Trends In ST-elevation Myocardial Infarction Hospitalisation Among Young Adults: A Binational Analysis

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MINAP: The authors do not have the authorization to share the data, but it can be accessed through contacting the National Institute for Cardiovascular Outcomes Research (NICOR) upon approval.

NIS: The National Inpatient Sample (NIS) database can be accessed through contacting the Agency for Healthcare Research and Quality after completing the Data use agreement training and upon reasonable request.

Abstract

Background: ST-segment myocardial infarction (STEMI) is typically associated with increased age, but there is an important group of patients that suffer STEMI under the age of fifty, that are not well characterized in studies.

Methods & Results: We analysed results from Myocardial Ischemia National Audit Project (MINAP) from the United Kingdom (UK) between 2010-2017 and the National Inpatient Sample (NIS) from the United States (US) between 2010-2018. After exclusion criteria, there were 32,719 STEMI patients aged ≤50 from MINAP, and 238,952 patients' ≤50 from the NIS. We analysed temporal trends in demographics, management, and mortality. The proportion of females increased, 15.6% (2010-2012) to 17.6% (2016-2017) (UK) and 22.8% (2010-2012) to 23.1% (2016-2018) (US). The proportion of white patients decreased, from 86.7% (2010) to 79.1% (2017) (UK) and 72.1% (2010) to 67.1% (2017) (US). Invasive coronary angiography (ICA) rates increased in UK (2010-2012: 89.0%, 2016-2017: 94.3%), while decreased in US (2010-2012: 88.9%, 2016-2018: 86.2% (US). After adjusting for baseline characteristics and management strategies, there was no difference in all-cause mortality in the UK in 2016-2017 compared to 2010-2012 (OR:1.21, 95% CI:0.60-2.40), but there was a decrease in the US in 2016-2018 compared to 2010-2012 (OR: 0.84, 95% CI: 0.79-0.90).

Conclusion: The demographics of young STEMI patients have temporally changed in the UK and US, with increased proportions of females and ethnic minorities. There was a significant increase in the frequency of diabetes mellitus over the respective time periods in both countries.

Introduction

Despite a reduction in mortality from coronary artery disease (CAD) both in the United Kingdom (UK) and the United States (US) over the past four decades, hospitalizations from acute myocardial infarction (AMI) amongst young adults, defined as those <50 years of age, have not declined[1]. Young patients have been shown to have increasing cardiometabolic risk factor profiles with growing rates of hypertension, hypercholesterolemia, obesity, and type 2 diabetes mellitus (DM)[2, 3]. In addition, an increasing prevalence of adverse health behaviors such as cigarette smoking have led to an increased incidence of AMI at a younger age[3, 4].

Many of the health care trends reported in patients with ST-segment elevation myocardial infarction (STEMI), such as disparities in ethnicity or sex, are well established in older populations. There remains a gap in knowledge about health care delivery and outcomes in younger patients. Furthermore, it is likely that different populations derived from different countries will have varying trends, given the variations in the healthcare systems and the phenotype of the population.

Thus, using data derived from a large national registry in England and Wales and a large US administrative database, our study aims to examine and analyse the trends of STEMI amongst young patients in both the UK and US.

Methods

Study design:

United Kingdom

We used the Myocardial Ischemia National Audit Project (MINAP), a prospective national registry of patients admitted to hospitals in the UK with an acute coronary syndrome. The MINAP dataset consists of 130 variables including baseline demographics and clinical characteristics, comorbid conditions, management strategies, pharmacotherapy, place of care, in-hospital clinical outcomes and diagnoses on discharge[5, 6]. Data are submitted by hospital clinical and clerical staff with approximately 90,000 pseudonymised records uploaded annually to the National Institute for Cardiovascular Outcomes Research (NICOR).

United States

The National Inpatient Sample (NIS) is the largest publicly available all-payer longitudinal database of hospital inpatient discharges in the US containing anonymized discharge-level data from >7 million hospitalizations annually. It was developed by the Agency for Healthcare Research and Quality (AHRQ), under the Healthcare Cost and Utilization Project, and represents a 20% stratified sample of the US community hospitals, excluding rehabilitation and long-term acute care hospitals. It provides sampling weights to calculate national estimates representing more than 95% of the US hospitalized population[7].

Study population:

United Kingdom

We included patients admitted with a diagnosis of STEMI in any of the 230 participating hospitals in England and Wales between 1st January 2010 to 31st March 2017. The discharge diagnosis of STEMI was determined by local clinicians according to presenting history, clinical examination, and the results of inpatient investigations in keeping with the consensus document of the Joint European Society of Cardiology and American College of Cardiology[8]. Patients were excluded if they were <18 or >50 years old (**Figure 1a**). Individual patient's baseline risk was assessed using the Global Registry of Acute Coronary Events (GRACE) scoring systems. MINAP does not record GRACE explicitly, so a validated method was used to calculate patients' GRACE score[9]. Incidence of young STEMI rates per 100,000 population were calculated using Office of National Statistics (ONS) mid-year population estimates for each year. MINAP data was only available for three months of 2017 (January-March), so a crude estimation of incidence for 2017 for comparison purposes was made by multiplication. In the UK, the ethnic minorities group included those whose ethnicity in MINAP was recorded as Black (including Caribbean, African, Black British, any other Black background) and Asian (including Indian, Pakistani, Bangladeshi, Asian British, any other Asian Background—but excluding Chinese) and other Non-White ethnicity.

United States

All hospitalizations of young adults (18-50 years) with a principal discharge diagnosis of ST-elevation myocardial infarction (STEMI) between January 2010 and December 2018 were included (**Figure 1b**). All diagnoses were defined according to the presence of International Classification of Diseases, ninth and tenth revision (ICD-9 and ICD-10,

respectively), depending on the dataset period (**Supplementary Table 1**). The *National Inpatient Sample* database was based on the *International Classification of Diseases – 9th modification* (ICD-9) up to September 2015, and after that it was based on the *International Classification of Diseases – 10th modification* (ICD-10). Incidence of young STEMI rates per 100,000 population were calculated using the United States Census mid-year population estimates for each year. The sex and ethnicity of the patient was self-reported in both datasets. In the US, the 'other' ethnic group includes patients who identified themselves differently from the preceding categories. This ethnic category is the least prevalent in the cohort and could include the following ethnic groups: 'Romani Americans' or 'Aboriginal/Indigenous Australians', or other multi-ethnic groups (such as 'Métis', 'Creole', or 'Mulatto').

Outcomes

All outcomes were limited to in-hospital period and were evaluated as trends across the study period. Key patient characteristics such as sex, ethnicity, and comorbidities were analysed. Clinical outcomes included all-cause mortality, major bleeding, acute ischemic stroke, acute haemorrhagic stroke, and the composite of all-cause mortality, acute ischemic stroke and reinfarction (major adverse cardiovascular and cerebrovascular events [MACCE]). Management-related outcomes included invasive coronary angiography (ICA), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) surgery and thrombolysis.

