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ORIGINAL ARTICLE

Pronounced increase in risk of acute ST-segment elevation myocardial infarction in younger smokers

Amelia Lloyd,[1] Lloyd Steele,[1] James Fotheringham,[2] Javaid Iqbal,[1,3] Ayyaz Sultan,[3] M Dawn Teare,[2] Ever D Grech[3]

[1]The University of Sheffield, Sheffield, UK
[2]The School of Health and Related Research (ScHARR), The University of Sheffield, Sheffield, UK
[3]The South Yorkshire Cardiothoracic Centre, Northern General Hospital, Sheffield, UK

Correspondence to
Dr Ever D Grech, The South Yorkshire Cardiothoracic Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK; Ever.Grech@sth.nhs.uk

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ABSTRACT

Objectives Previous studies have shown that smokers presented with ST-segment elevation myocardial infarction (STEMI) a decade earlier than non-smokers. However, no account has been made for population smoking trends, an important deficit addressed by this study.

Methods The combination of admission data on patients with acute STEMI undergoing percutaneous coronary intervention and demographic data supplied by the Office for National Statistics for the South Yorkshire population between 2009–2012 were analysed to generate incidence rates and rate ratios (RR) to quantify the relative risk of STEMI from smoking, overall and by age group.

Results There were 1795 STEMI patients included of which 72.9% were male. 68 patients were excluded as they had no smoking status recorded, leaving 48.5% of the remaining population as current smokers, 27.2% ex-smokers and 24.3% never smokers. Smokers were over-represented with overall smoking prevalence in South Yorkshire calculated at 22.4%. The incidence of STEMI in smokers aged under 50, 50–65 and over 65 years was 59.7, 316.9 and 331.0 per 100 000 patient years at risk compared to 7.0, 60.9 and 106.8 for the combined group of ex- and never smokers. This gave smokers under the age of 50 years an 8.47 (95% CI 6.80 to 10.54) increase in rate compared to non-smokers of the same age, with the 50–65 and over 65 age groups having RRs of 5.20 (95% CI 4.76 to 5.69) and 3.10 (95% CI 2.67 to 3.60), respectively.

Conclusions Smoking was associated with an eightfold increased risk of acute STEMI in younger smokers, when compared to ex- and never smokers. Further efforts to reduce smoking in the youngest are needed.

INTRODUCTION

Cigarette smoking was first identified as a risk factor for cardiovascular disease with the Framingham Heart Study of the 1950s.[1 2] This landmark project was one of the first, alongside Doll and Hill,[3 4] to publicise the ill-effects of smoking. Large epidemiological studies have since demonstrated the link between tobacco smoking and acute myocardial infarction (AMI) and have established that smokers present at an earlier age than non-smokers. In particular, the National Registry of Myocardial Infarction 2 (NRMI2) found that smokers presenting with AMI were on average 14 years younger than non-smokers,[5] and the multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) trials showed that the prevalence of smokers was up to 81% in young patients aged 35–39 years with AMI.[6]

However, there remains uncertainty as to the magnitude of the effect of tobacco smoking on the younger smoker. No study has compared the incidence of ST-segment elevation myocardial infarction (STEMI) within young smokers and young non-smokers by using local population data as a denominator. This is likely due to a lack of comparative analysis of local population data with the population suffering a STEMI. This study was carried out to provide a clear incidence analysis and to quantify the risk of acute STEMI in the South Yorkshire region of the UK.

METHODS

Participants

To calculate the incidence analysis of STEMI in South Yorkshire, this study analysed two populations. The first was the case data of all South Yorkshire patients over the age of 18 years who had undergone percutaneous coronary intervention (PCI) for acute STEMI at the South Yorkshire Cardiothoracic Centre, Sheffield, UK. A continuous population of patients aged ≥18 years were studied between 1 January 2009 and 6 April 2012. The second dataset was derived from responses from South Yorkshire residents ≥aged 18 years participating in the Office for National Statistics Integrated Household Survey (ONS-IHS) between April 2009 and March 2012.[7]

Procedures

Each patient included in the STEMI cohort had full demographic, risk factor and procedural information collected from the individual hospital case records and the hospital database. Smoking status was recorded as 'current smoker', 'ex-smoker' or 'never smoker'. An ex-smoker did not have a minimum duration of cessation needed to fit into this category, although when data were available, duration of cessation was recorded. This was due to difficulties in obtaining the smoking cessation duration, as this was not routinely recorded in admission documentation. In a small number of cases there was insufficient record keeping of the smoking status, and these were excluded from the rate ratio (RR) incidence analysis.

