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Title:
Relative contribution of trends in myocardial infarction event rates and case fatality to declines in mortality: an international comparative study of 1·95 million events in 80·4 million people in four countries

Date:
2022-03-01

Citation:
Camacho, X., Nedkoff, L., Wright, F. L., Nghiem, N., Buajitti, E., Goldacre, R., Rosella, L. C., Seminog, O., Tan, E. J., Hayes, A., Hayen, A., Wilson, N., Blakely, T. & Clarke, P. (2022). Relative contribution of trends in myocardial infarction event rates and case fatality to declines in mortality: an international comparative study of 1·95 million events in 80·4 million people in four countries. Lancet Public Health, 7 (3), pp.e229-e239. https://doi.org/10.1016/S2468-2667(22)00006-8.

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Relative contribution of trends in myocardial infarction event rates and case fatality to declines in mortality: an international comparative study of 1·95 million events in 80·4 million people in four countries

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Summary

Background Myocardial infarction mortality has declined since the 1970s, but contemporary drivers of this trend remain unexplained. The aim of this study was to compare the contribution of trends in event rates and case fatality to declines in myocardial infarction mortality in four high-income jurisdictions from 2002–15.

Methods Linked hospitalisation and mortality data were obtained from New South Wales (NSW), Australia; Ontario, Canada; New Zealand; and England, UK. People aged between 30 years and 105 years were included in the study. Age-adjusted trends in myocardial infarction event rates and case fatality were estimated from Poisson and binomial regression models, and their relative contribution to trends in myocardial infarction mortality calculated.

Findings 1 947 895 myocardial infarction events from a population of 80·4 million people were identified in people aged 30 years or older. There were significant declines in myocardial infarction mortality, event rates, and case fatality in all jurisdictions. Age-standardised myocardial infarction event rates were highest in New Zealand (men 893/100 000 person-years in 2002, 536/100 000 person-years in 2015; women 482/100 000 person-years in 2002, 271/100 000 person-years in 2015) and lowest in England (men 513/100 000 person-years in 2002, 382/100 000 person-years in 2015; women 238/100 000 person-years in 2002, 173/100 000 person-years in 2015). Annual age-adjusted reductions in event rates ranged from –2·6% (95% CI –3·0 to –2·3) in men in England to –4·3% (–4·4 to –4·1) in women in Ontario. Age-standardised case fatality was highest in England in 2002 (48%), but declined at a greater rate than in the other jurisdictions (men –4·1%/year, 95% CI –4·2 to –4·0%; women –4·4%/year, –4·5 to –4·3%). Declines in myocardial infarction mortality rates ranged from –6·1%/year to –7·6%/year. Event rate declines were the greater contributor to myocardial infarction mortality reductions in Ontario (69·4% for men and women), New Zealand (men 68·4%; women 67·5%), and NSW women (60·1%), whereas reductions in case fatality were the greater contributor in England (60% in men and women) and for NSW men (54%). There were greater contributions from case fatality than event rate reductions in people younger than 55 years in all jurisdictions, with contributions to mortality declines varying by country in those aged 55–74 years. Event rate declines had a greater impact than changes in case fatality in those aged 75 years and older.

Interpretation While the mortality burden of myocardial infarction has continued to fall across these four populations, the relative contribution of trends in myocardial infarction event rates and case fatality to declining mortality varied between jurisdictions, including by age and sex. Understanding the causes of this variation will enable optimisation of prevention and treatment efforts.

Funding National Health and Medical Research Council, Australia; Australian Research Council; Health Research Council of New Zealand; Canadian Institutes of Health Research, Canada; National Institute for Health Research, UK.

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Introduction

The morbidity and mortality burden associated with coronary heart disease (CHD) has declined over the past four decades in most developed countries.[1] Public health efforts have contributed to reductions in the prevalence of major cardiovascular risk factors, which—alongside improvements in acute care and secondary prevention after myocardial infarction—underpin downward trends in CHD mortality rates.[2,3] Despite these improvements, CHD remains the leading cause of years of life lost globally and is a major contributor to life expectancy inequalities associated with low socioeconomic status.[4,5]

Population-based surveillance of myocardial infarction is important for understanding the disease burden

Lancet Public Health 2022; 7: e229–39

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Research in context

Evidence before this study

We searched Ovid Medline for articles published up to Sept 17, 2021, using search terms "myocardial infarction" or "ischaemic heart disease" or "coronary heart disease" AND "mortality" or "survival" or "case fatality" or "event rate" AND "trends". We also identified papers of this type through a grey literature search, and specifically targeted papers published by the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study. We identified a number of studies that investigated trends in myocardial infarction event rates, case fatality, or mortality, but most focused on only one or two of these measures, and few quantified the contribution of trends in event rates and case fatality to declines in myocardial infarction mortality, or undertook comparative analyses across populations. The MONICA study included data from 37 countries in people aged 25–64 years, and reported that there was a greater contribution to declines in myocardial infarction mortality from falls in event rates (two thirds) than from reductions in case fatality (one third). One study from England used the MONICA method to show that half of the decline in myocardial infarction mortality was due to event rate reductions between 2002 and 2010. Another study reported declining myocardial infarction event rates and case fatality from six European population registries, demonstrating differing magnitude of decline dependent on population and age group; however, there was no direct estimate of the contribution of these trends to mortality rate declines.

Added value of this study

To our knowledge, our study is the first since the MONICA study to quantify the effect of changes in event rates and case fatality on myocardial infarction mortality trends across populations. We included a broad age range (30–105 years) compared with earlier studies in which the upper age limit was restricted to 64 years. Event rate declines contributed to around two-thirds of the reductions in myocardial infarction mortality in women in Ontario, Canada; New Zealand; and New South Wales (NSW), Australia, while reductions in case fatality were the greater contributor in England and in men in NSW, Australia. Because our study population included 80·4 million people with nearly 2 million events, it allowed for robust estimates, particularly in smaller strata such as people aged younger than 55 years, where we saw a greater impact of case fatality reductions on mortality declines compared with the impact of event rate declines, and limited improvement in trends in event rates. Our broader age range than previous studies allowed us to investigate trends in the oldest age groups, showing that falling event rates generally underpinned reductions in myocardial infarction mortality rates in those aged 75 years and older.