Statistical Analysis:

United Kingdom:

Demographics, clinical characteristics and crude adverse outcomes of adult patients <50 were compared by year using the Pearson chi-squared test for categorical variables. Continuous

variables were compared using Student's t-test if normally distributed and using Wilcoxon Rank Sum test if not. Normality of distribution was assessed using Shapiro-Wilks test. Continuous variables are presented as medians and interquartile ranges (IQR) and categorical variables by proportions. Multivariable regression analysis was applied to dataset, for each binary outcome of interest, to estimate the risk of adverse outcomes between groups. Logistic regression models were fitted using maximum likelihood estimation and were adjusted for sex, ethnicity, heart rate, blood pressure, family history of coronary artery disease (CAD), previous coronary artery bypass graft (CABG) surgery, ischaemic ECG changes, history of HF, LVSD, prior percutaneous coronary intervention (PCI), co-morbid conditions (history of diabetes mellitus, hypercholesterolaemia, angina, previous myocardial infarction, cerebrovascular accident, peripheral vascular disease, hypertension, smoking, asthma/COPD), cardiac arrest, procedures and investigations including ICA, PCI and CABG surgery during admission.

United States

Multiple imputation method was performed to account for the missing cases. An automatic method that decides imputation methods based on the data scan was used, with a total of 10 iterations for each imputation. It was done for the overall STEMI cohort, in the following variables: age (n=76), weekend admission (n=10), mortality (n=1,036), sex (n=163), length of stay (n=44), primary expected payer (n=3,146), median household income (n=33,448), ethnicity (n=111,096), total charges (22,265), hospital bedsize (n=4,440), and hospital location/teaching status (n=4,440). Data were summarized using medians (interquartile range) for continuous non-parametric data and as counts (percentages) for categorical data. Quantitative data were analysed with Wilcoxon Rank Sum test, and

categorical data with Chi-squared test. Trend analysis with a Mantel-Haenszel extension of the chi-square test of trend (linear-by-linear association) was conducted to establish trends of outcomes over the study period. Multivariable regression analysis was applied to dataset, for each binary outcome of interest, to estimate the risk of adverse outcomes between groups. Logistic regression models were fitted using maximum likelihood estimation and were adjusted for sex, ethnicity, history of ischemic heart disease, previous coronary artery bypass graft (CABG) surgery, prior percutaneous coronary intervention (PCI), co-morbid conditions (history of diabetes mellitus, hypercholesterolaemia, previous myocardial infarction, cerebrovascular accident, hypertension, smoking, asthma/COPD), cardiac arrest, procedures and investigations including ICA, PCI and CABG surgery during admission. All analyses were conducted with appropriate sampling weights provided by the AHRQ, for each individual discharge. Statistical analyses were performed with Stata 14.2 (College Station, Texas, USA). All statistical analyses were two-tailed, and an alpha of 5% was used throughout.

Results:

Between January 2010 to March 2017, there were 223,858 patients admitted to hospital in England and Wales with a diagnosis of STEMI. Applying relevant exclusion criteria produced a study cohort of 32,719 adult patients <50 years old (15%). Of these, there were 14,176 admissions between 2010-2012, 13,703 admissions between 2013-2015 and 4,840 admissions between 2016-2017 (**Figure 1a**). The incidence rate per 100,000 of the population fell from 8.1 in 2010 to 5.9 in 2017 (**Supplementary Figure 1a**). Between January 2010 to December 2018, there were 1,681,507 patients admitted to hospital in the US with a diagnosis of STEMI. Applying relevant exclusion criterion produced a study cohort of

238,952 patients (14.2%) aged <50 years old. Of these, there were 87,877 admissions between 2010-2012, 79,770 admissions between 2013-2015 and 71,305 admissions between 2016-2018 (**Figure 1b**). The incidence rate per 100,000 of the population varied fell from 10.3 in 2010 to 8.6 in 2014 to 6.1 in 2018 (**Supplementary Figure 1b**).

Differences in clinical characteristics of adult patients <50 years in the UK at admission varying by year are shown in **Table 1**. Whilst there were no significant temporal variations in age, the proportion of female patients increased from 15.6% (2010-2012) to 17.6% (2016-2017). The proportion of patients who were ethnic minorities has also risen. Between 2010-2012, 14.2% of presentations were from ethnic minorities, increasing to 20.4% between 2016-2017. Whilst the frequency of diabetes has increased from 11.1% (2010-2012) to 14.6% (2016-2017), the frequency of current smoking has declined from 69.5% (2010-2012) to 63.4% (2016-2017).

Differences in clinical characteristics of adult patients <50 years in the US at admission varying by year are shown in **Table 1a**. Similar to UK data, there were no significant temporal variations in age. There was a year-on-year decrease in the proportion of Caucasian patients (2010-2012: 71.4%, 2016-2018: 69.3%) and a parallel rise in ethnic minorities. With respect to comorbidities, there was a year-on-year increase in the frequency of patients with prior AMI (2010-2012: 7.2%: 2016-2018: 9.8%), atrial fibrillation (2010-2012: 3.4%, 2016-2018: 3.7%), and diabetes mellitus (2010-2012: 23.4%, 2016-2018: 27.3%), through the study period.

Figures 2a and **2b** show the proportion of young patients across the study period who have been diagnosed with STEMI. In the UK, there was a clear decline from 15.6% in 2010-2012 to 13.0% in 2017. Data derived from the US shows a similar trend with a reduction in the frequency of admissions between 2010-2012 (1%) and 2016-2018 (15.1%).

Management strategies & unadjusted crude clinical outcomes of the UK data are presented in **Table 2**. There was an increase in the use of invasive therapies with increased use of ICA (2010-2012: 89.0%, 2016-2017: 94.3%, P<0.001) and PCI (2010-2012: 67.4%, 2016-2017: 83.5%, P<0.001). Both in-hospital mortality (2010-2012: 1.5%, 2016-2017: 2.7%, P<0.001), cardiac mortality (2010-2012: 1.4%, 2016-2017: 2.5%, P<0.001) and MACE (2010-2012: 2.6%, 2016-2017: 3.8%, P<0.001) all increased through the study period. **Figure 3a** shows the all-cause mortality and **Figure 4a** shows the invasive management strategy of young patients across the study period in the UK.

After adjustment for differences in baseline clinical and treatment characteristics on multivariate analysis, there was no difference in odds of all-cause mortality (OR:1.05, 95% CI: 0.61-1.77), cardiac mortality (OR:1.01, 95% CI: 0.57-1.75), major bleeding (OR: 0.74, 95% CI: 0.46-1.19) and MACE (OR:1.13, 95% CI:0.82-1.56) in 2013-2015 when compared to 2010-2012. Similarly, there was no difference in odds of all-cause mortality (OR:1.21, 95% CI: 0.60-2.4), cardiac mortality (OR:1.29, 95% CI: 0.60-2.6), major bleeding (OR:0.68, 95% CI: 0.34-1.35) and MACE (OR: 1.32, 95% CI: 0.87-2.03) in 2016-2017 when compared to 2016-2017 (**Table 3**).

