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# Geographic variation in long-term health outcomes following myocardial infarction in England

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## ABSTRACT

**Background** Nationwide studies report the high incidence of major health outcomes following myocardial infarction (MI). This cohort study investigates variation in incidence of health outcomes following MI between health commissioning areas within England.

**Methods** All adults ≥18 years of age with index MI admitted to hospital within all 106 integrated care board (ICB) subpopulations in England were included (2008–2017). The cumulative incidence of all-cause mortality and non-fatal health outcomes (subsequent MI and first hospitalisation for heart failure, atrial fibrillation, cerebrovascular disease, peripheral arterial disease, severe bleeding, renal failure, diabetes mellitus and depression) within 9 years of follow-up was calculated from flexible parametric survival models adjusted for age, sex, year of MI and deprivation. Choropleth maps and funnel plots were used to visualise the degree of variation in incidence of outcomes by ICB subpopulation. The intraclass correlation coefficient (ICC) was used to determine the degree of variation explained at the area versus patient level.

**Results** A total of 381 518 individuals with MI (n=2 807 195 hospital admissions) were included in the study. The crude incidence of post-MI health outcomes varied between areas, including heart failure (range 20.2%–47.9%), severe bleeding (14.3%–34.6%), renal failure (23.7%–38.0%) and all-cause mortality (34.3%–47.7%). The incidence of each major health outcome following MI fell within expected range (between 95% control limits) after adjusting for patient demographics with the exception of two sub-ICBs in Lancashire and South Cumbria, where rates were higher than expected. Overall, variation observed was predominantly explained by region-specific patient demographic profiles rather than at the ICB subpopulation level (ICC <5% for all outcomes).

**Conclusions** This research provides region-specific data for the incidence of 10 major health outcomes following MI in England. The findings can support commissioners to target resources to those areas with populations at greatest risk of major health outcomes following MI.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Individuals who have had a myocardial infarction (MI) have a greater risk of developing a number of major health outcomes compared with individuals without MI in the adult population of England. However, the extent to which the incidence of long-term health conditions following MI varies geographically is unknown.

### WHAT THIS STUDY ADDS

⇒ This study provides high-resolution data regarding the incidence of health outcomes following MI, stratified by integrated care board (ICB) subpopulations in England. While the incidence of health outcomes varied considerably by health commissioning area, the majority of this variation was explained by patient-level factors rather than area-level factors. Nonetheless, a small number of ICB subpopulations were identified in which the incidence of post-MI disease was higher than expected, based on their patient population profile.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Understanding variation in health outcomes following MI by health commissioning area is important to enable targeted resource allocation to areas of greatest need, in order to reduce the significant burden of disease for the growing population of survivors of MI.

## INTRODUCTION

Despite improvements in long-term survival following myocardial infarction (MI), attributed to increased use of pharmacological therapies and percutaneous coronary intervention over recent decades,[1 2] MI remains a significant contributor to global mortality rates and is associated with a significant excess long-term health burden. In the decade following MI, individuals frequently accrue major health conditions across a range of body systems—with 3 in 10 developing heart failure or renal failure and 4 in 10 dying.[3]

Our earlier work has reported the excess incidence of all-cause mortality, subsequent MI, heart failure, renal failure, atrial fibrillation, severe bleeding, cerebrovascular disease, peripheral arterial disease, diabetes mellitus, vascular dementia and depression following MI, over and above that of age- and sex-matched individuals without MI in England.[3] These outcomes were associated with significant health inequality, including earlier onset of heart failure with increased deprivation, and increased risk of depression following MI among women and for those who experience MI at a younger

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age.[3] Previous studies have highlighted geographical variation in the management of MI and its impact on outcomes,[4–6] yet the extent to which the long-term consequences of MI vary within regions of England is not known. Given that health and care in the National Health Service (NHS) is managed through the local contracting of specialist services, it is important to understand region-specific data. Moreover, the NHS long-term plan also calls for more accurate assessment of health inequalities and unmet needs in local areas to support long-term funding allocations.[7]

This study aimed to provide a detailed overview of the incidence of long-term health outcomes post-MI for each integrated care board (ICB) subpopulation in England, assess the degree of variation between areas and determine the relative contribution of patient mix and commissioning group. This research aims to support targeted resource allocation decisions at the commissioning level and enable strategies for enhanced surveillance and detection of major health outcomes following MI focused on those areas of greatest need.

## METHODS

This is a retrospective cohort study of all adults with index MI, admitted to one of 229 NHS hospitals within 106 ICB subpopulations in England between 1 January 2008 and 31 January 2017. We analysed all-cause mortality as well as non-fatal health outcomes including subsequent MI and first hospital-recorded diagnoses for heart failure, atrial fibrillation, cerebrovascular disease, peripheral arterial disease, severe bleeding, renal failure, diabetes mellitus and depression. Health outcomes were identified a priori based on previous work quantifying the excess incidence over and above that of age and sex-matched population of England.[3] We hypothesise that this incidence differs between the 106 ICB subpopulations (previously clinical commissioning groups), which are responsible for planning health services and driving improvements in the outcomes of their local population.

### Data sources

Hospital Episode Statistics (HES) data, containing prospectively collected clinical and demographic data for every hospitalisation to NHS hospitals in England,[8] were extracted from the Admitted Patient Care dataset by NHS England and linked with all-cause mortality data from the Office for National Statistics (censoring date 27 March 2017). This research adheres to General Data Protection Regulation as per our privacy notice. Data minimisation standards were met through pseudonymisation, month/year aggregation of exact dates and exclusion of patients aged <18 years of age.

### Cohort definition

The primary analytical cohort included all individuals aged 18 years or over hospitalised with index MI within the study period. Index MI, as well as the first hospital-coded diagnoses of each of the included health outcomes, were identified from all diagnosis and procedure codes across all hospitalisation episodes per individual. All health outcomes were identified using the ICD10 and OPCS4.5 codes used in our previous work[3] (online supplemental table A). Each individual was allocated to one of 106 ICB subpopulations based on their area of residence (or area of General Practitioner (GP) practice if area of residence not recorded) at the closest point in time to the date of their index MI. All individuals with MI or any hospital-coded diagnoses of the health outcomes of interest recorded in HES prior to the study start date or prior to MI were excluded from the study (at source by NHS England). Furthermore, all individuals with missing geographical information (area of residence and area of GP practice), individuals who lived outside of England or individuals in the Armed Forces at time of MI were excluded.

### Statistical analysis

Patient demographics including age at index MI (continuous), sex (male/female), socioeconomic deprivation (Index of Multiple Deprivation (IMD)), year (single year of index MI), crude mortality (at 30 days, 5 year and the full follow-up period), Kaplan-Meier failure rate over the full follow-up period and diagnosis of subsequent MI and first occurrence of heart failure, atrial fibrillation, cerebrovascular disease, peripheral arterial disease, severe bleeding, renal failure, diabetes mellitus, vascular dementia and depression were summarised for England, as well as by seven broad NHS regions (North East & Yorkshire, North West, Midlands, East of England, London, South East and South West).

The crude and adjusted absolute risk of each outcome over the 9-year follow-up period (overall and by ICB subpopulation) was calculated through standardised cumulative incidence functions (CIFs) derived from flexible parametric survival models for each outcome, stratified by area, using the *standsurv* post-estimation command in Stata 19.[9] Models were adjusted for continuous age, sex, calendar year and IMD, treating death without outcome as a competing risk. Nonlinearity of age was modelled using restricted cubic splines (3 degrees of freedom). CIFs were linked with 2021 ICB subpopulation boundary data (from ONS Open Geography Portal[10]), to visualise variation by area using choropleth maps. In addition, we developed a web application which presents the cumulative incidence data and 95% CIs for each ICB subpopulation by outcome in a series of interactive maps (https://multimorbidity-research-university-of-leeds.shinyapps.io/postMI_CIF_spatial/).