Implications of all the available evidence

Many studies show that there continues to be substantial reductions in measures of myocardial infarction burden across most developed countries, including for mortality, event rates, and case fatality. However, our study revealed heterogeneity in the contribution of case fatality and event rate trends to declines in myocardial infarction mortality, particularly related to age and sex, and indicates further opportunities for reducing cardiovascular disease burden. Specific targeting of acute management approaches after myocardial infarction in older adults could further reduce case fatality in this patient group. In younger adults, the limited declines in myocardial infarction event rates, particularly in women, highlight that targeting this measure could contribute to even greater mortality declines in this and older age groups. The value of these comparative analyses across populations is that they highlight which population groups to target and where improvements in acute management or prevention are required.

associated with CHD.[6] Whole-population trends in myocardial infarction mortality are influenced by changes in myocardial infarction event rates and case fatality, and indicate the effectiveness of prevention and treatment. Declines in myocardial infarction incidence and event rates have been driven by reductions in smoking, high blood pressure, and dyslipidaemia.[7] Reductions in case fatality are associated with increasing use of evidence-based medicines and percutaneous coronary intervention (PCI) in patients presenting to hospital with myocardial infarction.[8,9] However, increasing prevalence of diabetes and obesity, and the shift from ST-elevation myocardial infarction (STEMI) to non-ST-elevation myocardial infarction (NSTEMI) could influence trends in event rates and case fatality,[1,2] with the combined effects of these changes on myocardial infarction mortality rates unknown.

The multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study[10] investigated the contribution of changes in event rates and case fatality to trends in myocardial infarction mortality across 37 countries. The MONICA study reported that from 1983 to 1993, two-thirds of the reduction in myocardial infarction mortality was attributed to declines in myocardial infarction event rates, and one-third to reductions in case fatality. However, this pattern was not homogenous across all countries, differed by sex in some, and was restricted to people aged 25–64 years. In subsequent years, increases in life expectancy, greater understanding of treatment effectiveness in elderly populations,[11] and recent adverse trends in myocardial infarction rates in adults aged 35–54 years,[12] could mean that the relative contribution of event rates and case fatality to the myocardial mortality burden might differ in contemporary settings. Results from a 2012 study demonstrated that half of the decline in myocardial infarction mortality in England from 2002 to 2010 was due to reductions in myocardial infarction event rates, indicating a potential shift from the previous pattern.[13]

The potential for interjurisdictional differences and the changing epidemiology of myocardial infarction means that a contemporary study is needed to determine whether changes in event rates or case fatality are driving trends in mortality from myocardial infarction. We used whole-population data from four jurisdictions—the state of New South Wales (NSW) in Australia, the province of Ontario in Canada, New Zealand, and England, UK. We first aimed to measure trends in myocardial infarction mortality, event rates, and case fatality, and quantify the relative contribution of changes in myocardial infarction event rates and case fatality to trends in myocardial infarction mortality across these four jurisdictions between 2002 and 2015; and second, to determine if these relative contributions differed by age and sex.

Methods

Setting and data sources

We used administrative hospital and mortality records to identify myocardial infarction events and deaths in each jurisdiction. We included national data from England and New Zealand, and state and provincial data from Australia (NSW) and Canada (Ontario), because the latter jurisdictions did not have whole-country linked data sources at the time the study was undertaken. Data were obtained from the relevant government departments in each jurisdiction.

Due to data custodian restrictions, we used a distributed approach whereby linkage and analysis of unit-level hospital and mortality data was undertaken within each jurisdiction independently, and only summary results shared across international boundaries. A common analysis plan was developed, including use of international coding systems: England used the WHO International Statistical Classification of Diseases and Related Health Problems tenth revision (ICD-10); Ontario used the enhanced Canadian version of ICD-10 (ICD-10-CA); and New Zealand and NSW used the ICD-10 Australian Modification (ICD-10-AM), all hereafter termed ICD-10. Comparable analysis code was developed in the study coordinating centre and distributed to all jurisdictions, with aggregated data from all centres combined at the coordinating centre. Less than 0·1% of all records in NSW, England, and New Zealand had invalid or missing values for sex, age, admission, or death dates; those that did were excluded from the study, while there were no missing data in the Ontario dataset.

Study population

The study population included all individuals aged between 30 years and 105 years who had a myocardial infarction between Jan 1, 2002, and Dec 31, 2015—the period representing the maximum window of available data across most jurisdictions. Changes to underlying cause of death coding in Ontario in 2013 rendered subsequent years of data unreliable, hence the study period for Ontario was restricted to Jan 1, 2002, to Dec 31, 2012.

Event definitions were chosen to maintain alignment with earlier studies.[10,13] Myocardial infarction events comprised sudden myocardial infarction deaths and admissions. Sudden myocardial infarction deaths were those in which myocardial infarction was the underlying cause of death (ICD-10 I21, I22) with no hospitalisation record for myocardial infarction in the previous 30 days. Myocardial infarction admissions were emergency hospitalisations with a principal diagnosis of myocardial infarction (ICD-10 I21, I22), in those discharged alive from hospital and with a length of stay of more than 1 day to avoid potential misclassification (there was no restriction on length of stay for myocardial infarction admissions resulting in an in-hospital death). Because of known re-admission practices for myocardial infarction including intrahospital and interhospital transfers and early re-admissions for diagnostic and revascularisation procedures for the same event, any hospital admissions or death occurring within 30 days of a myocardial infarction admission were counted as part of the same event.

Myocardial infarction events were also classified as non-fatal or fatal. Fatal myocardial infarction events included sudden myocardial infarction deaths and fatal myocardial infarction admissions, where death from any cause occurred within 30 days of hospital admission for myocardial infarction. Fatal myocardial infarction admissions, where myocardial infarction was the underlying cause of death, and sudden myocardial infarction deaths were collectively termed myocardial infarction deaths.

As a sensitivity analysis, we applied a broader definition encompassing all CHD events and deaths. CHD was identified using a similar method as described for myocardial infarction, with an expanded set of diagnosis codes (ICD-10 I20–I25), and including emergency and elective hospitalisations.

Statistical analysis

All analyses were stratified by sex. The main analyses were conducted including all people aged 30–105 years. We also stratified analyses by broad age groups (30–54 years, 55–64 years, 65–74 years, 75–84 years, and ≥85 years).