Management strategies and unadjusted clinical outcomes from the US data are shown in **Table 2a**. Throughout the study period, the use of ICA showed a slight decline (2010-2012: 88.9%, 2016-2018: 86.2%, P<0.001). However, there was an increase in the use of PCI (2010-2012: 81.5%, 2016-2018: 85.1%, P<0.001) year-on-year. There was a corresponding decrease in the frequency of CABG surgery (2010-2012: 4.2%, 2016-2018: 3.4%, P<0.001) through the study period. There was a progressive increase in the in-hospital mortality (2010-2012: 2.9%, 2013-2015: 3.4%, 2016-2018: 3.1%, P<0.001) through the study period, but a decrease in MACCE (2010-2012: 7.6%, 2016-2018: 3.8%, P<0.001) owing to a decrease in ischemic stroke and reinfarction (P<0.001). **Figure 3b** shows the all-cause mortality and

Figure 4b shows the invasive management strategy of young patients across the study period in the US.

After multivariable adjustment, there was a fluctuation in all-cause mortality across the years with higher mortality (OR 1.10, 95% CI 1.03-1.17) in 2013-2015 when compared to 2010-2012, and lower mortality (OR 0.84, 95% CI 0.79-0.90) in 2013-2015 when compared to 2010-2012. However, when looking at major bleeding (OR 0.92, 95% CI 0.85-0.99 in 2013-2015, and OR 0.58, 95% CI 0.53-0.64 in 2016-2018) and MACCE (OR 0.93, 95% CI 0.89-0.97 in 2013-2015, and OR 0.41, 95% CI 0.38-0.43 in 2016-2018), there was a significant decline across the years when compared to 2010-2012 (**Table 3**).Figure 5 (central illustration figure shows our key findings)

Discussion:

We demonstrate several key trends in primary STEMI hospitalizations in young adults over a 7-year span in the UK and a 8-year span in the US. First, in both the UK and US there was a steady decline in the proportion of young patients presenting with STEMI. Second, in the UK, there was a marked increase in the proportion of female young patients presenting with STEMI over the study period. Third, in both UK and US data, there was an increase in presentations of ethnic minorities with STEMI. This was particularly profound in Black and Hispanic patients in the US and Asian patients in the UK. Fourth, temporal changes in the cardiometabolic risk factor profiles of young patients differed between the UK and US. In the UK, there was a decline in the frequency of smoking across the study period, whereas the opposite was found in the US. The proportion of patients with DM steadily increased in both countries through the respective study periods. Fifth, in unadjusted data, all-cause mortality in both countries appeared to increase over time, but this was not found when

adjusting for baseline characteristics and demographics. Finally, there was a marked year-on-year increase in the use of PCI across both countries, with a corresponding decrease in the use of CABG surgery in the US.

In recent years, despite the rates of AMI decreasing in the general population, this trend has not been seen in younger patients[1]. Yang et al utilized the Partners YOUNG-MI registry – a study that focuses on patients who experience an AMI at less than or equal to 50 years, and found an increase of 1.7% per year in the proportion of very young (<40y) individuals presenting with MI from 2007 to 2016[4]. Similarly, Arora et al, as part of the Atherosclerosis Risk in Communities (ARIC) Surveillance study found that the overall population of AMI admissions attributable to young patients steadily increased from 27% in (1995-1999) to 32% in (2010-2014), with the largest increase observed in young women[2]. Our study found that in both the UK and US there was a decline in the proportion of STEMI patients that were aged under 50 from 2010 to 2017.

The risk factor profile of patients is likely a key determinant as to why they present with STEMI at a young age. We report that both in the UK and US, the proportion of young patients with DM is steadily increasing with an absolute 6% increase in the UK population and a 4% increase in the US over the respective study periods. DM has been previously identified as a major risk factor for the development of coronary artery disease, with a higher incidence of AMI in patients with DM than those without it[10, 11]. This may also explain the increase in unadjusted mortality in both countries with DM patients having significantly higher rates of mortality when presenting with AMI[12]. The growing incidence of DM amongst young patients is likely due to changes in lifestyle and availability of certain diets (high sugars, saturated fats, low fibre), with obesity the leading risk factor in its development[13]. Yandrapalli et al found that the prevalence of obesity almost doubled between 2005 to 2015 in young adults with a first presentation of AMI[13]. The metabolic effects of

diabetes including increased coagulability, oxidative stress, endothelial dysfunction and autonomic neuropathy may explain why as the incidence of diabetes has risen in this young population, the in-hospital mortality outcomes have worsened[14]. The increased incidence of STEMI hospitalisation in females is likely multifactorial. Prior studies have shown that relative to young men, young women have a higher comorbidity burden, with increased risk of traditional modifiable risk factors. In the US, female patients are more likely to be insured compared to their male counterparts, which may influence health seeking behavior. Similarly, the increased incidence of STEMI in young ethnic minority patients is likely to be explained by their burden of modifiable risk factors; with Asian patients have the highest rate of DM and Black patients having the highest rates of hypertension

Interestingly, the frequency of smokers in the UK population significantly declined throughout the study period. Smoking has previously been identified as one of the most prevalent risk factors amongst young patients presenting with MI[13]. Palmer et al as part of their retrospective ecological study examined a total of 3,343 patients. Their study showed that the rates of MI in smokers were approximately 9 and 13-fold higher than in non-smokers in males and females respectively[15]. The UK health policy on smoking changed in 2017, recognizing that smoking was not a lifestyle choice but a dependence requiring treatment[16]. The National Health Service (NHS) long term plan has set out a commitment that by 2023 to 2024, all patients admitted to, an acute or mental health hospital will be offered funded tobacco dependency treatment. In addition, in the UK, smoking is illegal in indoor spaces, bars, and restaurants[16]. Whilst the US is adopting similar policies this is not unified in all states and thus may explain why the frequency of smoking has not declined in young patients in the US.

In both countries there is an increased mortality in absolute percentages over the study period (except 2016-2018 in the US). In adjusted data, the mortality was equivocal amongst

different year groups in both countries with the exception that in the US the mortality in 2013-2015 was significantly higher than in 2010 to 2012. These findings were not replicated when comparing the data from 2016-2018 in comparison to 2010-2012. Given improvements in invasive strategy, medications and processes of care for STEMI hospitalisations in both countries, these findings are unusual. Whilst there are well known risk factors that predispose patients of all ages to CAD, it is important to note that there is an inherent risk of "no-risk", with respect to cardiovascular modifiable risk factors. Population-based data such as the INTERHEART study concluded that nine conventional risk factors explained >90% of premature AMI[17-19]. Emerging evidence has shown that patients with no standard cardiovascular modifiable risk factors (coined SMuRF-less) have in fact significantly worse in-hospital mortality outcomes compared to those with > 1 SMuRF[20, 21]. This condition is of particular importance in this young demographic of patients with STEMI as there are likely genetic variations, and differences in presentation that may explain their earlier presentation and there are likely biomarkers and other pathophysiological differences which have not yet been fully explored, which may account for why they present at a younger age and why there are increased mortality rates. SMuRF-less patients presenting with STEMI have been shown to increasingly present as a cardiac arrest numbers, which may explain the increasing cardiac arrest proportions in this young demographic. It is important to note however, that adjusting for demographics and management strategies mitigated this increased risk of mortality, particularly in the UK. Furthermore, there are likely biological differences between the different sexes and ethnicities which may account for the changing demographic of young patients presenting with STEMI. Our study showed that in both the UK and US there were increases in the proportion of patients who were female and ethnic minorities. Ethnic minority patients have previously been shown to have worse cardiometabolic risk factor profiles with an increasing frequency of DM, hypercholesterolemia, and hypertension[22].