While we implemented a flexible parametric survival modelling approach to calculate adjusted CIFs, we implemented a series of Cox proportional hazards (PH) models with the same set of adjustments including the non-linear effect of age, sex, calendar year of MI and IMD to facilitate subsequent analyses of (1) unwarranted variation in outcomes between sub-ICB populations and (2) quantification of the degree of variation in outcomes explained at the ICB subpopulation level, over and above the variation explained by direct patient demographic variables. This was necessary given the required methodology (adjusted hazard ratio (aHR) funnel plots and calculation of the intraclass correlation coefficient (ICC)) is not currently extended to the flexible parametric framework. The aHRs for each outcome were generated and plotted against 95% and 99% control limits to produce a series of funnel plots following methods by Silcocks.[11] This approach enabled us to incorporate the full survival curve when assessing unwarranted variation in favour of funnel plots of the incidence rates directly which would provide a cross-sectional view only. When constructing the funnel plot control limits, we used a robust variance estimation approach (Winsorisation) to address over-dispersion. Winsorisation was used solely to stabilise estimation of the dispersion parameter and was not applied to the ICB-level outcome estimates. This ensured that control limits reflect typical between-ICB variability and avoid undue widening of funnels driven by a small number of extreme observations. In order to quantify the degree of variation in outcomes explained at the ICB subpopulation level, over and above the variation explained by direct patient demographic variables, we calculated the ICC and corresponding 95% CIs from a Cox PH

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model with a random intercept for ICB subpopulation.[12] First, we determined the unadjusted ICC from the model containing only the random intercept, and subsequently we derived the adjusted ICC from a model additionally including the non-linear effect of age, sex, calendar year of MI and IMD. Finally, in order to quantify the direct effect of each patient demographic factor with each outcome, we report demographic-specific aHRs. For each demographic exposure, the set of covariates included for adjustment was determined a priori using directed acyclic graphs (online supplemental figure A) to avoid a Table 2 Fallacy.[13]

This study has been reported against Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

## PPIE

The research team have an established patient and public involvement and engagement (PPIE) group comprised of individuals who have, or care for someone who has, cardiovascular disease and other multiple long-term health conditions. The importance of local data to patients and the public was frequently raised at several of our workshops. These discussions highlighted the desire for our national-level findings to be disaggregated by geographical area and to make this information available to patients. The PPIE group identified the need for clear lay summaries of research projects to ensure the findings are accessible to all, which will form part of our post publication dissemination strategy.

## RESULTS

Of the 433 361 individuals aged 18 or older with a recorded hospital admission of index MI in England, 47 244 (10.9%) were excluded due to incomplete geographical information, and a further 4599 (1.1%) were excluded due to ICB subpopulations (or clinical commission groups) which are outside of England (online supplemental table B). The final analytical cohort comprised 381 518 individuals with MI relating to 2 807 195 hospital admissions across 106 ICB subpopulations within the seven NHS regions of England (figure 1). Individuals with MI were admitted to hospital at a mean age of 66.9 years (SD 14.2), predominantly male (65.8% (n=251 077)) and had a 30-day mortality rate of 7.4% (n=28 042) (table 1). Differences in age at index MI and sex between regions were minimal; however, individuals in the South East and South West tended to be slightly older at index MI (68.2 (14.3) and 68.5 (13.9)) compared with individuals with MI in London (65.2 (14.9)). There were a modestly higher proportion of males with MI in London and the Midlands (67.0% and 67.9%, respectively) compared with those in the North East & Yorkshire and the North West regions (64.5% and 64.4%, respectively). Variation in socioeconomic deprivation of individuals with MI by region was high. The North West and North East & Yorkshire regions had the highest proportion of MI individuals in the most deprived quintile of IMD (34.0% and 29.7%, respectively) compared with only 7.6% of individuals with MI in the South East region belonging to the most deprived IMD quintile.

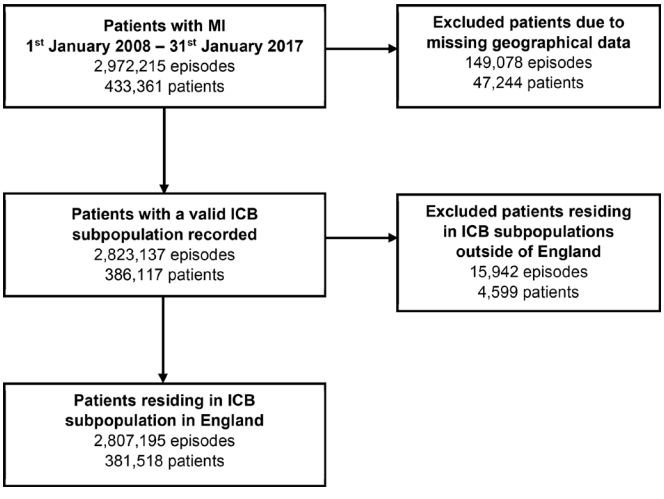



**Figure 1** Cohort definition for the MI population in England. ICB, Integrated Care Board; MI, myocardial infarction.

### Cumulative incidence of health outcomes and all-cause mortality by ICB subpopulation

The largest degree of variation in the crude incidence of health outcomes after MI between ICB subpopulations was observed for heart failure which ranged from 20.2% to 47.9% between areas (average incidence of heart failure following MI in England: 31.8%). The crude incidence of severe bleeding (England average, 19.2%; range across ICB subpopulations 14.3%–34.6%), diabetes mellitus (20.5%; 14.5%–30.1%), renal failure (29.2%; 23.7%–38.0%), all-cause mortality (40.1%; 34.3%–47.7%) and atrial fibrillation (23.4%; 17.5%–29.2%) all varied by more than 10% across ICB subpopulations. While the overall incidence of subsequent MI, peripheral arterial disease and depression following MI was lower than that of other health outcomes investigated in this study (8.9%, 7.2% and 9.3% in England, respectively), there was a high degree of variation in crude incidence for each of these outcomes (subsequent MI range: 5.3% to 12.8%; peripheral arterial disease range 4.0%–10.4%; depression range 5.8%–14.2%). Choropleth maps of crude incidence are found in figure 2, and the crude and adjusted cumulative incidence for each area is provided in online supplemental table E.

After standardisation for age, sex, socioeconomic deprivation and year of MI, the incidence of each major health outcome following MI falls within the 95% control limits of the funnel plot analyses for the vast majority of ICB subpopulations (figures 3–5 and online supplemental figure C), thereby displaying an expected level of variation in health outcomes and all-cause mortality after accounting for population demographics within each area.

Overall, there were five ICB subpopulations where the excess hazard exceeded the 99% control limits for at least one of the health outcomes investigated after standardisation for population demographics (Morecambe Bay, Fylde and Wyre, Coventry and Warwickshire, Frimley, Calderdale) and 12 ICB subpopulations where the excess hazard fell between the upper 95% and 99% control limits (Morecambe Bay, Fylde and Wyre, Calderdale, Trafford, Frimley, Coventry and Warwickshire, Basildon and Brentwood, Bassetlaw, Blackburn With Darwin, Brighton and Hove, Cambridgeshire and Peterborough, Cheshire) for at least one health outcome (figure 6). Two ICB subpopulations had consistently higher than expected incidence of long-term health outcomes following MI (Morecambe Bay and Fylde and Wyre, both part of the Lancashire and South Cumbria ICB) which had excess rates for all outcomes investigated in this study, and all outcomes except diabetes and severe bleeding, respectively. Conversely, two ICB subpopulations had consistently lower than expected incidence of health outcomes following MI (North Staffordshire and North East Essex) across all outcomes.