Annual event and mortality rates per 100 000 person-years were calculated. The numerators comprised myocardial infarction events and myocardial infarction deaths, respectively. The denominators were based on the mid-year population estimates for each year from each jurisdiction, sourced from the Office of National Statistics (England), the Australian Bureau of Statistics (NSW), Statistics New Zealand, and the Ministry of Health (Ontario). Event and mortality rates were directly age standardised by 5-year age groups with the 2013 European Standard Population as the standard.[14] 30-day

	NSW		Ontario*		New Zealand		England	
	Men	Women	Men	Women	Men	Women	Men	Women
Population size (all ages)†	3 776 574	3 839 594	6 581 938	6 808 694	2 275 300	2 358 400	27 029 286	27 757 041
Population size (age <65 years)†	3 225 881	3 206 121	5 707 686	5 713 731	1 961 100	1 981 600	22 628 085	22 446 670
Myocardial infarction events	124 140	79 248	193 609	122 801	92 892	61 611	784 347	489 247
Mean age, years	69·1 (14·1)	77·9 (13·1)	67·8 (13·9)	75·8 (13·2)	69·5 (13·8)	77·2 (12·9)	69·2 (13·6)	77·2 (12·4)
Median age, years	70·0 (58·5–80·4)	80·8 (70·3–87·5)	68·0 (57·0–79·0)	78·0 (67·0–86·0)	71·0 (59·0–81·0)	80·0 (69·0–87·0)	70·0 (59·0–80·0)	80·0 (70·0–86·0)
Myocardial infarction admissions	103 124 (83·1%)	58 951 (74·4%)	167 299 (86·4%)	103 538 (84·3%)	76 452 (82·3%)	47 979 (77·9%)	588 425 (75·0%)	351 103 (71·8%)
Myocardial infarction deaths‡	26 553 (21·4%)	24 982 (31·5%)	36 114 (18·7%)	28 021 (22·8%)	20 739 (22·3%)	17 565 (28·5%)	243 903 (31·1%)	182 921 (37·4%)
Fatal myocardial infarction events	30 336	27 840	45 607	36 160	22 521	19 026	262 904	199 347
Mean age, years	77·2 (12·2)	84·2 (9·9)	75·0 (12·6)	81·6 (10·8)	76·3 (12·4)	83·2 (10·4)	74·6 (12·1)	81·2 (10·3)
Median age, years	80·0 (70·0–86·0)	86·0 (80·0–91·0)	77·0 (67·0–85·0)	84·0 (76·0–89·0)	79·0 (69·0–85·0)	85·0 (78·0–90·0)	77·0 (67·0–84·0)	83·0 (76·0–88·0)
Fatal myocardial infarction admission	9320 (30·7%)	7543 (27·1%)	19 297 (42·3%)	16 897 (46·7%)	6081 (27·0%)	5397 (28·4%)	66 982 (25·5%)	61 203 (30·7%)
Sudden death	21 016 (69·3%)	20 297 (72·9%)	26 310 (57·7%)	19 263 (53·3%)	16 434 (73·0%)	13 647 (71·7%)	195 922 (74·5%)	138 144 (69·3%)
Myocardial infarction events by age groups, years								
30–54	22 712 (18·3%)	5576 (7·0%)	38 444 (19·9%)	9867 (8·0%)	15 258 (16·4%)	4248 (6·9%)	128 606 (16·4%)	30 271 (6·2%)
55–64	25 388 (20·5%)	7876 (9·9%)	41 859 (21·6%)	14 383 (11·7%)	18 192 (19·6%)	6519 (10·6%)	155 062 (19·8%)	46 919 (9·6%)
65–74	28 101 (22·6%)	13 495 (17·0%)	43 040 (22·2%)	22 994 (18·7%)	21 414 (23·1%)	10 974 (17·8%)	189 369 (24·1%)	91 801 (18·8%)
75–84	30 179 (24·3%)	24 404 (30·8%)	46 576 (24·1%)	40 050 (32·6%)	24 150 (26·0%)	19 032 (30·9%)	207 162 (26·4%)	165 375 (33·8%)
≥85	17 760 (14·3%)	27 897 (35·2%)	23 690 (12·2%)	35 507 (28·9%)	13 884 (14·9%)	20 844 (33·8%)	104 148 (13·3%)	154 881 (31·7%)

Data are n, mean (SD), median (IQR), or n (%). NSW=New South Wales. *Ontario data covers the period 2002–12. †Based on the estimated residential population in 2015 for NSW, New Zealand, and England, and 2012 for Ontario. ‡Myocardial infarction deaths comprise fatal myocardial infarction admissions where cause of death is myocardial infarction, plus sudden myocardial infarction deaths. Myocardial infarction admissions can also be classified as myocardial infarction deaths. Sum of percentages will not necessarily add up to 100%. Minor inconsistencies between fatal events, fatal admissions and sudden deaths in New Zealand are due to privacy restrictions.

Table 1: **Descriptive characteristics of myocardial infarction events by country and sex, 2002–15**

case fatality was calculated using fatal myocardial infarction admissions and sudden myocardial infarction deaths as the numerator, and all myocardial infarction events as the denominator. The number of myocardial infarction events in each 5-year age group were summed across all jurisdictions, and the weights from each age group used as the standard population for case fatality.

Poisson regression was used to estimate the annual percentage change in myocardial infarction event and mortality rates, with 95% CIs. The dependent variable was the number of events or myocardial infarction deaths, respectively, and the independent variables were 5-year age group and calendar year. The average annual change was calculated as $-100\times[1-\exp(\beta)]$ where β is the coefficient for calendar year. Poisson models were checked for overdispersion and, where present, a dispersion parameter was included in the model. Trends in case fatality were estimated using a generalised linear model with binomial distribution and log link function with the same dependent and independent variables as above.

The approach for estimating the relative contribution of event rates and case fatality to trends in myocardial infarction mortality was based on published methods.[10,13] First, an estimated annual trend in mortality was calculated by adding the average annual changes in event rates and case fatality, expressed as percentages. Here, mortality rate (M)=event rate (E)×case fatality (C) in each year, and $M'/M=E'/E+C'/C$, where M', E', and C' represent the average annual change for each rate in absolute terms. Estimating the average annual change in percentage terms $\Delta M=(M'/M)$, $\Delta E=(E'/E)$, and $\Delta C=(C'/C)$, gives $\Delta M=\Delta E+\Delta C$. Next, the change in mortality rate was divided by the change in event rates and case fatality, respectively, to calculate the relative contributions of each. The sum of the relative contributions of case fatality and event rates adds to 100%.