Previous medical history of ischaemic heart disease (IHD), hypertension, diabetes, dyslipidaemia, transient ischaemic attack/stroke, peripheral vascular disease, and family history of IHD were recorded.

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The ONS-IHS uses a multi-stage population weighting procedure which accounts for the probability of selection and adjusts for non-response, enabling responses from South Yorkshire ONS-IHS to be weighted to represent the entire South Yorkshire population.[7] As this weighting is specific to the period when the ONS-IHS data are collected it also accounts for people entering or leaving the population. Therefore, these data were presented as patient year at risk to reflect most accurately the open and changing population.

Statistical methods

Univariate categorical analysis of risk factors across smoking status within the STEMI cohort was performed using the χ^2 test, with multivariate adjustment for age using logistic regression.

The incidence rate of STEMI in South Yorkshire was calculated using the STEMI and ONS-IHS populations using the following equation. 'Person-time at risk' is measured in patient-years, and represents the true time that each patient spent in this at-risk population. For example, a person who moved into the geographical area served by the South Yorkshire Cardiothoracic Centre part way through the study would have less person-time at risk, compared to a person who always lived in the catchment area.

$$\text{Incidence rate} = \frac{\text{Number of acute STEMI cases with disease in time period}}{\text{Total person} - \text{time at risk during that time period}}$$

Rate ratios were used to compare incidence rates of STEMI between different groups (eg, smokers and non-smokers).

$$\text{Rate ratio} = \frac{\text{Incidence rate in smokers}}{\text{Incidence rate for ex} - \text{smokers and never smokers}}$$

Analyses were performed with Stata V.12.1 (STATA Corp, Texas) and SPSS software 23 (IBM).

RESULTS

A total of 1795 patients were included in the STEMI data. In 68 (3.8%) patients, the smoking status was unobtainable and was excluded from incidence analysis. The mean age of the patients was 63.0 years (95% CI 62.38 to 63.56) and 72.9% of the population was male.

Just under half of the population with known smoking status were current smokers (48.5%). At presentation, the mean age of the current smokers was 57.4 years (95% CI 56.63 to 58.13) which was around 10–11 years less than ex- and never smokers (ex-smokers: 68.5 years, 95% CI 67.48 to 69.61; and never smokers: 66.7 years, 95% CI 65.50 to 67.84).

ONS-IHS data allowed calculation of smoking prevalence rates for the South Yorkshire area, as shown by age group in figure 1. With this population, the overall smoking prevalence was 22.4% and the highest prevalence of current smoking was found in those under the age of 50 (27.3%). However, this was much higher in those under the age of 50 who had suffered an acute STEMI (74.8%).

Risk factor profiles of current, ex- and never smokers

Logistic regression analysis allowed further study of the likelihood of risk factors being present in those who were current or ex-smokers compared to those patients who had never been exposed to cigarette smoking (table 1). Current smokers presenting with STEMI requiring PCI were less likely to have hypertension or diabetes, but more likely to have a family history of IHD ($p<0.05$ for all three). However, after adjusting for age, the differences in the odds of these risk factors were not statistically significant. Ex-smokers and current smokers were more likely than never smokers to have a previous history of IHD, including after adjustment for age (OR 2.37, 95% CI 1.69 to 3.31, $p<0.001$; and OR 1.45, 95% CI 1.03 to 2.05, $p<0.05$, respectively). Lastly, current smokers were three times more likely than never smokers to suffer with peripheral vascular disease (OR 3.44, 95% CI 1.56 to 7.59, $p<0.005$).

Incidence of acute STEMI in South Yorkshire

Ex-smokers and never smokers had similar incidence rates of acute STEMI, whereas this was much higher in the current smokers (figure 2). This peaked in the 60–69 year age group with an incidence rate of over 350 cases per 100 000 patient years at risk. By comparison, the peak age for incidence of STEMI in ex- and never smokers was 10 years later, in the 70–79 year age group, with over 100 cases per 100 000 patient years at risk. The incidence of STEMI in smokers aged under 50, 50–65 and over 65 years was 59.7, 316.9 and 331.0 per 100 000 patient years at risk compared to 7.0, 60.9 and 106.8 for the combined group of ex- and never smokers.