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**Table 1** Patient demographics by NHS region for the MI population in England

| | North East & Yorkshire | North West | Midlands | East of England | London | South East | South West | England total | Missing N (%) |
|---|---|---|---|---|---|---|---|---|---|
| Integrated Care Boards (ICBs) (N) | 23 | 27 | 19 | 14 | 5 | 11 | 7 | 106 | |
| Cases (N) | 70 409 | 53 119 | 76 684 | 43 725 | 40 957 | 55 783 | 40 841 | 381 518 | 0 |
| Age at study entry, years (mean, SD) | 66.3 (14.0) | 66.1 (14.1) | 66.5 (14.0) | 67.8 (14.2) | 65.2 (14.9) | 68.2 (14.3) | 68.5 (13.8) | 66.9 (14.2) | 59 (0.02) |
| Sex (N, % male) | 45 444 (64.5) | 34 186 (64.4) | 51 372 (67.0) | 28 640 (65.5) | 27 809 (67.9) | 36 783 (65.9) | 26 843 (65.7) | 251 077 (65.8) | 38 (0.01) |
| Period of study entry (N, %) | | | | | | | | | 0 |
| 2008-2010 | 21 532 (30.6) | 15 484 (29.1) | 22 402 (29.2) | 12 503 (28.6) | 11 731 (28.6) | 16 452 (29.5) | 11 407 (27.9) | 111 511 (29.2) | |
| 2011-2013 | 25 650 (36.4) | 19 244 (36.2) | 28 019 (36.5) | 16 111 (36.8) | 15 240 (37.2) | 20 479 (36.7) | 15 423 (37.8) | 140 166 (36.7) | |
| 2014-2017 | 23 227 (33.0) | 18 391 (34.6) | 26 263 (34.2) | 15 111 (34.6) | 13 986 (34.1) | 18 852 (33.8) | 14 011 (34.3) | 129 841 (34.0) | |
| Socioeconomic status | | | | | | | | | 2762 (0.7) |
| 1 – Least deprived | 8759 (12.4) | 7789 (14.7) | 12 719 (16.6) | 10 926 (25.0) | 3809 (9.3) | 17 901 (32.1) | 7608 (18.6) | 69 511 (18.2) | |
| 2 | 12 605 (17.9) | 8602 (16.2) | 15 373 (20.0) | 10 966 (25.1) | 6087 (14.9) | 12 644 (22.7) | 9766 (23.9) | 76 043 (19.9) | |
| 3 | 12 774 (18.1) | 8407 (15.8) | 15 686 (20.5) | 10 275 (23.5) | 8017 (19.6) | 11 902 (21.3) | 11 121 (27.2) | 78 182 (20.5) | |
| 4 | 15 029 (21.3) | 9954 (18.7) | 15 042 (19.6) | 7757 (17.7) | 11 681 (28.5) | 8808 (15.8) | 8189 (20.1) | 76 460 (20.0) | |
| 5 – Most deprived | 20 935 (29.7) | 18 051 (34.0) | 17 465 (22.8) | 3562 (8.1) | 10 511 (25.7) | 4227 (7.6) | 3809 (9.3) | 78 560 (20.6) | |
| Health outcomes following MI* | | | | | | | | | N/A |
| Subsequent MI | 4039 (5.7) | 2598 (4.9) | 3886 (5.1) | 2183 (5.0) | 2221 (5.4) | 2775 (5.0) | 2097 (5.1) | 19 799 (5.2) | |
| Heart failure | 19 380 (27.5) | 15 931 (30.0) | 18 262 (23.8) | 11 269 (25.8) | 11 211 (27.4) | 12 681 (22.7) | 11 777 (28.8) | 100 511 (26.3) | |
| Atrial fibrillation | 13 544 (19.2) | 11 388 (21.4) | 15 353 (20.0) | 9259 (21.2) | 7870 (19.2) | 11 915 (21.4) | 8702 (21.3) | 78 031 (20.5) | |
| Cerebrovascular disease | 5787 (8.2) | 5030 (9.5) | 6814 (8.9) | 4397 (10.1) | 4647 (11.4) | 6015 (10.8) | 4089 (10.0) | 36 779 (9.6) | |
| Peripheral arterial disease | 3295 (4.7) | 2741 (5.2) | 3690 (4.8) | 2201 (5.0) | 2086 (5.1) | 3022 (5.4) | 2304 (5.6) | 19 339 (5.1) | |
| Severe bleeding | 10 617 (15.1) | 9161 (17.5) | 11 262 (14.7) | 7093 (16.2) | 6502 (15.9) | 8234 (14.8) | 6124 (15.0) | 58 993 (15.5) | |
| Renal failure | 13 437 (19.1) | 10 826 (20.4) | 14 526 (18.9) | 8217 (18.8) | 8449 (20.6) | 10 452 (18.7) | 8563 (21.0) | 74 470 (19.5) | |
| Diabetes mellitus | 11 265 (16.0) | 8753 (16.5) | 13 474 (17.6) | 6881 (15.7) | 9211 (22.5) | 8707 (15.6) | 5947 (14.6) | 64 238 (16.8) | |
| Depression | 4817 (6.8) | 4166 (7.8) | 4754 (6.2) | 2767 (6.3) | 2515 (6.1) | 3362 (6.0) | 2539 (6.2) | 24 920 (6.5) | |
| All-cause mortality (N, %) | | | | | | | | | N/A |
| 30 days | 4867 (6.9) | 3972 (7.5) | 5755 (7.5) | 3272 (7.5) | 3079 (7.5) | 4272 (7.7) | 2816 (6.9) | 28 033 (7.3) | |
| 5 years | 14 564 (20.7) | 11 448 (21.6) | 15 811 (20.6) | 9427 (21.6) | 8369 (20.4) | 12 340 (22.1) | 8640 (21.2) | 80 599 (21.1) | |
| 9 years | 16 974 (24.1) | 13 104 (24.7) | 18 249 (23.8) | 10 809 (24.7) | 9610 (23.5) | 14 177 (25.4) | 9968 (24.4) | 92 891 (24.3) | |
| Kaplan-Meier estimate (95% CI)† | 39.3 (38.6 to 40.1) | 39.5 (38.7 to 40.3) | 38.7 (38.0 to 39.4) | 40.5 (39.5 to 41.4) | 37.6 (36.7 to 38.5) | 41.1 (40.2 to 42.0) | 40.7 (39.7 to 41.7) | 39.6 (39.3 to 39.9) | N/A |

*Code lists for each health outcome are available in online supplemental table A. The definitions were based on our previously published work.[3]
†Over the full follow-up period.
MI, myocardial infarction; NHS, National Health Service.