Given the increased incidence of these patients presenting with a STEMI at a young age, there may be an opportunity to target these patients more aggressively with respect to primary prevention therapies.

Reassuringly, our study showed that in both the UK and US there was an increase in the frequency of patients who underwent PCI through the study period. This is important as an invasive strategy for STEMI "is a class 1 indicated" recommendation from both European[23] and American[24] guidelines. Whilst we do not have the American data on pharmacotherapy, the UK data showed an increase in the use of guideline directed therapies with an increase over the study period in the use of statins, ACE inhibitors/ARB's and beta blockers. This is important as the use of statins, for example, has been shown to have an early and sustained survival benefit on patients with AMI and is a key secondary prevention strategy for patients with STEMI[25, 26]. Data from the *PROVE-IT-Trial*, have shown that an intensive lipid lowering statin regimen for patients with AMI has a prognostic benefit in reducing mortality, even in patients without elevated cholesterol levels[27].

Strengths and limitations

There are several strengths to this study. Our analysis represents the largest study from two nations of differing healthcare systems that analyses the trends in young patients over a significant time period. The MINAP database encapsulates an almost complete record of STEMI patients admitted in the UK and represents one of the largest national "real-world" databases of this cohort of patients in the world. Similarly, the NIS database gives insight into the "real world" in-hospital clinical outcomes on a large and unselected cohort of patients with STEMI, including those that are high risk and have multiple comorbid illness, such that they are either not included or under-represented in clinical trials. We have looked at two large western affluent countries with similar practices of care, but differing healthcare

systems, in order to ascertain differences between the two countries. Due to the size of the databases, there is sufficient power to detect differences in adverse clinical outcomes between the two cohorts of interest.

Despite these strengths, there are a number of important limitations common to observational studies of this type. MINAP shares the weakness of other national data sets, including self-reporting of adverse events where there is no external validation of these. There are also limitations to the data collected by each registry. For instance, neither database captures the severity of coronary artery disease, socioeconomic or psychosocial risk factors, access to use of health care, the rationale for specific medications or an exhaustive list of comorbid conditions. Neither database captures the frequency of patients with myocardial infarction with non-obstructive coronary arteries (MINOCA). This is particularly important, as there is an important group of young patients, particularly young females who present with this. Furthermore, the databases do not capture markers of inflammation, biomarkers or less common risk factors such as malignancy, lipoprotein(a) or clonal haematopoiesis of indeterminate potential. In addition, neither database captures substance use, particularly the use of cocaine and marijuana, with prior studies showing up to 10% of patients with young AMI previously using these substances[4]. Both databases only record in-hospital clinical outcomes and it is likely that long term follow-up data may reveal further differences over the study period, particularly with respect to mortality rates, given the evolving pharmacotherapy. In addition, whilst the overall diagnosis of STEMI is relatively homogenous in nature, it is important to note that the UK defaults to National Institute for Health and Care excellence (NICE) guidelines; whereas the US uses American College of Cardiology (ACC) guidelines. The subtle differences between guidelines may have contributed to a small difference between incidence rates. We acknowledge that the differences between the two datasets are a limitation to making meaningful comparisons, as

there are differences in the source of data (from insurance claims in NIS) and there are marked differences in population demographics between the UK and US. Furthermore, whilst there is overlap, the study period between the two countries differs, which may affect interpretation. Data for the entire national population was used as a surrogate for calculating incidence rates per 100,000 population, as accurate mid-year estimates for 18-50 years old were not available. A further limitation of our study was that gender identity was not captured in either data set. Also, due to inherent limitations of the database, it is not possible to surely detect exact timing of events. It is important to note that over time, the overall population of ethnic minorities may have changed in both countries. In the UK for example, 14% of patient identified as ethnic minorities in 2011; whereas this was 18.3% in 2021. Factors including migration are likely to account for this and may reduce the generalizability of the results. Finally, there is no fixed consensus as to what constitutes a 'young patient' with STEMI. Whilst the majority of studies use a cut of <50 years old, there is variability in studies which can make some degree of difficulty in exact like-for-like comparisons.

Conclusion

In conclusion, our study found that over a 7-year span in the UK and 8-year span in the US, whilst the frequency of STEMI in young patients has diminished, the demographic has significantly changed with an increase in the proportion of female patients and ethnic minorities. There was an overall decrease in the proportion of smokers in the UK and a reduction in the frequency of hypercholesterolemia, which was not mirrored in the US. The incidence of diabetes has increased in both countries as has the overall unadjusted mortality rate for this young demographic. Further work is required with respect to primary and secondary prevention to reduce the proportion of STEMI in the young.

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Table 1. Baseline patient characteristics in the young STEMI cohort (≤50 years) according to time period (MINAP, UK).

Characteristics	2010-2012 (43.3%)	2013-2015 (41.9%)	2016-2017 (n=14.8%)	*P*-value
Number of hospitalizations	14,176	13,703	4,840	
Age (years), median (IQR)	45.7 (48-42)	46 (48-42)	46 (48-42)	0.05
Women, %	15.6	16.4	17.6	0.005
Caucasians, %	85.8	82.6	79.6	<0.001
Ethnic Minorities, %	14.2	17.4	20.4	<0.001
Basal crepitations, %	4.3	4.7	4.3	<0.001
Pulmonary oedema, %	1.5	1.7	1.6	0.06
Cardiogenic shock, %	1.9	2.7	2.6	<0.001
Grace risk score groups. %				<0.001
High risk GRACE score >140	30.4	32.9	47.7	
Intermediate risk GRACE score 109-140	47.2	47.4	47.2	
Low risk GRACE score <109	22.4	19.7	5.1	
Previous smoker, %	13.3	14.6	12.8	<0.001
Current smoker, %	69.5	66.7	63.4	<0.001
Chronic renal failure, %	0.9	1.1	1.0	0.31
Prior percutaneous coronary intervention, %	6.5	6.9	7.6	0.02
Diabetes, %	11.1	12.8	14.6	<0.001
Hypercholesterolemia, %	25.4	23.8	24.0	0.02
Previous MI, %	8.4	8.9	9.1	0.30
Angina, %	6.7	6.4	5.2	0.003
Cerebrovascular disease, %	1.5	1.4	1.8	0.32
Peripheral vascular disease, %	1.1	1.1	1.1	0.34
Hypertension, %	25.3	25.5	26.0	0.38
Asthma / COPD, %	6.5	7.0	7.7	0.55
Family history of CAD, %	49.6	44.1	42.0	<0.001
Heart rate, bpm, median (IQR)	78 (90-67)	79 (91-68)	80 (91-68)	0.20
Systolic blood pressure, median (IQR)	130 (148-116)	130 (146-114)	130 (148-115)	0.001
Moderate LVSD, %	25.0	32.8	36.6	<0.001
Severe LVSD, %	4.9	6.8	7.3	<0.001

Cardiac arrest, %	10.1	11.7	13.7	<0.001
Previous CABG surgery, %	0.7	0.6	0.8	0.85

Abbreviations: CABG – coronary artery bypass grafting surgery; PCI – percutaneous coronary intervention; MI – myocardial infarction; BMI – body mass index; GRACE – global registry of acute coronary events; ECG – electrocardiogram; CCF – congestive cardiac failure; COPD – chronic obstructive pulmonary disease; CAD – coronary artery disease; IQR – interquartile range; LVSD – left ventricular systolic dysfunction; EF – ejection fraction; UK – United Kingdom

Table 1a. Baseline patient characteristics in the young STEMI cohort (≤50 years) according to time period (NIS, US).