Incidence RR analysis

RR analysis to compare incidence rates between current smokers and their age-matched ex- and never smoking counterparts was performed (figure 3). Although not statistically significant for risk factors other than a previous history of IHD, ex-smokers tended towards higher odds for each risk factor than never smokers. Combining these two groups therefore provides a more conservative estimate of the comparison with current smokers than comparing to never smokers alone. This analysis showed that for all ages, current smokers were 3.26 (95% CI 2.98 to 3.57) more likely to suffer acute STEMI than ex- and never smokers grouped together. Stratification by age group showed the highest RR in the youngest age group analysed. Current smokers under 50 years of age were 8.47 (95% CI 6.80 to 10.54) times more likely to suffer an acute STEMI compared to their age-matched ex- and never smokers. The incidence RR subsequently decreased in the older age groups. Those aged 50–65 years had a RR of 5.20 (95% CI 4.76 to 5.69) and those aged over 65 years the RR was 3.10 (95% CI 2.67 to 3.60).

DISCUSSION

The main finding of this study is that for all age groups, current smokers were over three times more likely to have an acute STEMI than the comparison group comprising ex- and never smokers. Although previous studies have demonstrated a significant increase in risk of AMI in smokers, our analysis is the first to quantify this risk using incidence RR analysis.[8–12] The detrimental effect of smoking was most pronounced in the younger age group; smokers under 50 years of age had >8 times the risk of an acute STEMI compared to their age-matched ex- and never smokers.

In this incidence analysis of STEMI patients the population was predominantly male and smoking prevalence was higher in the younger age groups. There was a mean age difference of 10–11 years between current and non-smokers. These results mirrored other large AMI studies.[10 13 14] However, one other AMI reported an even larger 14 year age difference.[5]

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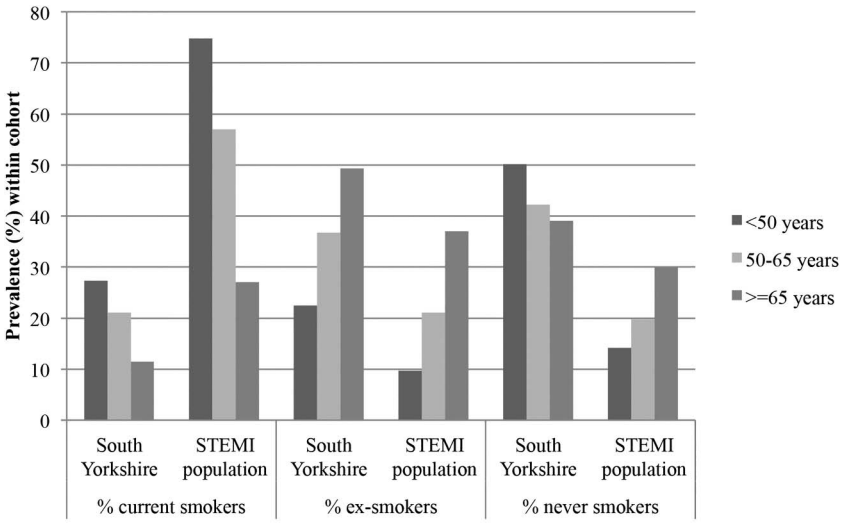

Figure 1 Smoking prevalence (%) within the ST-segment elevation myocardial infarction (STEMI) cohort and in South Yorkshire derived from Office for National Statistics Integrated Household Survey (ONS-IHS) responses. Weighted patient years for the IHS are presented, with unweighted responses reported in brackets.

Age group	Current smokers		Ex-smokers		Never smokers	
	South Yorkshire	STEMI population	South Yorkshire	STEMI population	South Yorkshire	STEMI population
<50	27.3	76.1	22.5	9.5	50.2	14.4
50-65	21.1	57	36.7	21.1	42.2	19.8
65 and over	11.5	27	49.3	37	39.1	29.9
n	576927 (3277)	838	814569 (4914)	470	1182134 (6706)	419

Ex-smokers and never smokers share similar incidence rates of STEMI

Incidence rate analysis clearly shows that smokers who quit or those who have never smoked have a significantly lower incidence rate of acute STEMI. Of note is the similarity of incidence of acute STEMI between ex-smokers and never smokers. Both ex-smokers and never smokers presented at similar ages with acute STEMI, and the mean age difference was not statistically significant (ex-smoker mean age 68.54 years, 95% CI 67.48 to 69.61; never smoker mean age 66.67 years, 95% CI 65.50 to 67.84). These data indicate that giving up smoking reduces the incidence of acute STEMI to that of someone who has never smoked, in all age groups. One study has suggested that ex-smokers can approach the same risk of a first or second MI as never-smokers, but this benefit may be seen after 15 years of smoking cessation.[9] However, another study found an elevated risk of a major IHD event remained even at 20 years of smoking cessation.[10] Undoubtedly, however, smoking cessation is associated with a notable reduction in coronary heart disease mortality.[11]