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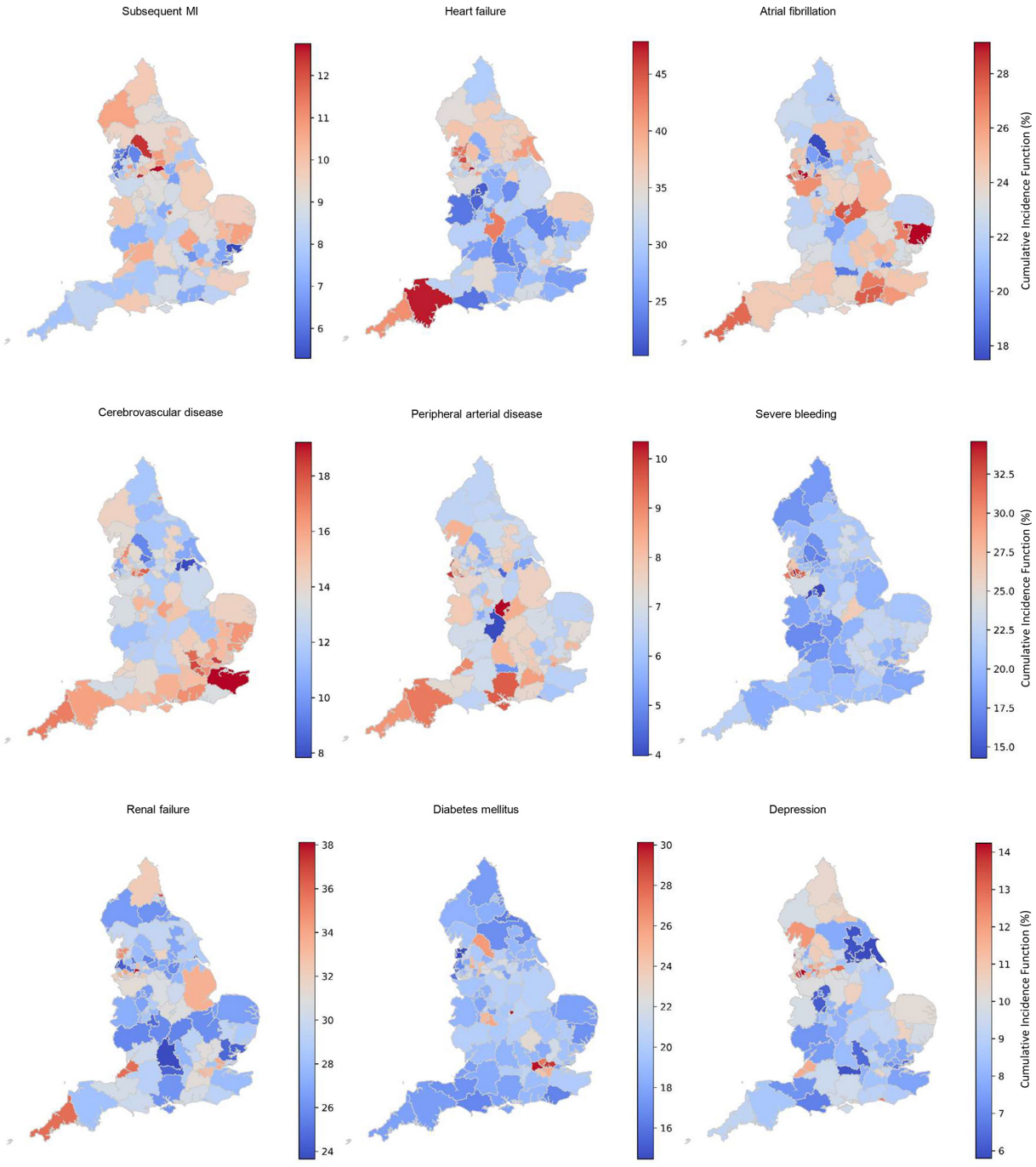



**Figure 2** Choropleth maps of crude cumulative incidence functions by ICB subpopulation for each health outcome. ICB, Integrated Care Board; MI, myocardial infarction.

### Determinants of long-term health outcomes following MI

ICCs, which quantify the degree of variation in incidence explained by geographical area over and above that of patient case mix within each area (age, sex, IMD and year of MI), were below 5% for all health outcomes investigated. The smallest degree of variation explained at the ICB subpopulation level was observed for all-cause mortality (0.2% (95% CI 0.1% to 0.3%)), atrial fibrillation (0.6% (95% CI 0.4% to 0.8%)) and renal failure (0.9% (95% CI 0.6% to 1.2%)), with a higher degree of variation in incidence explained at the area level for heart failure (2.6% (95% CI 2.0% to 3.5%)) (tables 2 and 3). Therefore, the majority of the variation in incidence observed was explained by differences within ICB subpopulations (patient level factors), rather than variation between ICB subpopulations (area level factors).

The risk of developing all major health outcomes within areas, except depression, increased with age. This was most pronounced for all-cause mortality (HR=2.44; 95% CI 2.41 to 2.47 for age 70 vs 60 and HR=2.59; 95% CI 2.56 to 2.61 for age 80 vs 70 years) and renal failure (HR=2.53; 95% CI 2.49 to 2.56 for age 70 vs 60 and HR=2.31; 95% CI 2.29 to 2.34 for age 80 vs 70 years) (tables 2 and 3). In the post-MI period, females had a reduced risk of developing peripheral arterial disease (HR 0.75; 95% CI 0.72 to 0.77), severe bleeding (HR 0.86; 95% CI 0.85 to 0.88), atrial fibrillation (HR 0.91; 95% CI 0.90 to 0.92), diabetes (HR 0.91; 95% CI 0.90—0.93), renal failure (HR 0.92;



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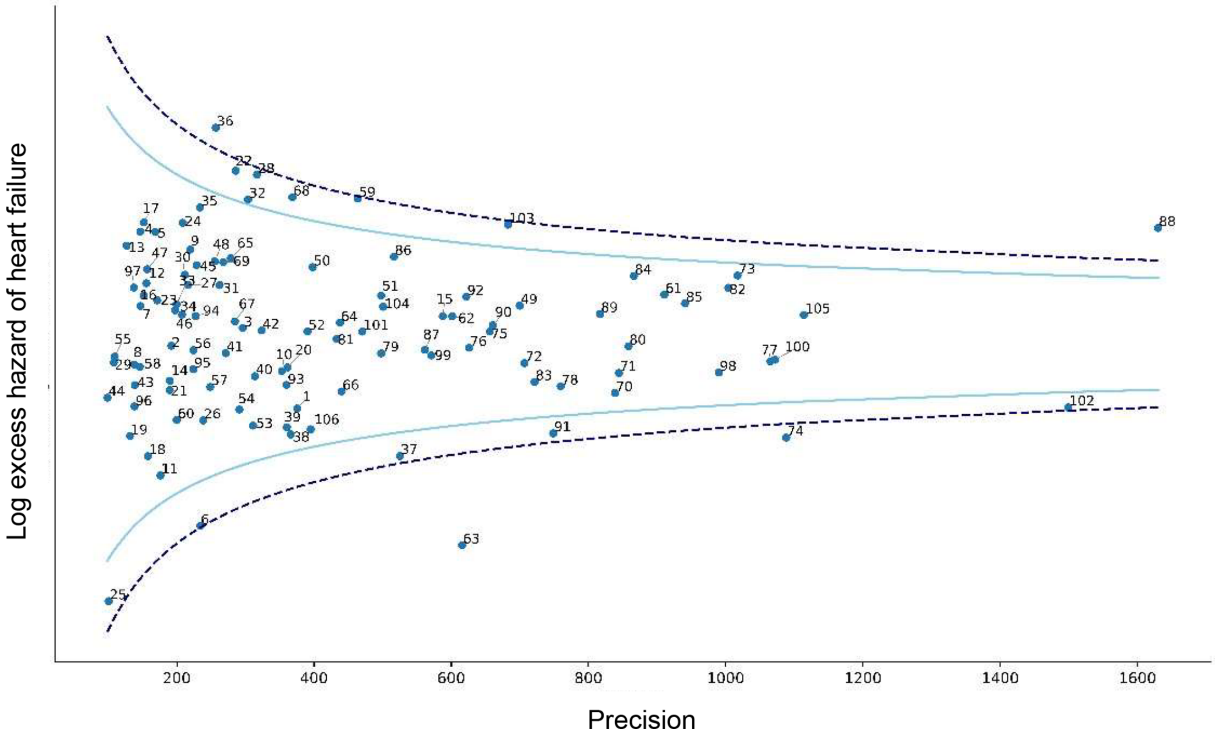



**Figure 3** Funnel plot of the excess hazard of heart failure by ICB subpopulation showing the 95% and 99% control limits. A lookup from the ID in the plot to ICB subpopulation code and name is provided in online supplemental table C. ICB, Integrated Care Board.

