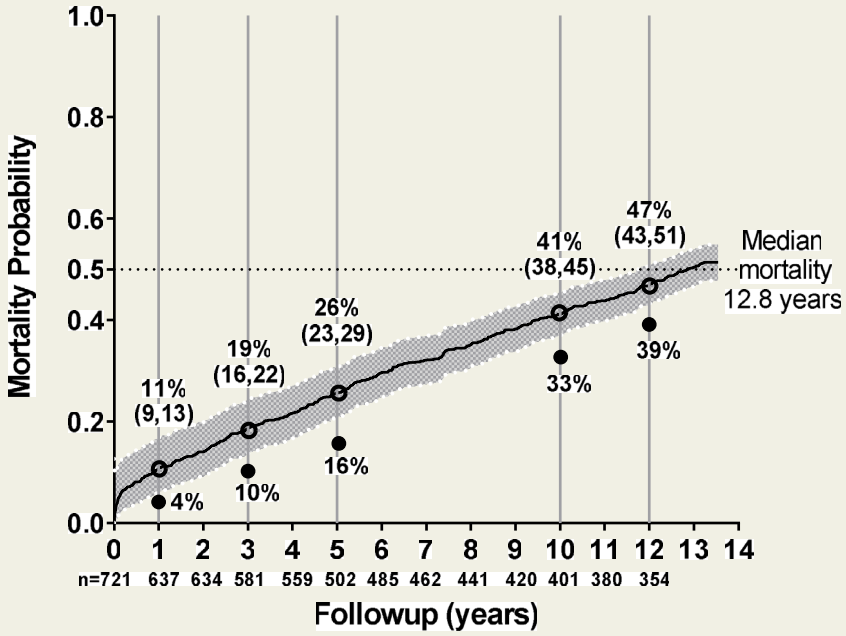

Figure 3 Kaplan-Meier All Cause mortality (n = 721), Compared to an age, sex, Māori ethnicity-matched population. Number of patients at risk at each time point is shown below the figure.
All-cause survival solid line; 95% confidence interval dashed line. Numbers (solid circle) below the line are percentage dying at each time point for an age/sex/Māori-ethnicity matched population. Numbers above the line are the percentage dying (95% CI) for the ACS cohort (open circles).

There have also been older 3- and 12-year follow-up studies of the MONICA (MONitoring of trends and determinants in CArdiovascular disease) registry from New Zealand [31] and Australia [32] However, as the registry was only of patients aged 35 to 64 years, with follow-up only of those who survived to 28 days *after* a myocardial infarction, there is a limited applicability to contemporary ACS cohorts.

Disease Coding Studies

A disease coding study using the ICD-10-AM classification and the national hospitalisation and mortality datasets from New Zealand has reported on a 1-year follow-up of ACS patients hospitalised from 2007 to 2009 [33]. Over 3 years, 42,920 New Zealand residents with their first ACS hospitalisation were data linked with ACS type recorded as STEMI: 18%; NSTEMI: 56%; UAP: 22%; and 'unspecified' MI: 4%. Overall 21% of ACS patients were reported to have died at 1 year of follow-up, which is a worse prognosis than the 2002 New Zealand cohort with a 12% ACS mortality at 1 year.

The differences may be related to the fact that while disease coding studies with subsequent data linking can provide very useful information by the use of large numbers of patients, data accuracy is dependent on the accuracy of individual discharge summary records. One of many potential problems is that these studies may include patients whose outcome was a terminal MI following hospitalisation, or an MI during hospitalisation for an unrelated cause, which is a different cohort of patients compared to those who present with an ACS admission.

A disease coding study from New South Wales (NSW) has used hospital admissions data to identify patients aged >18 years admitted to a NSW hospital with a principle diagnosis of AMI (ICD10 codes: 121.0 to 121.4) between 1 July 2004 and 30 June 2008 [34]. A total of 39,798 patients were linked with the NSW deaths registry to obtain mortality data. At a median follow-up of 2.8 years, overall mortality was 26.6%. The comparative figure from the 2002 New Zealand cohort was a similar overall mortality after a MI (STEMI and NSTEMI) of 26% (95% CI, 25.1 to 30.4) at a median follow up of 2.8 years.

Study Limitations

The 2002 ACS data was estimated to have missed 4% of ACS patients across New Zealand, at the time of the audit [10,11]. The 2002 ACS cohort definition of UAP patients relied on less sensitive troponin assays, which were available in 2002, and has probably resulted in a higher proportion of UAP patients in this study, than would be found in more modern cohorts [6]. The follow-up data are reliant on patients dying in New Zealand; any who had emigrated and then died will not be counted, so the mortality rate could potentially be worse. The age, sex and Māori ethnicity matched population also includes patients with ACS, and hence a matched population excluding ACS patients would have a better prognosis than described. Hence the estimate of eight lives per 100 who die at a younger age, following an ACS, may be something of an under-estimate.