Analyses were done in Australia using SAS version 9.4, in New Zealand and Ontario using SAS Enterprise Guide 7.1, and in England using Stata version 14.1. This study was approved by the University of Toronto Health Sciences Research Ethics Board, NSW Population and Health Services Research Ethics Committee (2016/09/654), the New Zealand Health and Disability Ethics Committees (H13/049), and the Central and South Bristol Multi-Centre Research Ethics Committee (04/Q2006/176).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing the manuscript.

Results

Between 2002 and 2015, 1 947 895 myocardial infarction events occurred in 80 426 827 people aged 30 years or older across all jurisdictions. Of these events, 1 496 871 were myocardial infarction admissions and 580 798 were myocardial infarction deaths (table 1), with 129 765 events included in both myocardial infarction admissions and deaths definitions (figure 1). The proportion of total myocardial infarction events occurring in men in each jurisdiction was 60·1% in New Zealand, 61·2% in Ontario, 61·6% in England, and 61·0% in NSW. The mean age of a myocardial infarction event in men ranged from 67·8 years (SD 13·9) in Ontario to 69·5 years (SD 13·8) in New Zealand. Women were around 8 years older than men from the same jurisdiction at the time of a myocardial infarction event.

643 741 fatal myocardial infarction events occurred, with more than two-thirds of these being sudden deaths in most jurisdictions (table 1), except Ontario, where sudden deaths comprised a smaller proportion of fatal myocardial infarction events (57·7% in men and 53·3% in women). The majority of fatal myocardial infarction admissions had myocardial infarction reported as the cause of death (figure 1). The mean age of fatal myocardial infarction events was older than for myocardial infarction events, ranging from 74·6 years in men in England to 77·2 years in NSW, with women on average 6–7 years older than men at the time of death.

Age-standardised myocardial infarction event rates were highest in New Zealand, declining between 2002 and 2015 from 893/100 000 person-years to 536/100 000 person-years in men, and from 482/100 000 person years to 271/100 000 person-years in women (figure 2; table 2). The lowest event rates were in England, declining from 513/100 000 person-years to 382/100 000 person-years in men, and 238/100 000 person-years to 173/100 000 person-years in women. There were significant age-adjusted reductions in myocardial infarction event rates in men and women, with the largest declines in men seen in Ontario (–4·0%/year, 95% CI –4·1 to –3·8) and New Zealand (–3·9%, –4·1 to –3·8). In women, annual reductions of just over 4%/year were observed in Ontario and New Zealand, with smaller declines in NSW (–3·6%/year, –3·8 to –3·4) and England (–2·9%/year, –3·2 to –2·6). Overall trends in myocardial infarction event rates were underpinned by larger reductions in people aged 65 years or older (appendix p 2). The lowest rates of decline were in people aged 30–54 years. In men, these declines ranged from –0·4%/year in England to –1·9%/year in New Zealand. Women in this age group in NSW, Ontario, and England had no significant improvement in myocardial infarction event rates, whereas in New Zealand, an annual reduction of –1·2%/year (–2·0 to –0·5) was observed.

Age-standardised case fatality was highest in England, but declined at a greater rate than in other jurisdictions (men –4·1%/year, 95% CI –4·2 to –4·0%; women –4·4%/year, –4·5 to –4·3; figure 2; table 2). Annual age-adjusted reductions in other jurisdictions ranged from –1·7%/year (–2·0 to –1·5%) in men in Ontario to –3·4%/year (–3·6 to –3·1%) in men in NSW. There were marginally greater declines in case fatality in women than men in England, whereas in NSW reductions were greater in men. In Ontario and New Zealand there was limited difference in trends by sex. Overall trends in case fatality were underpinned by significant declines across all age groups (appendix p 2).

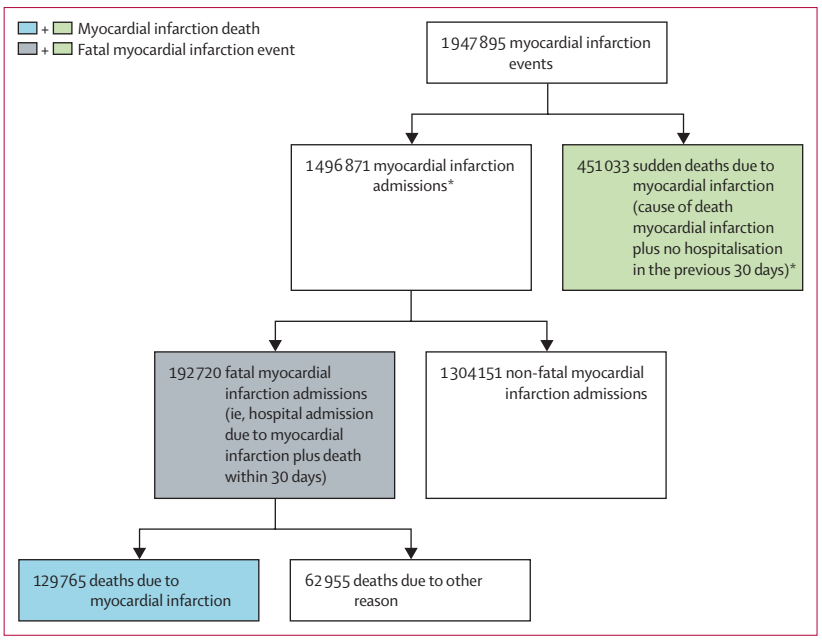


Figure 1: **Definition of myocardial infarction events**

Fatal myocardial infarction admissions are included in the definitions of myocardial infarction events and myocardial infarction deaths. *The sum of myocardial infarction admissions and sudden myocardial infarction deaths does not add up to the total of myocardial infarction events, and the sum of fatal myocardial infarction admissions plus sudden myocardial infarction deaths does not add to total fatal myocardial infarction events. This is because privacy restrictions in some jurisdictions limit reporting of event counts where cell sizes are very small.