95% CI 0.91 to 0.93), subsequent MI (HR 0.93; 95% CI 0.90 to 0.96), heart failure (HR 0.96; 95% CI 0.95 to 0.97) and all-cause mortality (HR 0.96; 95% CI 0.95 to 0.98) when compared with males. Conversely, females had an increased risk of depression (HR 1.96; 95% CI 1.91 to 2.02) and cerebrovascular disease (HR 1.13; 95% CI 1.11 to 1.16).

For all health outcomes, the incidence was higher among people living in more deprived areas compared with those living in the least deprived areas. This was most pronounced for depression (HR 1.64; 95% CI 1.57 to 1.72) and diabetes (HR 1.60; 95% CI 1.56 to 1.65). The cumulative incidence of most health outcomes following MI reduced over the study period including

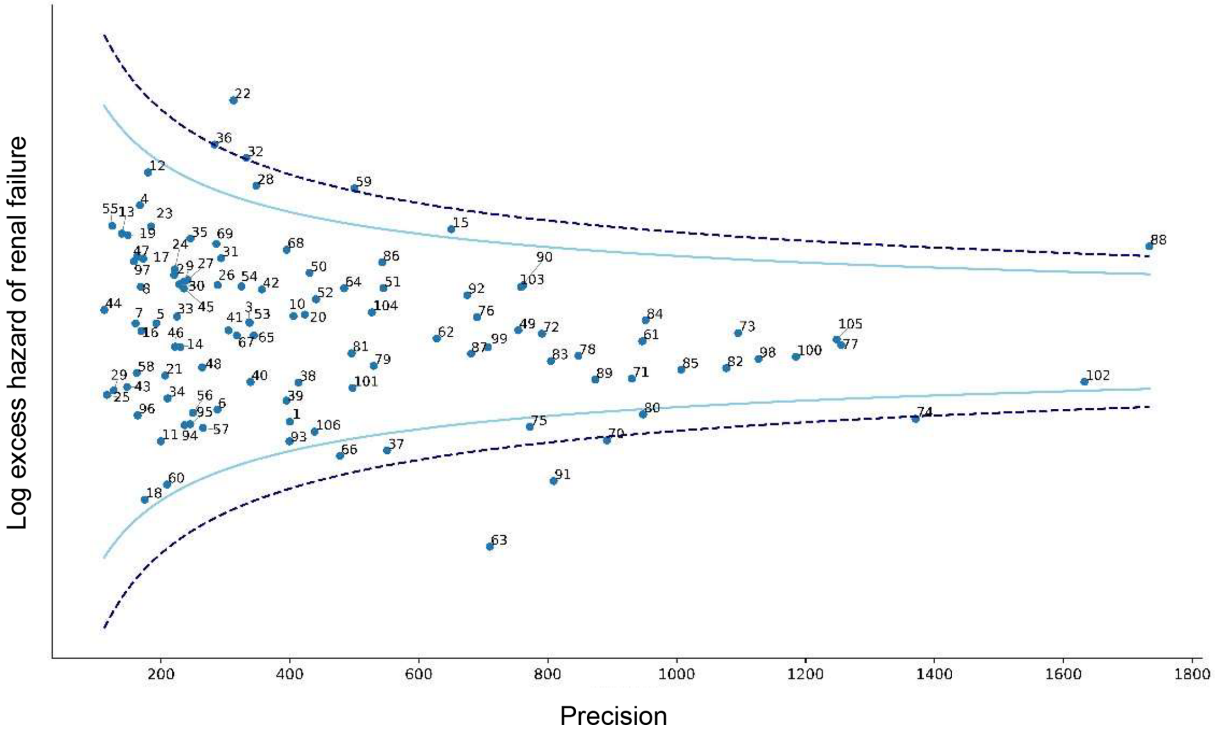



**Figure 4** Funnel plot of the excess hazard of renal failure by ICB subpopulation showing the 95% and 99% control limits. A lookup from the ID in the plot to ICB subpopulation code and name is provided in online supplemental table C. ICB, Integrated Care Board.



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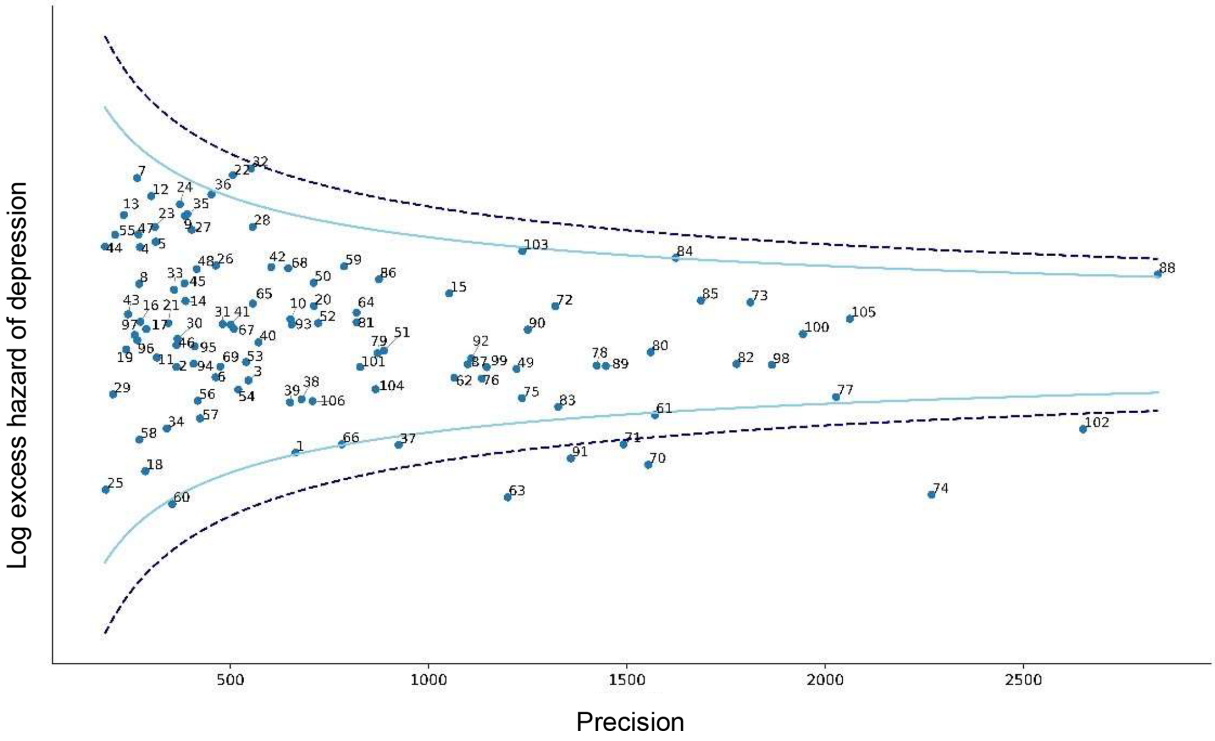