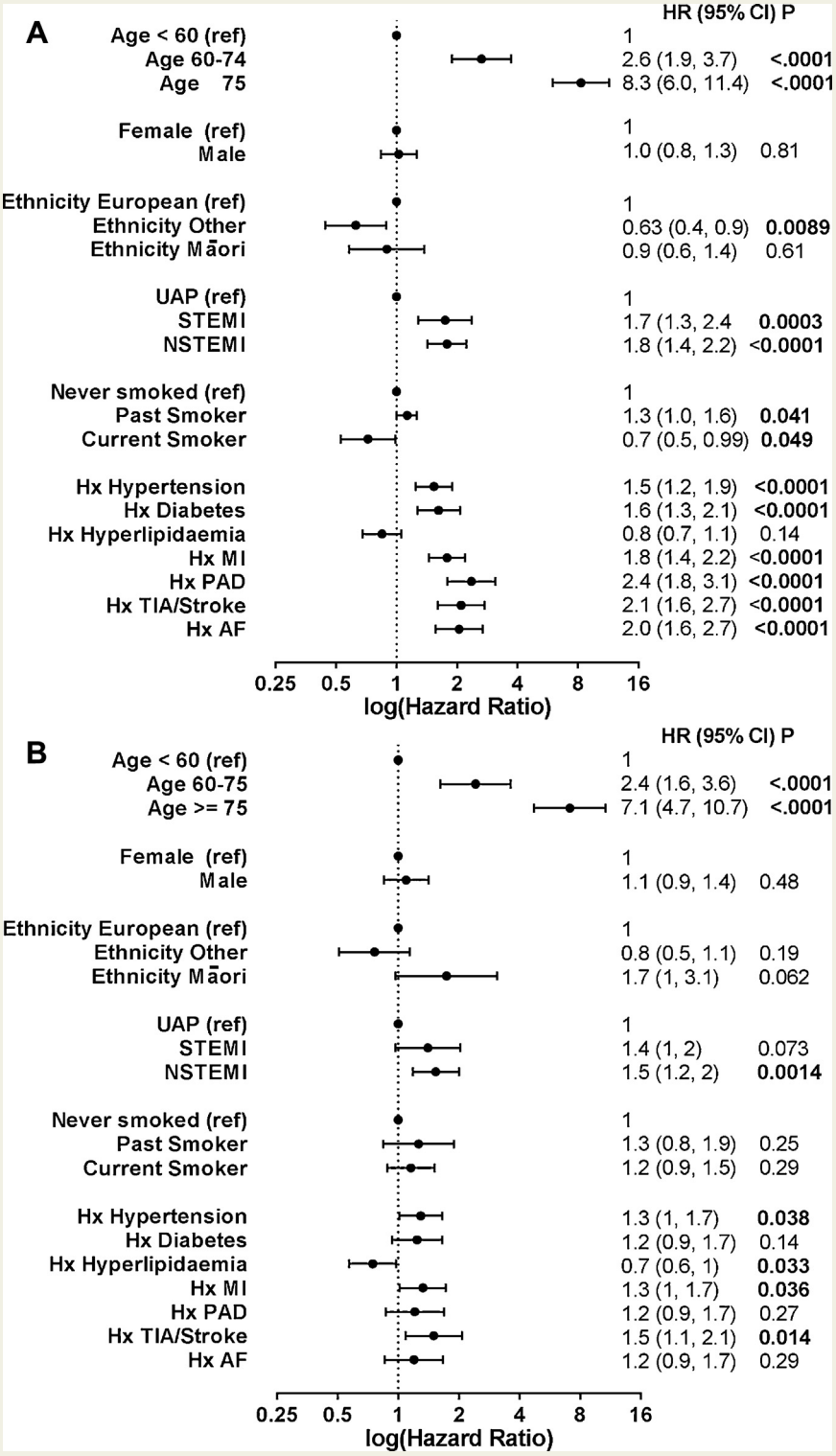

Figure 4 (a) Hazard of all-cause death following an ACS Admission: Forest plot of univariate analysis (median follow-up is 12.7 years, maximum follow-up is 13.5 years). (b) Hazard of all-cause death following an ACS Admission: Forest plot of multivariable adjusted hazard of all cause death (median follow-up is 12.7 years, maximum follow-up is 13.5 years).