See Online for appendix

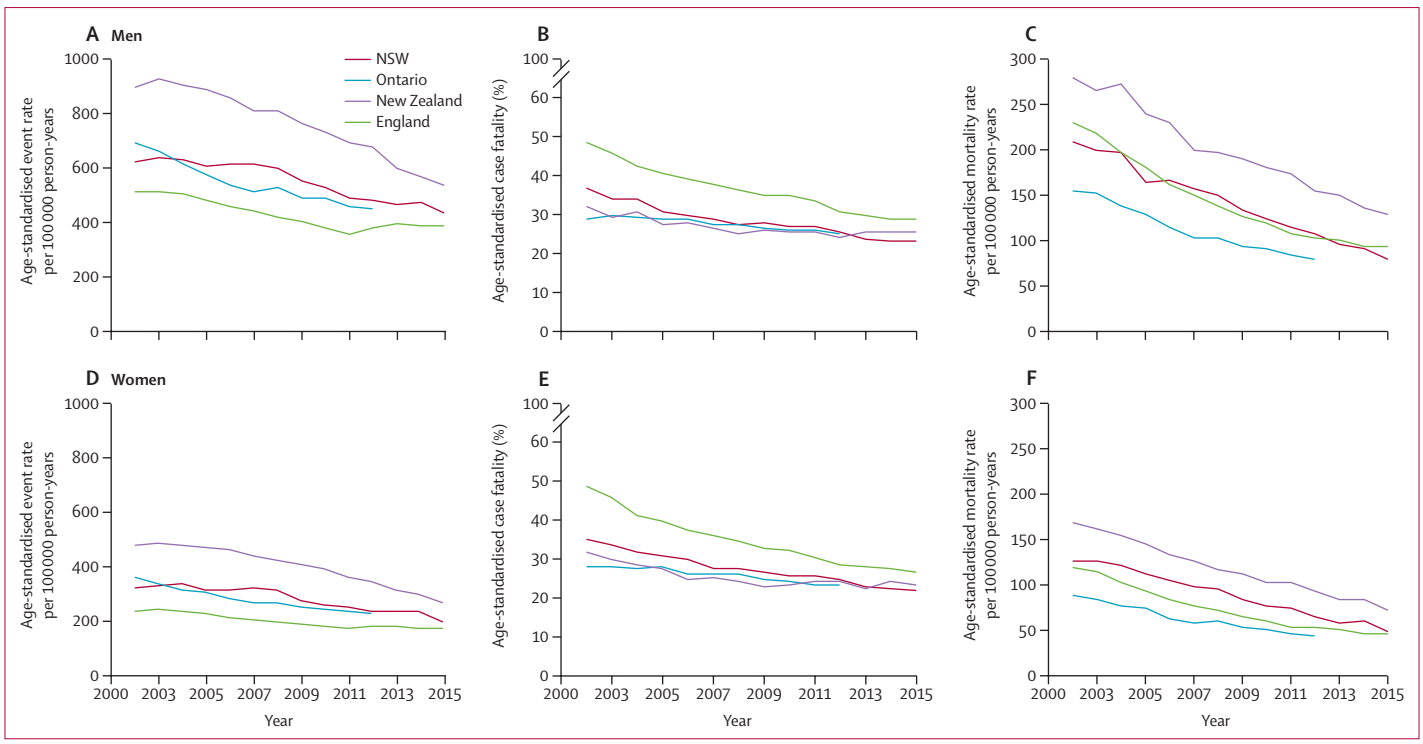


Figure 2: **Annual age-standardised myocardial infarction event rates in men (A) and women (D), case fatality in men (B) and women (E), and mortality rates in men (C) and women (F) aged 30 years or older, 2002–15**
NSW=New South Wales.

Reductions were generally similar in each age group in people aged 30 to 74 years, while smaller rates of decline were seen in people aged 75 years or older.

There were marked declines in age-standardised myocardial infarction mortality rates in men and women across all jurisdictions (figure 2; table 2). Annual reductions ranged from –6·1%/year in men (95% CI –6·4 to –5·7) in New Zealand to –7·4%/year (–7·7 to –7·1) in men in England, whereas in women, declines ranged from –6·2%/year (–6·5 to –5·9) in New Zealand to –7·6%/year (–7·9 to –7·3) in England. Reductions in myocardial infarction mortality rates were seen in all age groups (appendix p 2). There were generally greater rates of decline in men and women aged 65–84 years in Ontario, New Zealand, and England, whereas in NSW, the greatest declines were among people aged 55–84 years.

In New Zealand and Ontario, nearly 70% of the overall downward trend in myocardial infarction mortality rates was due to declines in myocardial infarction event rates, with around 30% attributable to declines in case fatality, with similar contributions in men and women (table 2). In England, the reductions in case fatality were the stronger driver of declines in mortality rates (61% in men and 60% in women). In NSW, the contributions differed by sex: in men, the relative contribution from declines in event rates (46%) was less than that from case fatality (54%), whereas in women there was a greater relative contribution from trends in event rates (60%).

The relative contribution of reductions in event rates versus reductions in case fatality varied substantially with age (figure 3; appendix p 2). In people aged 30–54 years, the reductions in myocardial infarction mortality were mainly attributable to declining case fatality in all jurisdictions. In older age groups (65 years and older in Ontario and New Zealand, and 75 years and older in NSW women), the reductions in myocardial infarction mortality were primarily attributable to reductions in event rates. This pattern was particularly apparent in people aged 85 years or older, except in England where reductions in case fatality outweighed reductions in event rates in older age groups.

The composition of fatal myocardial infarction cases across jurisdictions is shown in figure 4. Nearly three-quarters of fatal cases in New Zealand, NSW, and England were sudden deaths, with little change in this pattern during the study period. In contrast, in Ontario, around 58% of fatal cases in men and 53% in women were sudden deaths.

When the broader definition of CHD was used, downward trends in CHD event rates were the main contributor to declines in CHD mortality (appendix pp 4, 7). The limited improvements in case fatality for CHD in these jurisdictions, particularly in Ontario, New Zealand, and NSW women, meant that contributions from case fatality trends were generally small and

underpinned by limited contributions across all age groups (appendix p 5).

Discussion

Our study of 1·95 million myocardial infarction events in a combined population of 80·4 million people demonstrates substantial reductions in myocardial infarction mortality rates in all jurisdictions, underpinned by declines in myocardial infarction event rates and case fatality. However, there is heterogeneity in the relative contribution from changes in these measures by jurisdiction, age, and sex. For example, the contribution of reductions in myocardial infarction event rates to declines in mortality varied from 40% to 70%, depending on the jurisdiction. In general, there were greater contributions from reductions in case fatality in younger age groups, and a greater contribution from event rate declines in older age groups. Of note was the pattern in people aged 30–54 years, where declines in event rates were lower than all other age groups, or in the case of women in NSW, Ontario, and England, where there was no significant reduction over the study period.