**Figure 5** Funnel plot of the excess hazard of depression by ICB subpopulation showing the 95% and 99% control limits. A lookup from the ID in the plot to ICB subpopulation code and name is provided in online supplemental table C. ICB, Integrated Care Board.

subsequent MI (HR 0.91; 95% CI 0.90 to 0.91), atrial fibrillation (HR 0.96; 95% CI 0.96 to 0.97), cerebrovascular disease (0.97; 95% CI 0.96 to 0.97), peripheral arterial disease (0.97; 95% CI 0.96 to 0.97), severe bleeding (0.96; 0.96–0.97) and diabetes (0.96; 0.95–0.96) per year over the study period. However, the incidence of heart failure (HR 1.01, 95% CI 1.01 to 1.01), renal failure (HR 1.04; 95% CI 1.04 to 1.05) and depression (HR 1.04; 95% CI 1.03 to 1.05) increased over the study period.

## DISCUSSION

This study provides nationwide insights into geographic variation in the long-term cumulative incidence of major health outcomes and all-cause mortality following MI in England. The cumulative incidence of health outcomes within 9 years of MI varied considerably between ICBs, with major differences observed in heart failure (20.2 to 47.9%), severe bleeding (14.3 to 34.6%), diabetes mellitus (14.5 to 30.1%), renal failure (23.7 to 38.0%), atrial fibrillation (17.5 to 29.2%) and all-cause mortality (34.3 to 47.7%).

The majority of variation observed in the study fell within acceptable limits after accounting for patient population demographics within each area. We found that the observed variation in outcomes between ICB subpopulations reflects the patient population profile of that area for the vast majority of ICBs.

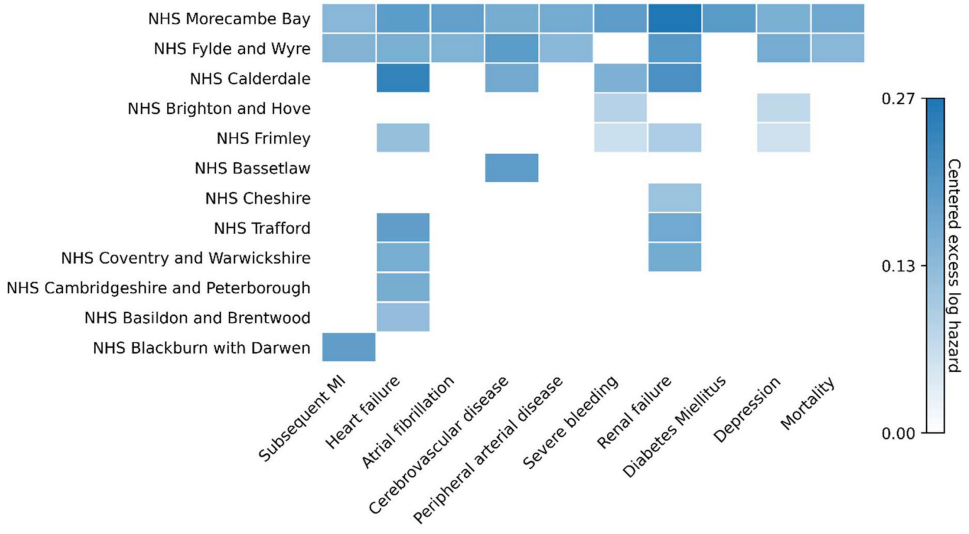



**Figure 6** Heat map showing ICB subpopulations where the excess hazard exceeds 95% control limits for each health outcome. ICB, Integrated Care Board; MI, myocardial infarction; NHS, National Health Service.



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**Table 2** Degree of variation in the incidence of cardiovascular health outcomes following MI at the ICB subpopulation level based on the intraclass correlation coefficient (ICC) and 95% CI and adjusted HRs for the direct effect of age, sex, calendar year of MI and Index of Multiple Deprivation on risk of cardiovascular health outcomes following MI

| | Subsequent MI | Heart failure | Atrial fibrillation | Cerebrovascular disease | Peripheral arterial disease | Severe bleeding |
|---|---|---|---|---|---|---|
| Unadjusted ICC (%)* | 1.5 (1.1–2.2) | 2.6 (2.0–3.4) | 0.9 (0.7–1.2) | 1.7 (1.3–2.4) | 1.4 (1.0–2.0) | 1.9 (1.4–2.5) |
| Adjusted ICC (%)† | 1.4 (1.0–2.0) | 2.6 (2.0–3.5) | 0.6 (0.4–0.8) | 1.6 (1.2–2.2) | 1.4 (1.0–2.0) | 1.9 (1.4–2.5) |
| Exposure of interest‡ | Adjusted hazard ratio (95% CI) | | | | | |
| Non-linear effect of age in years§ | | | | | | |
| Age 50 vs 40 years | 0.84 (0.82 to 0.87) | 1.07 (1.05 to 1.09) | 1.80 (1.73 to 1.88) | 1.19 (1.14 to 1.24) | 1.43 (1.34 to 1.52) | 1.10 (1.07 to 1.13) |
| Age 60 vs 50 years | 1.02 (1.00 to 1.03) | 1.34 (1.33 to 1.35) | 2.03 (1.99 to 2.07) | 1.61 (1.58 to 1.64) | 1.66 (1.62 to 1.71) | 1.32 (1.31 to 1.34) |
| Age 70 vs 60 years | 1.27 (1.24 to 1.29) | 1.67 (1.65 to 1.68) | 2.19 (2.17 to 2.22) | 2.12 (2.09 to 2.16) | 1.84 (1.79 to 1.88) | 1.56 (1.54 to 1.58) |
| Age 80 vs 70 years | 1.57 (1.55 to 1.59) | 1.65 (1.64 to 1.67) | 1.83 (1.81 to 1.84) | 1.92 (1.90 to 1.95) | 1.40 (1.37 to 1.42) | 1.44 (1.43 to 1.46) |
| Average linear effect for single year of age at MI | 1.03 (1.03 to 1.03) p<0.001 | 1.04 (1.04 to 1.04) p<0.001 | 1.06 (1.06 to 1.06) p<0.001 | 1.06 (1.06 to 1.06) p<0.001 | 1.04 (1.04 to 1.04) p<0.001 | 1.03 (1.03 to 1.03) p<0.001 |
| Sex | | | | | | |
| Male (ref) | 1 | 1 | 1 | 1 | 1 | 1 |
| Female | 0.93 (0.90 to 0.96) p<0.001 | 0.96 (0.95 to 0.97) p<0.001 | 0.91 (0.90 to 0.92) p<0.001 | 1.13 (1.11 to 1.16) p<0.001 | 0.75 (0.72 to 0.77) p<0.001 | 0.86 (0.85 to 0.88) p<0.001 |
| Index of Multiple Deprivation | | | | | | |
| IMD 5 (least deprived, ref) | 1 | 1 | 1 | 1 | 1 | 1 |
| IMD - 4 | 1.09 (1.04 to 1.15) p<0.001 | 1.08 (1.06 to 1.11) p<0.001 | 1.03 (1.00 to 1.05) p=0.024 | 1.09 (1.05 to 1.13) p<0.001 | 1.08 (1.03 to 1.13) p<0.001 | 1.03 (1.01 to 1.06) p<0.001 |
| IMD - 3 | 1.17 (1.12 to 1.23) p<0.001 | 1.14 (1.11 to 1.16) p<0.001 | 1.05 (1.03 to 1.08) p<0.001 | 1.14 (1.10 to 1.18) p<0.001 | 1.12 (1.07 to 1.18) p<0.001 | 1.07 (1.04 to 1.10) p<0.001 |
| IMD - 2 | 1.31 (1.25 to 1.37) p<0.001 | 1.21 (1.18 to 1.24) p<0.001 | 1.04 (1.02 to 1.07) p<0.001 | 1.21 (1.17 to 1.25) p<0.001 | 1.20 (1.14 to 1.25) p<0.001 | 1.13 (1.10 to 1.16) p<0.001 |
| IMD - 1 (most deprived) | 1.39 (1.32 to 1.46) p<0.001 | 1.32 (1.29 to 1.35) p<0.001 | 1.09 (1.06 to 1.12) p<0.001 | 1.34 (1.30 to 1.39) p<0.001 | 1.36 (1.30 to 1.43) p<0.001 | 1.17 (1.14 to 1.21) p<0.001 |
| Year of MI | 0.91 (0.90 to 0.91) p<0.001 | 1.01 (1.01 to 1.01) p<0.001 | 0.96 (0.96 to 0.97) p<0.001 | 0.96 (0.95 to 0.96) p<0.001 | 0.97 (0.96 to 0.97) p<0.001 | 0.96 (0.96 to 0.97) p<0.001 |