Characteristics	2010-2012 (19.2%)	2013-2015 (17.4%)	2016-2018 (15.5%)	*P*-value
Number of hospitalizations	87,877	79,770	71,305	
Age (years), median (IQR)	45 (48-41)	45 (48-41)	45 (48-41)	0.007
Female sex, %	22.8	22.3	23.1	0.001
Ethnicity, %				<0.001
White	71.4	70.5	69.3	
Black	11.2	12.2	13.3	
Hispanic	9.3	9.0	9.6	
Asian or Pacific Islander	2.8	3.1	3.0	
Native American	0.8	0.7	0.6	
Other	4.5	4.5	4.1	
Weekend admission, %	29.9	29.4	29.5	0.067
Primary expected payer, %				<0.001
Medicare	7.6	7.0	6.9	
Medicaid	15.3	20.0	22.3	
Private Insurance	50.1	50.2	51.0	
Self-pay	20.2	16.7	14.7	
No charge	1.7	1.9	1.2	
Other	5.0	4.1	3.9	
Homelessness, %	0.2	0.2	0.3	0.001
Median Household Income (percentile), %				<0.001
0-25th	29.5	30.9	31.6	
26th-50th	26.4	27.4	27.5	
51st-75th	24.8	23.9	23.5	
76th-100th	19.3	17.7	17.4	
Cardiogenic shock, %	5.0	6.6	5.5	<0.001
Cardiac arrest, %	5.0	6.6	5.5	<0.001
Comorbidities, %				

Atrial fibrillation	3.4	3.4	3.7	0.008
Dyslipidaemia	59.4	59.1	58.4	<0.001
Thrombocytopenia	2.0	2.2	2.1	0.006
Neutropenia	0.1	0.1	<0.1	<0.001
Smoking	61.7	58.8	58.0	<0.001
Previous AMI	7.2	8.1	9.8	<0.001
History of IHD	84.4	85.2	78.5	<0.001
Previous PCI	12.2	11.5	10.3	<0.001
Previous CABG	1.3	1.3	1.3	0.472
Previous CVI	1.5	1.8	2.3	<0.001
Anaemias	6.4	6.0	7.1	<0.001
Heart failure	11.4	13.7	16.0	<0.001
Valvular disease	0.2	0.5	2.9	<0.001
Arterial hypertension	51.7	55.3	48.8	<0.001
Peripheral vascular disorders	3.1	3.0	2.0	<0.001
Diabetes mellitus	23.4	25.8	27.3	<0.001
Hypothyroidism	3.2	3.4	3.7	<0.001
Chronic pulmonary disease	9.4	9.4	8.8	<0.001
Coagulopathy	2.8	3.1	3.8	<0.001
Dementia	0.1	<0.1	0.1	<0.001
Liver disease	1.2	1.3	1.7	<0.001
Chronic renal failure	3.4	3.9	4.6	<0.001
AIDS	0.3	0.3	0.4	0.003
Alcohol abuse	5.3	5.6	5.0	<0.001
Drug abuse	7.0	8.4	6.9	<0.001
Fluid and electrolyte disorders	13.8	16.4	17.7	<0.001
Obesity	17.0	21.1	24.0	<0.001
Metastatic cancer	0.2	0.2	0.2	0.019
Bed size of hospital, %				<0.001
Small	7.6	11.2	14.5	
Medium	21.6	27.9	29.1	
Large	70.8	60.9	56.5	

Hospital Region, %				<0.001
Northeast	17.6	16.9	18.2	
Midwest	24.8	24.3	25.9	
South	39.1	41.9	42.5	
West	18.5	16.9	13.4	
Location/teaching status of hospital, %				<0.001
Rural	6.7	5.3	6.2	
Urban non-teaching	41.6	31.8	23.9	
Urban teaching	51.7	62.8	69.9	

Abbreviations: AIDS – Acquired Immuno-deficiency Syndrome; AMI – Acute Myocardial Infarction; CABG – Coronary Artery Bypass Graft; CVI – Cerebrovascular Indicent; IHD – Ischemic Heart Disease; IQR – Interquartile Range; PCI – Percutaneous Coronary Intervention; RA – rheumatoid arthritis; STEMI – ST-elevation Myocardial Infarction; US - United States.

Table 2. Management strategies and crude clinical outcomes in the young STEMI cohort (≤50 years) according to time period (MINAP, UK).

Variables	2010-2012 (43.3%)	2013-2015 (41.9%)	2016-2017 (n=14.8%)	*P*-value
Coronary angiogram, %	89.0	92.3	94.3	<0.001
Percutaneous coronary intervention, %	67.4	80.1	83.5	<0.001
CABG surgery, %	1.3	1.2	1.4	0.68
Death, %	1.5	1.9	2.7	<0.001
Cardiac mortality, %	1.4	1.8	2.5	<0.001
Major bleeding, %	0.8	1.0	0.8	0.47
MACE*, %	2.6	2.8	3.8	<0.001

Abbreviations: CABG – coronary artery bypass grafting surgery; MACE – major adverse cardiovascular events (composite of in-hospital mortality and reinfarction), UK - United Kingdom

Table 2a. Procedural and clinical outcomes in the young STEMI cohort (≤50 years) according to time period (NIS, US).

Characteristics	2010-2012 (19.2%)	2013-2015 (17.4%)	2016-2018 (15.5%)	*P*-value
Procedural outcomes:				
Coronary angiography	88.9	89.6	86.2	<0.001
PCI	81.5	83.8	85.1	<0.001
CABG	4.2	3.7	3.4	<0.001
Systemic thrombolysis	5.3	4.4	2.9	<0.001
IABP, ECMO or assist devices	7.5	7.2	7.0	0.002
Pericardiocentesis	<0.1	0.1	<0.1	<0.001
Clinical outcomes:				
All-cause mortality	2.9	3.4	3.1	<0.001
MACCE	7.6	7.1	3.8	<0.001
Major bleeding	1.5	1.4	1.1	<0.001
Procedure-related bleeding	0.6	0.5	0.3	<0.001
Ischemic Stroke	1.1	1.3	0.7	<0.001
Haemorrhagic stroke	0.2	0.3	0.2	0.099
Subsequent infarction (reinfarction)	4.0	2.8	0.2	<0.001
Length of stay (days), median (IQR)	3 (4-2)	3 (4-2)	2 (3-2)	<0.001
Total charges (USD), median (IQR)	58,993 (89,247-40,487)	69,105 (103,123-48,193)	75,853 (114,755-52,346)	<0.001