Mortality from CHD has declined in most developed countries for the past four decades and these reductions have underpinned the substantial declines in cardiovascular disease mortality reported worldwide.[1] Declines in myocardial infarction mortality in our study were in the order of 6·1–7·6% per year in each jurisdiction, and declines in CHD mortality around 4·7–6·3% per year. These latter reductions are similar to WHO estimates for CHD trends before 2010; however, there is some evidence of a slowing of downward trends in cardiovascular disease mortality in high-income countries since that time.[15]

Understanding the decline in myocardial infarction mortality in a range of settings enables evaluation of past treatment and prevention strategies and quantifies the scope for further reduction. Few studies have directly measured the impact of event rate and case fatality trends on myocardial infarction mortality. A recent study of six European population registries showed differing rates of decline in case fatality and event rates between populations, although there was no direct quantification of the contribution to myocardial infarction mortality trends.[16] This study hypothesised that the smallest declines in event rates were likely due to higher risk factor prevalence, such as increasing obesity in men in the Spanish study region.

Our study complements and extends the findings of the MONICA study,[10] which is now more than two decades old and did not study trends in older populations. In the combined MONICA populations, there was a greater impact of declines in event rates relative to trends in case fatality; however, this pattern was not universal across our study populations. The countries in our study have reported falling myocardial infarction rates[12,17,18] and case fatality during our study

	Myocardial infarction events				Case fatality			Myocardial infarction mortality					Contribution to mortality decline*	
	Rate,† 2002	Rate,† 2015	Overall change (%)‡	Annual percentage change (95% CI)	Percentage,§ 2002	Percentage,§ 2015	Overall change (%)‡	Annual percentage change (95% CI)	Rate,† 2002	Rate,† 2015	Overall change (%)‡	Annual percentage change (95% CI)	Estimated annual trend (%)¶	Event (%)	Case fatality (%)
NSW															
Men	616·8	429·2	-30·4%	-2·9 (-3·0 to -2·7)	36·7%	22·8%	-37·8%	-3·4% (-3·6 to -3·1)	208·8	79·2	-62·1%	-7·3% (-7·6 to -7·0)	-6·2%	46·0	54·0
Women	322·8	201·5	-37·6%	-3·6 (-3·8 to -3·4)	35·1%	22·1%	-37·2%	-2·4% (-2·6 to -2·2)	124·9	47·8	-61·7%	-6·9% (-7·2 to -6·7)	-6·0%	60·1	39·9
Ontario‖															
Men	689·5	448·6	-34·9%	-4·0 (-4·1 to -3·8)	28·8%	24·7%	-14·3%	-1·7% (-2·0 to -1·5)	155·8	79·9	-48·7%	-6·7% (-7·0 to -6·4)	-5·7%	69·4	30·6
Women	358·8	231·0	-35·6%	-4·3 (-4·4 to -4·1)	27·8%	23·2%	-16·3%	-1·9% (-2·1 to -1·6)	87·8	44·0	-49·9%	-6·8% (-7·1 to -6·4)	-6·1%	69·4	30·6
New Zealand															
Men	892·8	536·3	-39·9%	-3·9 (-4·1 to -3·8)	31·9%	25·4%	-20·3%	-1·8% (-2·1 to -1·6)	280·6	128·4	-54·2%	-6·1% (-6·4 to -5·7)	-5·8%	68·4	31·6
Women	481·6	271·3	-43·7%	-4·2 (-4·4 to -4·0)	31·5%	23·3%	-26·1%	-2·0% (-2·3 to -1·7)	169·1	71·4	-57·7%	-6·2% (-6·5 to -5·9)	-6·2%	67·5	32·5
England															
Men	513·1	381·6	-25·6%	-2·6 (-3·0 to -2·3)	48·3%	28·6%	-40·9%	-4·1% (-4·2 to -4·0)	231·1	93·5	-59·6%	-7·4% (-7·7 to -7·1)	-6·8%	39·2	60·8
Women	237·7	172·7	-27·4%	-2·9 (-3·2 to -2·6)	48·7%	26·7%	-45·3%	-4·4% (-4·5 to -4·3)	119·3	45·2	-62·1%	-7·6% (-7·9 to -7·3)	-7·3%	39·9	60·1

NSW=New South Wales. *Calculate as (event or case fatality annual trend/estimated mortality trend)×100. †Age-standardised rate/100 000 person-years. ‡Overall change is calculated by dividing the difference between the 2002 and 2015 rate or percentage, by the rate or percentage in 2002. §Age-standardised case fatality. ¶Estimated annual change is average event change plus average case fatality change. ‖Data for Ontario covers 2002–12.

Table 2: **Trends in myocardial infarction event rates, 30-day case fatality and mortality rates by jurisdiction and sex, 2002–15**