*Intraclass correlation coefficient (ICC) and 95% CI obtained from an unadjusted multilevel mixed effects cox regression models, per outcome.
†ICC and 95% CI obtained from a multilevel mixed effects cox regression models adjusted for age, sex, Index of Multiple Deprivation and year of MI, per outcome.
‡The adjusted HR for each exposure-outcome relationship has been derived from a separate mixed effects Cox proportional hazards model, adjusted for appropriate confounders determined through direct acyclic graphs and accounting for clustering at the ICB subpopulation level.
§P values are omitted as they are not readily available post-estimation of age contrasts derived from a model fitted with restricted cubic splines (3 degrees of freedom) for the non-linear effect of age.
ICBs, Integrated Care Boards; MI, myocardial infarction.

However, there were a small number of areas for which the cumulative incidence of at least one health outcome after MI was higher than expected, exceeding the 95% control limits following standardisation for patient demographics. These included Morecambe Bay, Fylde and Wyre, Calderdale, Trafford, Frimley, Coventry and Warwickshire, Basildon and Brentwood, Bassetlaw, Blackburn with Darwin, Brighton and Hove, Cambridgeshire and Peterborough, Cheshire, Frimley and Calderdale. For two ICB subpopulations, Morecambe Bay and Fylde and Wyre, which both form part of the Lancashire and South Cumbria ICB, rates of health outcomes following MI were consistently higher than would be expected after standardising for the patient population demographic profile in these areas.

Causes of healthcare variation are numerous and complex. They may be due to differences in patient demographics which could be associated with the severity of illness, differences in local clinical guidelines and policies driving different clinician behaviours or the effects of incentives in the financing of healthcare.[14 15] There is a need to further investigate the small number of areas in which unwarranted variation in health outcomes following MI has been identified. Our earlier research has described the missed opportunities for care among patients who present to NHS hospitals with MI and that this was significantly associated with reduced survival.[4 16] In this study, the between ICB subpopulation variation was minimal overall (<5%) after standardising for patient case mix, suggesting that the incidence of long-term health outcomes following MI predominantly reflects patient demographic profiles in each area—with the exception of those areas where rates were significantly higher than expected. Our findings provide a practical framework to improve post-MI service planning. Comparison of observed vs expected outcome rates enables clinical commissioners to identify regions in which outcomes may be worse than anticipated given patient case mix, which may warrant targeted review of specific pathways including (i) cardiac rehabilitation, (ii) provision of secondary prevention and (iii) access to cardiology-led follow-up. Conversely, areas with lower-than-expected rates may offer insights into best practice that could be replicated in other areas. As most variation was explained by patient demographics, these results also support aligning resource allocation



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**Table 3** Degree of variation in the incidence of non-cardiovascular health outcomes following MI at the ICB subpopulation level based on the intraclass correlation coefficient (ICC) and 95% CI and adjusted HRs for the direct effect of age, sex, calendar year of MI and Index of Multiple Deprivation on risk of non-cardiovascular health outcomes following MI

| | Renal failure | Diabetes | Depression | Mortality |
|---|---|---|---|---|
| Unadjusted ICC (%)* | 0.8 (0.6–1.1) | 1.3 (1.0–1.7) | 2.2 (1.6–3.0) | 0.4 (0.3–0.6) |
| Adjusted ICC (%)† | 0.9 (0.6–1.2) | 1.3 (1.0–1.7) | 1.5 (1.1–2.1) | 0.2 (0.1–0.3) |
| Exposure of interest‡ | Adjusted hazard ratio (95% CI) | | | |
| Non-linear effect of age§ | | | | |
| Age 50 vs 40 years | 1.30 (1.25 to 1.35) | 1.20 (1.17 to 1.23) | 0.86 (0.83 to 0.88) | 1.34 (1.29 to 1.39) |
| Age 60 vs 50 years | 1.84 (1.81 to 1.87) | 1.22 (1.21 to 1.24) | 0.81 (0.80 to 0.82) | 1.81 (1.78 to 1.84) |
| Age 70 vs 60 years | 2.53 (2.49 to 2.56) | 1.20 (1.19 to 1.22) | 0.79 (0.78 to 0.81) | 2.44 (2.41 to 2.47) |
| Age 80 vs 70 years | 2.31 (2.29 to 2.34) | 0.96 (0.95 to 0.97) | 0.94 (0.92 to 0.95) | 2.59 (2.56 to 2.61) |
| Average linear effect for single year of age at MI | 1.08 (1.08 to 1.08) p<0.001 | 1.01 (1.01 to 1.01) p<0.001 | 0.99 (0.99 to 0.99) p<0.001 | 1.09 (1.09 to 1.09) p<0.001 |
| Sex | | | | |
| Male (ref) | 1 | 1 | 1 | 1 |
| Female | 0.92 (0.91 to 0.93) p<0.001 | 0.91 (0.90 to 0.93) p<0.001 | 1.96 (1.91 to 2.02) p<0.001 | 0.96 (0.95 to 0.98) p<0.001 |
| Index of Multiple Deprivation | | | | |
| IMD 5 (least deprived, ref) | 1 | 1 | 1 | 1 |
| IMD - 4 | 1.11 (1.08 to 1.14) p<0.001 | 1.11 (1.08 to 1.14) p<0.001 | 1.13 (1.08 to 1.18) p<0.001 | 1.09 (1.07–1.11) p<0.001 |
| IMD - 3 | 1.18 (1.15 to 1.21) p<0.001 | 1.24 (1.21 to 1.28) p<0.001 | 1.24 (1.18 to 1.29) p<0.001 | 1.16 (1.13 to 1.18) p<0.001 |
| IMD - 2 | 1.27 (1.224 to 1.30) p<0.001 | 1.38 (1.34 to 1.42) p<0.001 | 1.42 (1.36 to 1.49) p<0.001 | 1.27 (1.25 to 1.30) p<0.001 |
| IMD - 1 (most deprived) | 1.47 (1.44 to 1.51) p<0.001 | 1.60 (1.56 to 1.65) p<0.001 | 1.64 (1.57 to 1.72) p<0.001 | 1.43 (1.40 to 1.47) p<0.001 |
| Year of MI | 1.04 (1.04 to 1.05) p<0.001 | 0.96 (0.95 to 0.96) p<0.001 | 1.04 (1.03 to 1.05) p<0.001 | 1.03 (1.02 to 1.03) p<0.001 |