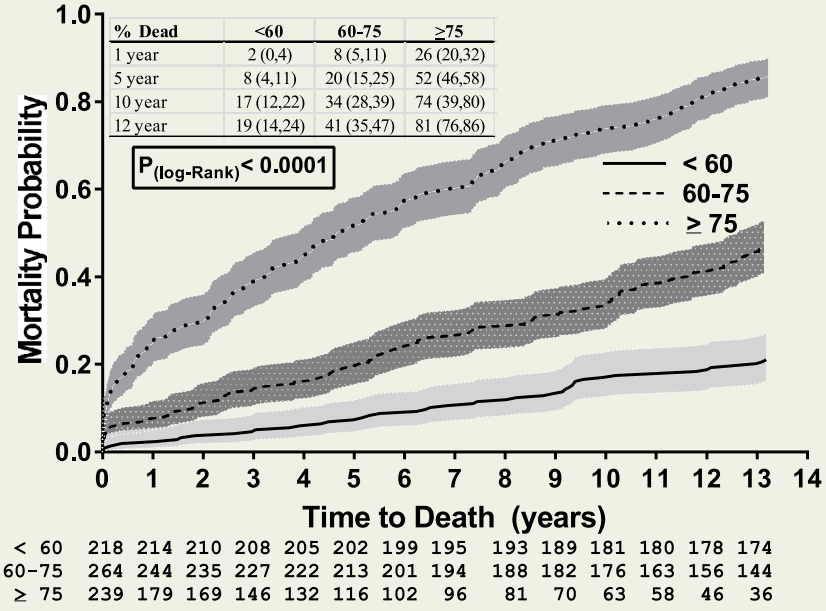

Figure 5 Kaplan-Meier All Cause unadjusted mortality from an ACS admission, by age. Number of patients at risk at each time point is shown below the figure.

Conclusion

Studies which report complete ACS patient cohorts are rare, as methods to collect these cohorts are limited in design. This unique study in a complete national cohort of ACS patients demonstrates that, by 12 years after an ACS hospitalisation in 2002, approximately 50% of patients have died. These figures emphasise the need to focus on optimal ACS patient management, both from the initial hospitalisation but also with long-term patient management and systematic follow-up.

Conflict of Interest Statement

The 2002 NZACS Audit Group was supported by small, unrestricted educational grants from Aventis Pharmaceuticals and MSD Pharmaceuticals, who responded to an Investigator initiated request to assist with data entry, statistical and administrative support. The project was however entirely devised and executed by the Steering Committee with total independence from these companies and endorsed by the Regional Cardiac Society of New Zealand. All collection of data was unfunded at local centres.

2002 NZACS Audit Group Hospitals (By Region and Latitude) Audit Leaders, Assistants, and Patient Numbers

Chairman; * Steering Committee member

Auckland/Northland North Island

Kawakawa Hospital, Dr P Burgoyne, Ms S August, Whangarei Hospital, Dr B Wong, Ms K O'Keefe, North Shore Hospital, Auckland, Dr H Hart, Ms J Wickham, Auckland Hospital, Dr C Ellis#*, Mr G Gamble*, Ms W Benjamin, Mercy Private Hospital, Auckland, Dr T Clarke, Green Lane Hospital, Auckland, Prof J French*, Prof H White*, Ms B Williams, Ascot Private Hospital, Auckland, Dr A Maslowski, Middlemore Hospital, Auckland, Dr A Ko, Dr M Lund, Dr H Oettli.

Waikato/Central North Island

Thames Hospital, Dr J Lennane, Dr Aftabuzzaman, Tauranga Hospital, Dr J Tisch, Dr G Porter, Ms V Watts, Ms J Braid, Waikato Hospital, Hamilton, Assoc Prof G Devlin*, Ms D Penney, Whakatane Hospital, Dr E Edwards, Ms D Garner, Rotorua Hospital, Dr K Logan, Ms A Morley, Tokoroa Hospital, Dr P Reeve, Dr F Kanan, Te Kuiti Hospital, Dr P Reeve, Dr J Pusupati, Taupo Hospital, Dr A Ludbrook, Gisborne Hospital, Dr F Aitcheson, Ms K Weytmans, Taumarunui Hospital, Dr P Reeve, Dr R Shepherd, New Plymouth Hospital, Dr I Ternouth.

Wellington/Southern North Island

Hastings Hospital, Dr R Luke, Ms J Mackenzie, Wanganui Hospital, Dr T Thompson, Ms K Olsen, Palmerston North Hospital, Dr R Shameem, Masterton Hospital, Dr T Matthews, Ms K Lee, Hutt Hospital, Assoc Prof S Mann*, Ms A Cuthbert, Wellington Hospital, Dr P Matsis*, Ms D Middlemitch, Ms B Scott, Wakefield Private Hospital, Wellington, Dr M Abernethy, Nelson Hospital, Dr A Hamer, Ms R Price, Blenheim Hospital, Dr M Heynike, Ms M Udy.

Christchurch, Canterbury, South Island

Greymouth Hospital, Dr Y Al Khairulla, Ms L Skeats, Christchurch Hospital, Assoc Prof J Elliott*, Prof M Richards, Ms L Campbell, Ms A Alspach, Ashburton Hospital, Dr N Abdul-Ghaffar, Ms A Smart, Timaru Hospital, Dr M Hills, Ms Maria Hammond, Ms C Barker.

Dunedin, Otago, South Island

Oamaru Hospital, Dr P Curzon, Dunstan Hospital Clyde, Dr G Nixon, Ms S Meaden, Dunedin Hospital, Prof MJ Williams*, Ms M McLelland, Invercargill Hospital, Dr C Renner, Dr A Maloney.

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Chris Lewis, Information Analyst, Analytical Services, Ministry of Health, New Zealand who constructed a spreadsheet which calculated the odds of a person dying each year matched to a person of the same age, sex and Māori/Non-Māori ethnicity. The individual year percentages were used to calculate the overall probability of a person living to 12.5 years from their start age. Date and cause of death data, where available, were also provided by the Ministry of Health from the National Mortality register.

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