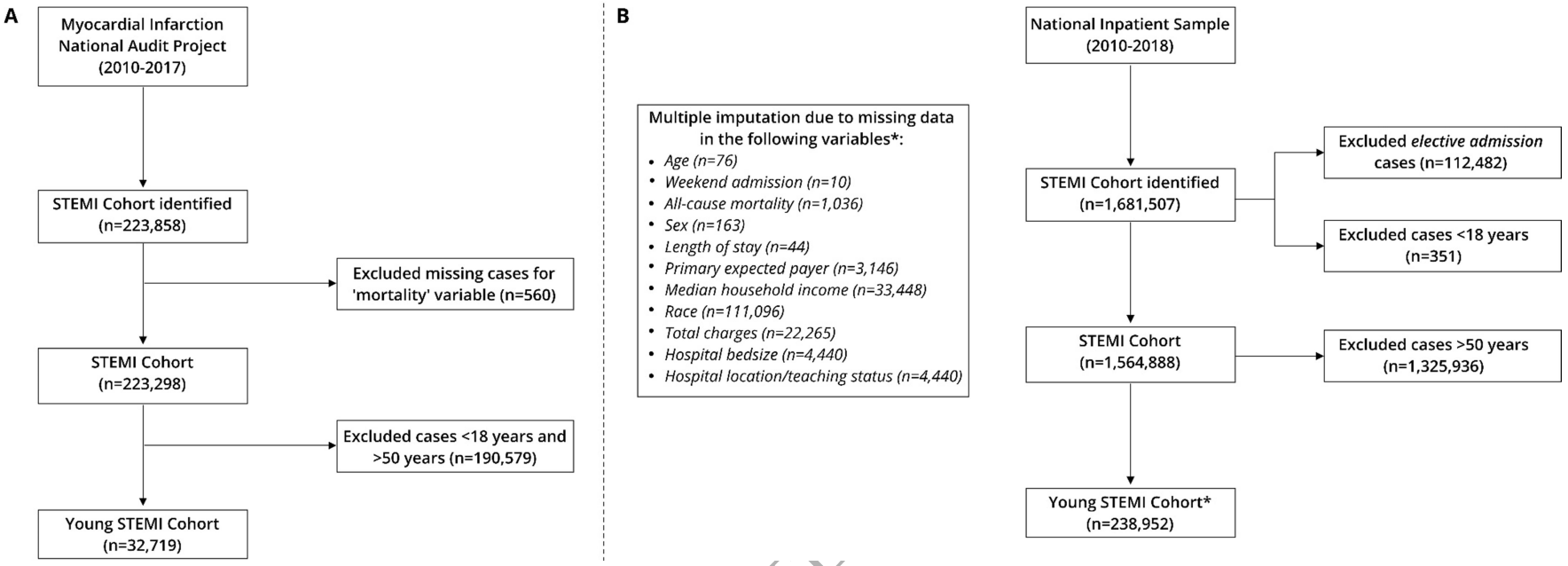
Abbreviations: CABG – Coronary Artery Bypass Graft; ECMO – extracorporeal membrane oxygenation; IABP – intraaortic balloon pump; IQR – interquartile range; MACCE – major adverse cardiovascular and cerebrovascular outcomes (composite of in-hospital mortality, ischemic stroke and reinfarction); PCI – Percutaneous Coronary Intervention; RA – rheumatoid arthritis; STEMI – ST-elevation Myocardial Infarction; USD – United States Dollar, US – United States.

Table 3. Adjusted analysis of management strategies and clinical outcomes in the young STEMI cohort (≤50 years) according to time period.

Variables		2013-2015	2016-2017 (2016-2018 in US)
		aOR (95% CI)	
Death	**MINAP (UK)**	1.04 (0.61-1.77), p=0.890	1.21 (0.6-2.4), p=0.570
	NIS (US)	1.10 (1.03-1.17), p=0.003	0.84 (0.79-0.90), p<0.001
Cardiac mortality	**MINAP (UK)**	1.01 (0.57-1.75), p=0.990	1.29 (0.60-2.60), p=0.480
	NIS (US)	n/a	n/a
Major bleeding	**MINAP (UK)**	0.74 (0.46-1.19), p=0.220	0.68 (0.34-1.35), p=0.270
	NIS (US)	0.92 (0.85-0.99), p=0.042	0.58 (0.53-0.64), p<0.001
MACE/MACCE*	**MINAP (UK)**	1.13 (0.82-1.56), p=0.450	1.32 (0.87-2.03), p=0.190
	NIS (US)	0.93 (0.89-0.97), p=0.001	0.41 (0.38-0.43), p<0.001

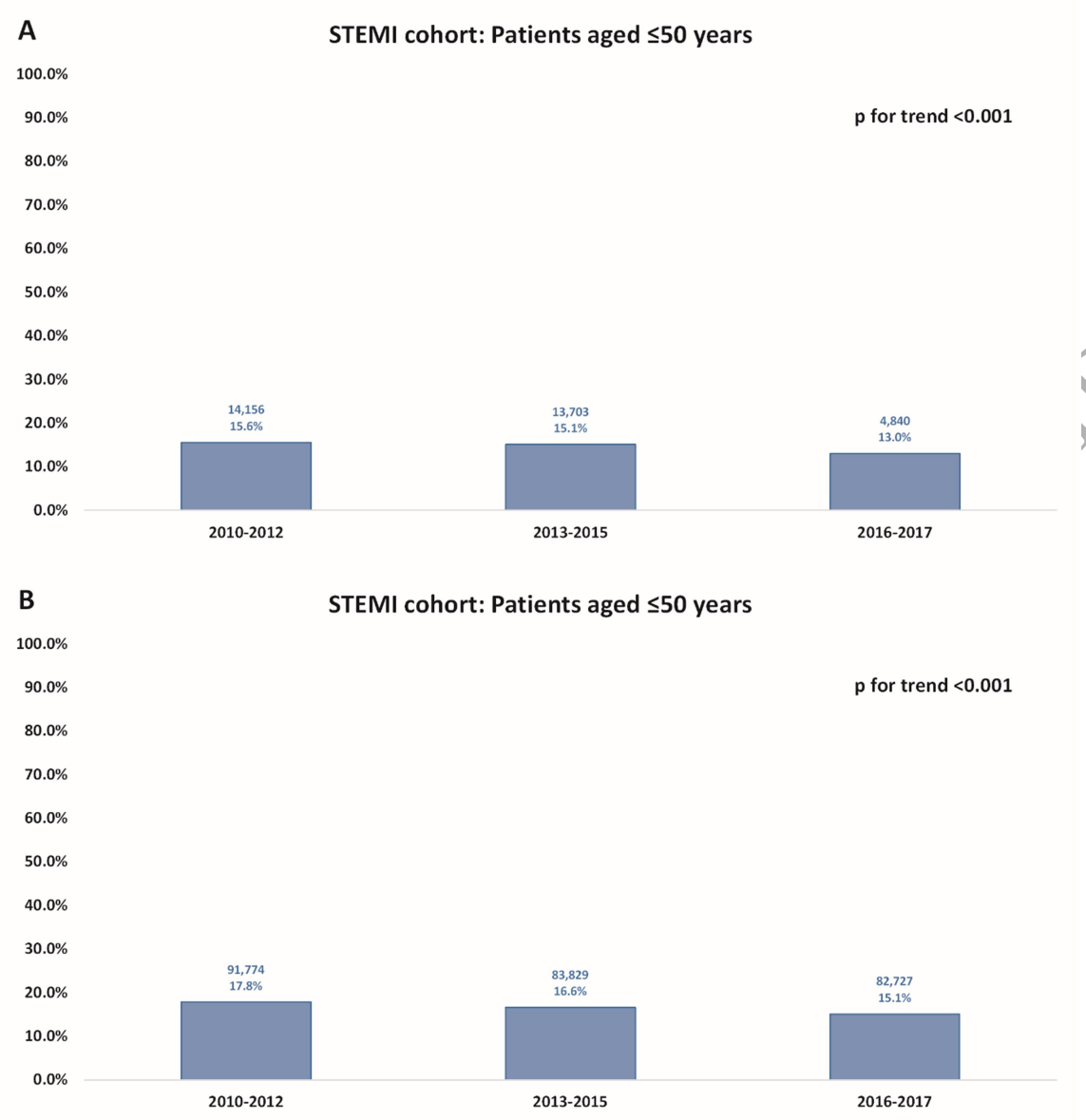
Abbreviations: MACE (for MINAP, UK) – major adverse cardiovascular events (composite of in-hospital mortality and reinfarction); MACCE (for NIS, US) – major adverse cardiovascular and cerebrovascular outcomes (composite of in-hospital mortality, ischemic stroke and reinfarction).