*Intraclass correlation coefficient (ICC) and 95% CI obtained from an unadjusted multilevel mixed effects cox regression models, per outcome.
†Intraclass correlation coefficient (ICC) and 95% CI obtained from a multilevel mixed effects cox regression models adjusted for age, sex, Index of Multiple Deprivation and year of MI, per outcome.
‡The adjusted HR for each exposure-outcome relationship has been derived from a separate mixed effects Cox proportional hazards model, adjusted for appropriate confounders determined through direct acyclic graphs and accounting for clustering at the ICB subpopulation level.
§P values are omitted as they are not readily available post-estimation of age contrasts derived from a model fitted with restricted cubic splines (3 degrees of freedom) for the non-linear effect of age.
ICB, Integrated Care Board; MI, myocardial infarction.

with local population risk profiles, alongside targeted evaluation of (and greater support for) outlier areas.

While we observed some reductions in the post-MI incidence of subsequent MI, atrial fibrillation, cerebrovascular disease, peripheral arterial disease, severe bleeding and diabetes over the study period, the incidence of heart failure, renal failure and depression increased. There is a clear need to shift focus to preventative measures aimed at reducing the ongoing significant burden of disease for individuals surviving MI. We identified an almost twofold increased risk of depression among females following MI compared with male counterparts, and the cumulative incidence of depression following MI varied by area from 5.8% to 14.2%. While these differences may be partly influenced by sex-related differences in health-seeking behaviour, our study captures hospital-coded diagnoses of depression which is likely reflective of clinically significant and persistent illness. While some degree of detection bias is likely present, our findings may be less susceptible to differential health-seeking behaviour than studies in primary care settings or self-reported symptoms. The consistent increased risk of depression among females, as well as higher incidence among younger and more socioeconomically deprived individuals also reported in previous analyses of post-MI depression,[3] supports consideration of targeted or enhanced screening and follow-up for depression in the post-MI setting with the aim of improving quality of life and longer-term outcomes.

The strengths of this study are its nationwide population coverage of individuals with MI, combined with robust statistical methodology producing high-resolution area-specific maps and tables to support health commissioning decisions. We do, however, acknowledge the study limitations. While we were able to examine the degree of variation observed at the ICB subpopulation level over and above that of key demographic factors associated with adverse post-MI outcomes (including age, sex, socioeconomic deprivation and year), the absence of more detailed clinical and treatment variables (eg, those relating to MI management, MI severity or uptake of cardiac rehabilitation) within these routinely collected data limited further adjustment. Therefore, we acknowledge that some residual differences between ICB subpopulations may reflect differences in clinical risk and care pathways rather than service-related variation. Nonetheless, we believe that the provision of area-specific rates of health outcomes will facilitate further local investigation and consideration of area-specific knowledge of service provision. As in our earlier study,[3] we acknowledge potential underestimation of the post-MI disease burden of diagnoses typically made in primary care. Our estimates reflect clinically recognised disease during hospital admission, rather than true population incidence. Geographic variation observed may therefore partly reflect differences in healthcare utilisation and, in particular, deprivation-related differences in healthcare-seeking behaviour. Despite this, our study provides evidence that the development of specific health outcomes following MI are common and have shown no signs of significant improvement over the study period. Our study identified that the variation in socioeconomic deprivation of individuals with MI by region was high; however, we cannot infer whether this was specific to MI or the population more generally from our data. Nonetheless, aggregate and crude IMD level data

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for the total population do show that the proportion of the general population in the most deprived quintile of IMD in the North West and North East & Yorkshire regions was 34% and 32% compared with 34% and 29.7% for this study's MI population. This suggests that the MI population deprivation is similar to the general population. We were unable to include data for individuals where geographical data were missing. These individuals were more likely to have been admitted earlier in the study period and had higher observed mortality (online supplemental table B). While this may indicate some selection towards a lower-risk cohort in the analytical sample, exclusion of individuals without geographic assignment is unlikely to bias comparisons *between* ICB subpopulations, which formed the primary focus of this study. Furthermore, we accounted for changes over time in our analyses to mitigate against potential bias arising from this exclusion.

While high-quality system-wide healthcare databases are increasingly accessible, major barriers remain in timely data access and the associated costs of both data access and scalable computational facilities to handle size, complexity and necessary security standards.[17] Addressing these barriers should remain a priority so that nationwide data can be systematically interrogated by health commissioning bodies to generate timely knowledge of health outcomes for an increasingly at-risk population and drive forward major public health initiatives.

In conclusion, this study found a high degree of variation in the incidence of severe bleeding, diabetes mellitus, atrial fibrillation, heart failure, renal failure and all-cause mortality by geographical area in England for individuals following MI. The degree of variation was reflective of patient case mix with minimal unwarranted variation at the ICB subpopulation level overall—except for in a small number of areas. This study presents an opportunity for health commissioners to target resource allocation to prevent the post-MI disease burden in areas with higher-than-expected rates. Given the increasing trends in incidence of post-MI heart failure, renal disease and depression, addressing the provision of long-term follow-up care for individuals surviving MI through stronger networks of post-MI care or performance-based commissioning is necessary. Overall, there is a need for enhanced post-MI health surveillance in order to mitigate increased healthcare usage, reduced quality of life and premature death for the growing population of survivors of MI.

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**Contributors** All authors meet the criteria for authorship, with individual contributions as follows: MH was responsible for conceptualisation, funding acquisition and data curation. MH, CS, TdT, EB and JAB were responsible for study design, methodology and interpretation of the findings. MH, CS, TdT and JAB were responsible for formal analysis of the data. CS and TdT were responsible for visualisation. MH and CS were responsible for writing the original draft of the manuscript. All authors were responsible for reviewing and editing of the manuscript and approved the final version. MH is the guarantor of the paper. MH provides assurance that all listed authors meet authorship criteria and that there is no one else who fulfils the criteria for authorship but has not been included as an author. MH accepts full responsibility for the work and conduct of the study, had access to the data and controlled the decision to publish.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not applicable.

**Ethics approval** This research adheres to General Data Protection Regulation (GDPR) (privacy notice). Data minimisation standards were met through pseudonymisation, month/year aggregation of date and exclusion of patients aged <18 years old and individuals with pre-existing conditions from the a priori defined outcomes. Data were stored and processed within the Leeds Analytic Secure Environment for Research (LASER) platform at the University of Leeds. Ethical approval was not required for this study, which solely relies on the secondary use of routinely collected, non-confidential healthcare data.

**Provenance and peer review** Not commissioned; externally peer-reviewed.

**Data availability statement** Data may be obtained from a third party and are not publicly available. Hospital episode statistics data used within this study are managed and released by NHS England. Anyone wishing to access these data must do so via direct application to the Data Access and Request Service. The specific extract provided to the research team cannot be shared by the research team according to the legally binding terms under which they were released. Our privacy notice defines the purpose and legal basis of our use of these data: https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics.

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