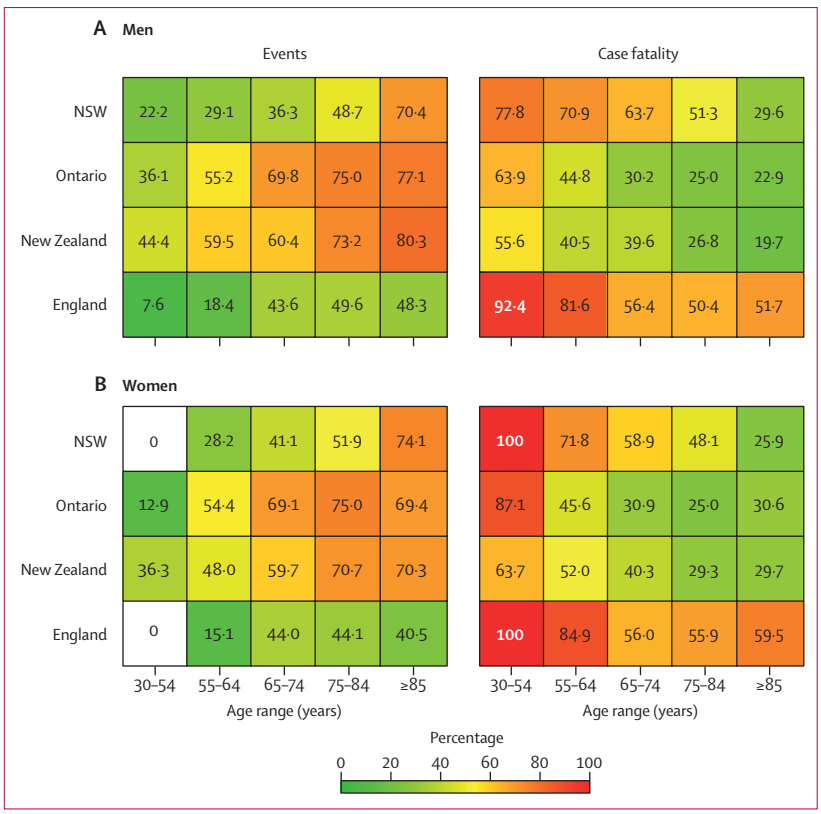


Figure 3: **Relative contribution of trends in event rates and case fatality to the overall decline in myocardial infarction mortality rates in people aged 30 years or older, 2002–15**
The numbers represent the percentage contribution of trends in event rates and case fatality to mortality rate declines. For example, in men aged 30–54 years in NSW, the declines in myocardial infarction event rates contributed to 22·2% of the decline in mortality rates in that age and sex grouping, while declines in case fatality contributed to 77·8% of the decline in mortality rates. The sum of the relative contributions of event rates and case fatality was set to 100%. Negative contributions are shown as 0. NSW=New South Wales.

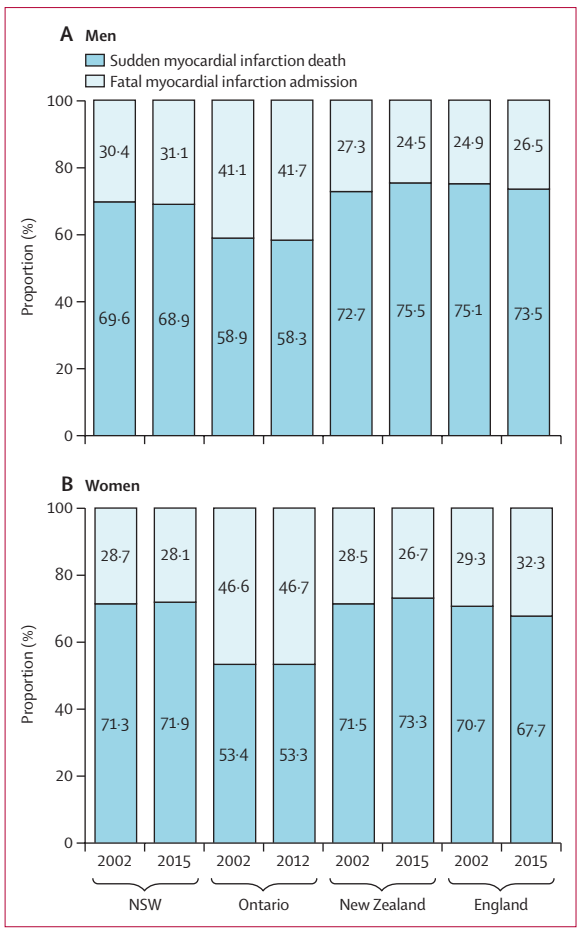


Figure 4: **Proportion of fatal myocardial infarction events classified as sudden death or fatal myocardial infarction admission in 2002 and 2015**
Ontario data ends in 2012. NSW=New South Wales.

period.[19] However, reductions in myocardial infarction hospitalisation rates have attenuated since the early 2000s due to increasing detection of NSTEMIs, with concurrent marked reductions in unstable angina. In New Zealand, while hospitalisation rates for unstable angina and NSTEMI decreased, the slower rate of decline in NSTEMIs indicates a likely shift in diagnosis.[18] Because this shift from unstable angina to NSTEMI can impact non-fatal myocardial infarction event rates and case fatality, it is unclear to what degree this has affected the relative contribution of each to myocardial infarction mortality declines. Other factors could also contribute to differences in trends, such as differing propensity to admit patients to hospital and health system factors, even though our study countries all have universal health-care systems.

Our study highlights the importance of extending age-specific analyses to younger and older age groups, as our data highlight variation by age and sex. The limited decline in event rates in adults aged younger than 55 years, particularly women, aligns with known trends in this age group,[12,20,21] with some studies also demonstrating increasing rates in women aged up to 65 years.[21] The lack of contribution to mortality reductions from declines in event rates has also been reported for men and women aged younger than 55 years for stroke.[22] These trends might partly reflect the obesity epidemic, and for myocardial infarction, the lower threshold for diagnosis with increasingly sensitive troponin assays. Although our sensitivity analyses showed significant reductions in CHD event rates in this age group, we have previously shown that this trend in England and Australia is underpinned by marked reductions in hospitalisations for unstable angina.[12] Conversely, the extension of substantial gains in early mortality reduction after myocardial infarction to people aged 65 years and older, implies increased application of evidence-based therapies in these age groups.

Declines in the prevalence of smoking, high blood pressure, and elevated serum cholesterol have coincided with declines in mortality from myocardial infarction in high-income countries.[23] A 2021 international comparison of lipid-modifying drugs involving all four countries

indicated rising use, although with some variation in consumption across countries, ranging from 39 389 units per 1000 population in Australia to 43 491 units per 1000 population in Canada.[24] Evidence from randomised controlled trials highlight the role of lowering cholesterol[25] and reducing sodium intake on cardiovascular disease rates,[26] whereas modelling studies demonstrate the impact of declines in hypertension, smoking, and dyslipidaemia on CHD mortality.[3,27,28] The severity of myocardial infarctions was likely falling before the introduction of troponin assays, contributing to falls in case fatality.[29] Improved risk stratification and early application of evidence-based drugs and PCI have also reduced early mortality after myocardial infarction, with PCI rates increasing in New Zealand over the past decade in both STEMI and NSTEMI patients.[18] An NSW-based study demonstrated that interhospital transfer was associated with lower levels of 30-day case fatality after myocardial infarction, even after exclusion of early in-hospital deaths.[30] The higher case fatality in England in the early 2000s relative to other high-income countries resulted in improvements in application of evidence-based treatments for acute myocardial infarction,[9] which might have contributed to a greater relative contribution from case fatality during our study.