Figure 1. Flow diagram of the cohort selection process: **A.** MINAP database (UK); **B.** NIS database (US).



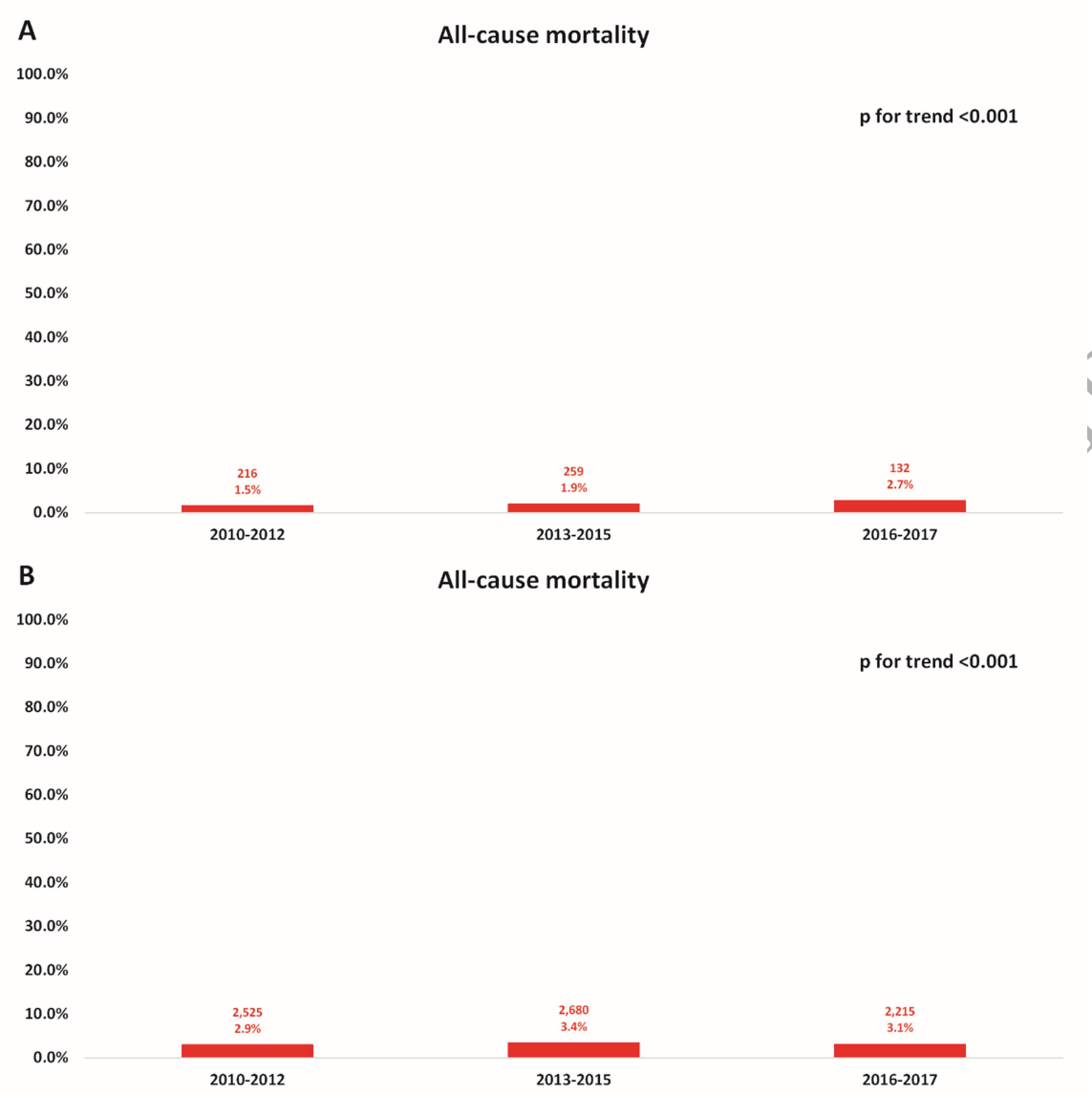
Abbreviations: MINAP – Myocardial Infarction National Audit Project (UK); NIS – National Inpatient Sample (US); STEMI – ST-segment elevation myocardial infarction; PCI – percutaneous coronary intervention, UK – United Kingdom, US – United States.

Figure 2. Proportion of young patients (≤50 years) in the STEMI cohort across the study years: **A.** MINAP database (UK); **B.** NIS database (US).



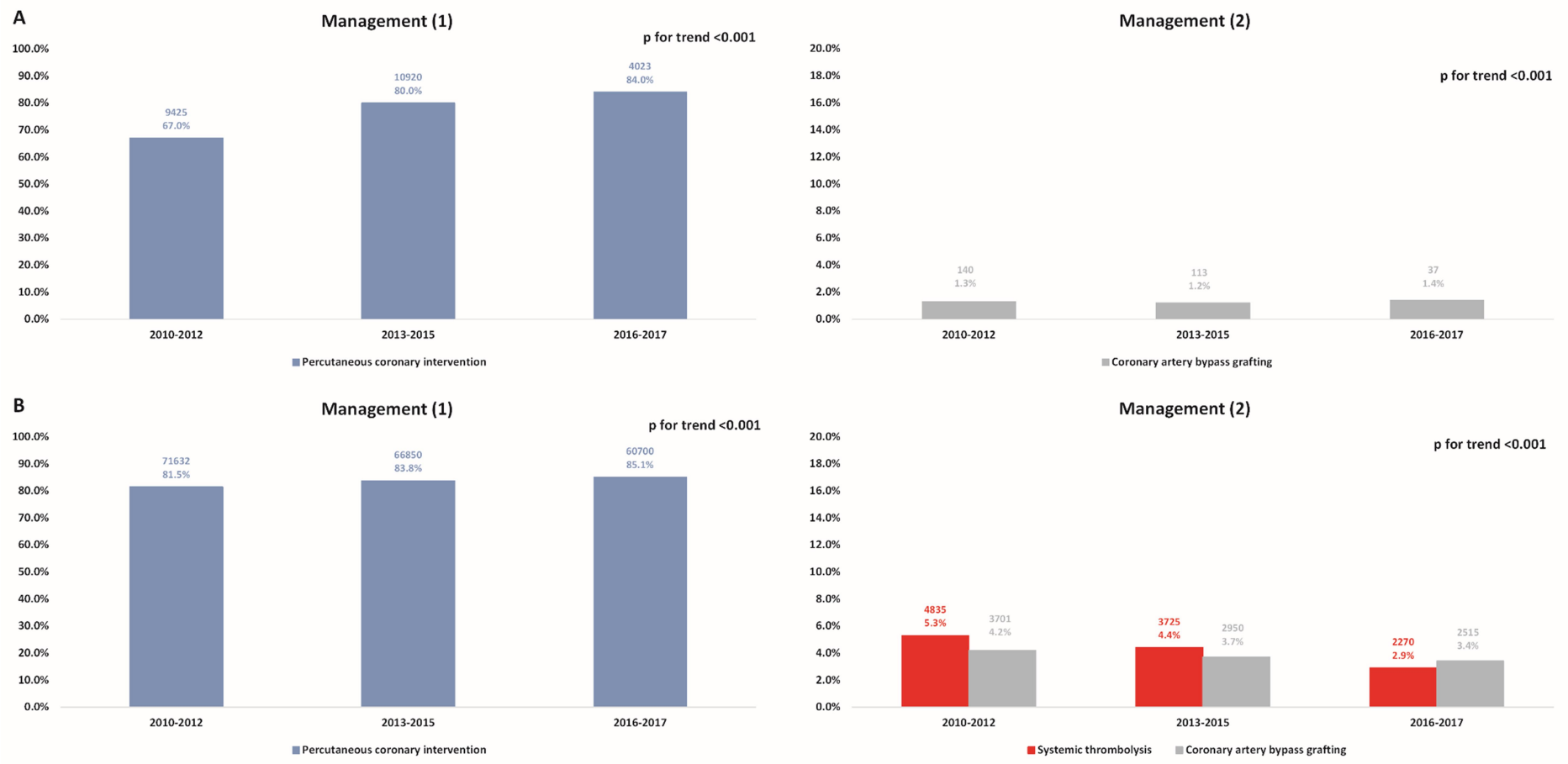
Abbreviations: MINAP – Myocardial Infarction National Audit Project (UK); NIS – National Inpatient Sample (US); STEMI – ST-segment elevation myocardial infarction.

Figure 3. All-cause mortality of young patients (≤50 years) with STEMI across the study years: **A.** MINAP database (UK); **B.** NIS database (US).



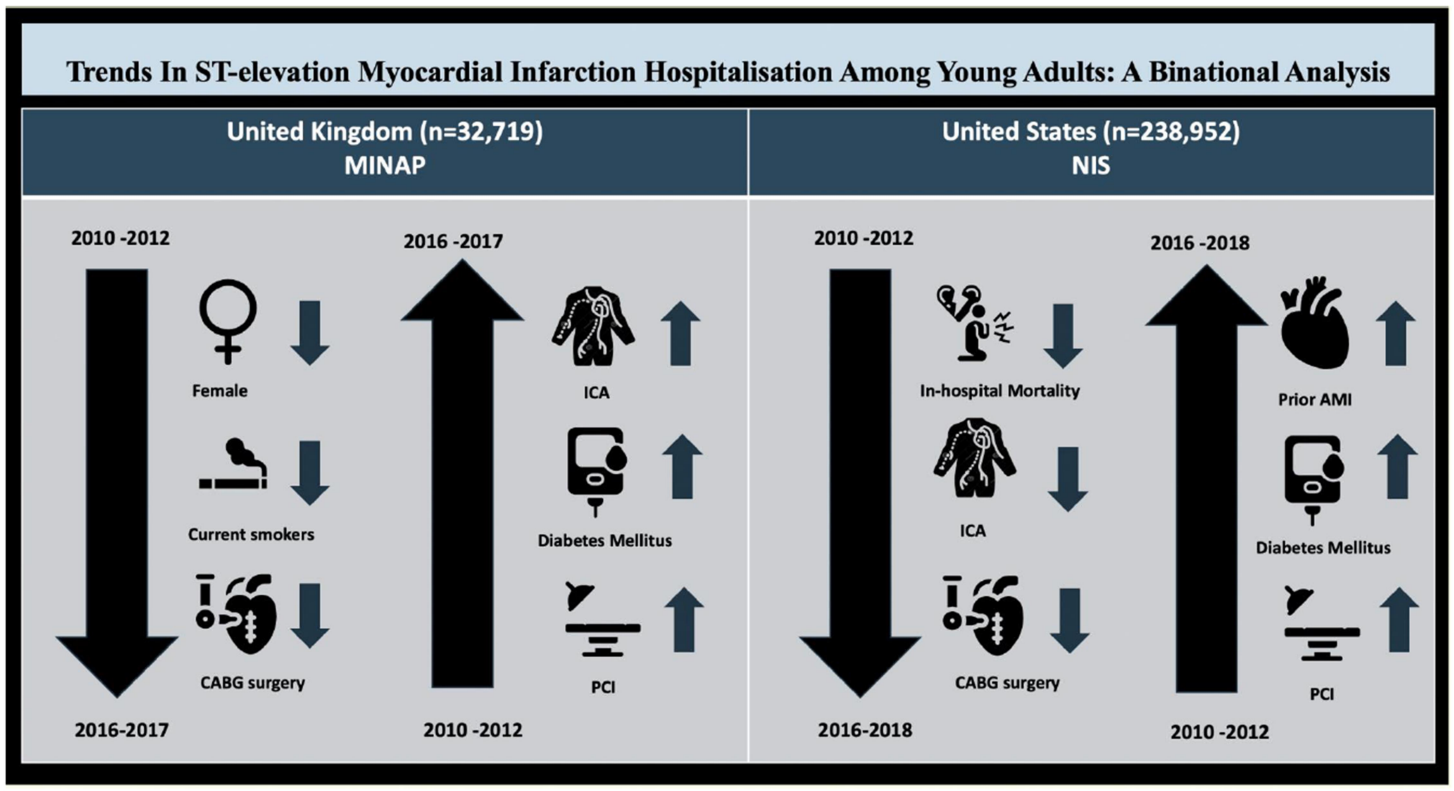
Abbreviations: MINAP – Myocardial Infarction National Audit Project (UK); NIS – National Inpatient Sample (US); STEMI – ST-segment elevation myocardial infarction.

Figure 4. Management among young patients (≤50 years) with STEMI across the study years: **A.** MINAP database (UK); **B.** NIS database (US).



Abbreviations: MINAP – Myocardial Infarction National Audit Project (UK); NIS – National Inpatient Sample (US); STEMI – ST-segment elevation myocardial infarction.

Figure 5. Central Illustration Figure



Abbreviations: MINAP – Myocardial Infarction National Audit Project (UK); NIS – National Inpatient Sample (US); STEMI – ST-segment elevation myocardial infarction, ICA; invasive coronary angiogram, PCI; percutaneous coronary intervention, AMI; acute myocardial infraction, CABG; coronary artery bypass grafting.