Our study provides a template for future international comparisons of cardiovascular disease trends. It takes advantage of routinely collected administrative hospital data linked to mortality data, which is increasingly available internationally.[31] International comparisons face many challenges, because it is often difficult to share data across borders. The protocol for this study, which involved sharing common analysis code, facilitates international comparison without the need for sharing individual-level data. It is also important to note that data sources were restricted to hospital and mortality data. No doubt greater insights could be obtained with additional data linkage such as pharmaceutical and primary care data, which are increasingly available in some countries.[32]

Our study has several limitations. While all jurisdictions in the study have high-quality record-linkage systems with high linkage and low false-positive rates,[33–36] each dataset is subject to the linkage methods in its own jurisdiction. Record linkage between hospital records and mortality records, and the quality of such linkage, might not be consistent between jurisdictions or across time. We have previously shown differences in local coding practices for coding myocardial infarction subtypes in hospital data between England and Australia,[37] hence our broader use of myocardial infarction codes. We were unable to stratify mortality rates by STEMI or NSTEMI status due to the high proportion of deaths coded as unspecified myocardial infarction. Understanding the impact of myocardial infarction subtype on myocardial infarction mortality declines could be achieved by restricting the study population to STEMI cases. Coding of STEMI in hospitalised cases appears to be more stable over time; however, assumptions about assigning sudden myocardial infarction deaths as STEMI would be required. We have included analyses of CHD to mitigate the impact of changing severity of myocardial infarction; however, nearly half of CHD hospitalisations in some jurisdictions are comprised of chronic CHD or stable angina admissions,[12] meaning that case fatality for CHD includes many low-severity cases in the denominator, and therefore definitional issues for case fatality require further attention. Disease coding in older people might be of lower accuracy because of the higher comorbidity burden leading to difficulties in correctly attributing cause of death. We are unable to draw conclusions about the reasons for differences in event rate or case fatality trends between countries, because we do not have data on risk factors and health system factors. The growing availability of data from electronic medical records enabling linkage of risk factors to event data, as occurs in New Zealand,[38] should enable these issues to be examined in more jurisdictions in the future. We could not investigate differences in contributions to myocardial infarction mortality trends by indigenous or ethnic status, as these variables were not uniformly available in our datasets. Our overall results could mask differing relative contributions and thus it is important that further studies investigate this in indigenous populations and other ethnic groups.

Despite impressive reductions in mortality from myocardial infarction in recent decades, our findings demonstrate opportunities for further gains in reducing cardiovascular disease burden. Extending improvements in case fatality to include people aged 75 years and older could have a marked impact on further reducing myocardial infarction mortality at a population level, but requires guideline-directed implementation. Better understanding of the combined impacts of cardiovascular disease risk factor and diagnostic changes on event rates, particularly for people under 55 years, is necessary as cumulative data across multiple populations provides an imperative to address the adverse trends in this age group, particularly in women. Comparative analyses across countries using standardised design and analytic approaches provide the most pragmatic means of undertaking such studies and can inform optimised approaches to prevention and treatment of myocardial infarction.

Contributors

PC, FLW, and XC conceptualised the study. XC was responsible for project administration and coordination of all analytical work. AnH, AlH, PC, NW, TB, NN, and LCR were responsible for funding acquisition. XC, LN, FLW, NN, NW, OS, EB, TB, LCR, and PC contributed to development of the study analysis plan. XC, EB, NN, and RG led the data and statistical analyses. RG, EB, NN, and XC had full access to the data in their relevant jurisdictions. All authors reviewed methods and interpreted results. LN, XC, FLW, and PC coordinated manuscript production. LN and XC drafted the manuscript and all authors reviewed and edited the final version of the manuscript. XC, LN,

FLW, and PC were responsible for the decision to submit the manuscript for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Access to the NSW data was provided with the permission of data custodians to researchers named and approved by the NSW Population and Health Services Research Ethics Committee. No additional data are available. Sharing of anonymised cohort data from New Zealand with other researchers or official agencies will generally be possible on request from the authors (pending approval of the relevant official agencies). Access to the anonymised data used in this study was provided by Statistics NZ under the security and confidentiality provision of the Statistics Act 1975. Only people authorised by the New Zealand Statistics Act 1975 will be allowed to see data about a particular person, household business, or organisation. The Ontario dataset for this study is held securely in coded form at ICES. Although legal data sharing agreements between ICES and data providers (eg, health-care organisations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access. English national Hospital Episode Statistics and linked mortality data may be obtained by successful application to National Health Service (NHS) Digital (www.digital.nhs.uk). Data sharing agreements between NHS Digital and Nuffield Department of Population Health prohibit the further sharing of any data other than statistical aggregates.

Acknowledgments

NSW, Australia: we acknowledge the NSW Ministry of Health for the provision of data for this study. The Cause of Death Unit Record File is provided by the Australian Coordinating Registry on behalf of Australian Registries of Births, Deaths and Marriages, NSW Coroner and the National Coronial Information System. The Centre for Health Record Linkage is acknowledged for their role in data linkage. LN was supported by a National Health and Medical Research Council of Australia (NHMRC) Early Career Fellowship and a National Heart Foundation Future Leader Fellowship. The research was supported by NHMRC project grant (1084347) and Centre of Excellence in Population Ageing Research, Australian Research Council (CE170100005). Ontario, Canada: this study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and the Ministry of Long-Term Care. This study also received funding from a Canadian Institutes for Health Research operating grant (FRN-142498). LCR is supported by a Canada Research Chair in Population Health Analytics. New Zealand: data is supplied by Statistics New Zealand. The results in this report are not official statistics. They have been created for research purposes from the Integrated Data Infrastructure, managed by Statistics New Zealand. Access to the anonymised data used in this study was provided by Statistics New Zealand under the security and confidentiality provision of the Statistics Act 1975. NN, TB, and NW were supported by the Health Research Council of NZ (grant 16/443). England, UK: data were provided by NHS Digital and held securely in coded form within the Nuffield Department of Population Health at the University of Oxford. The research was supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (NIHR-BRC-1215–20008), and by the Office for Health Improvement and Disparities, and Health Data Research UK (OXFD1). The Big Data Institute has received funding from the Li Ka Shing Foundation and Robertson Foundations, the Medical Research Council, British Heart Foundation, and is supported by the NIHR Oxford Biomedical Research Centre. We thank Nick Hall for his assistance in curating the English datasets used in this study. The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

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