Analysis of the risk factor profile of ex-smokers and never smokers may partly explain this similar incidence rate in the two groups. Other than a previous history of IHD, which was higher in ex-smokers, the risk factor profile between the two groups was largely similar. This may explain why similar levels of acute STEMI occurred. However, ex-smokers, who were much more likely to have a diagnosis of previous IHD, may have received secondary preventative therapy. It may also be a reflection of the benefits of smoking cessation regardless of duration of the cessation period, although this was not measured in this study.

Those who are youngest experienced the greatest risk from smoking

Using the incidence rates of acute STEMI in different groups, incidence RR analysis allowed comparison of risk associated

Table 1 Unadjusted and age-adjusted odds ratios for risk factors across smoking groups

	Age unadjusted risk factor prevalence				Age-adjusted risk factor prevalence (odds ratio)		
Risk factor	Current smoker n=838	Ex-smoker n=470	Never smoker n=419	p Value	Current smoker	Ex smoker	Never smoker
Hypertension	285 (34.0%)	209 (44.5%)	178 (42.5%)	<0.001	0.88 (0.69–1.14) p=0.337	1.03 (0.79–1.36) p=0.803	1
Previous history of IHD	139 (16.6%)	138 (29.4%)	61 (14.6%)	<0.001	1.45 (1.03–2.05) p=0.035	2.37 (1.69–3.32) p<0.001	1
Diabetes	87 (10.4%)	74 (15.7%)	60 (14.3%)	0.012	0.72 (0.50–1.04) p=0.080	1.11 (0.77–1.61) p= 0.580	1
Dyslipidaemia	316 (37.7%)	209 (44.5%)	163 (38.9%)	0.051	0.90 (0.70–1.16) p=0.431	1.27 (0.97–1.66) p=0.080	1
Family history of IHD	382 (45.6%)	184 (39.1%)	166 (39.6%)	0.033	0.87 (0.68–1.13) p=0.306	1.06 (0.81–1.40) p=0.664	1
Previous TIA/stroke	45 (5.4%)	35 (7.4%)	22 (5.9%)	0.251	1.59 (0.91–2.77) p=0.106	1.36 (0.78–2.36) p=0.283	1
Peripheral vascular disease	34 (4.1%)	18 (3.8%)	9 (2.1%)	0.206	3.44 (1.56–7.59) p=0.002	1.67 (0.74–3.78) p=0.218	1

IHD, ischaemic heart disease; TIA, transient ischaemic attack.

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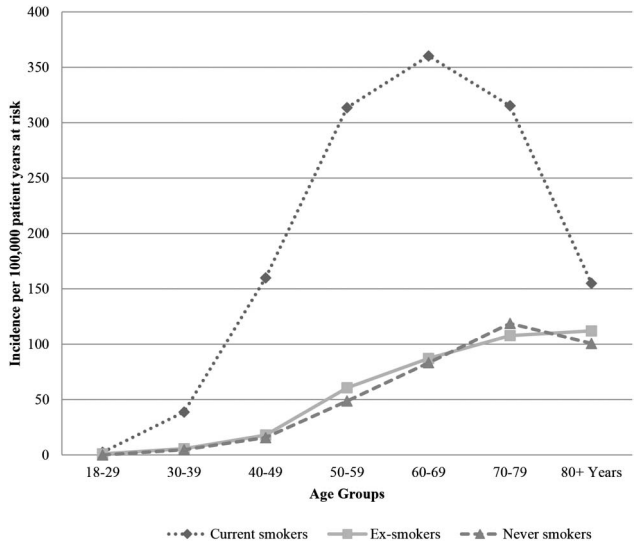

Figure 2 Incidence of acute ST-segment elevation myocardial infarction (STEMI) by smoking status in South Yorkshire, calculated using patient time from the Office of National Statistics Integrated Household Survey (ONS-IHS) and a cohort of patients presenting with STEMI. Current smokers had a peak incidence of acute STEMI at age 60–69 years, whereas for ex- and never smokers, the peak incidence was 10 years later at 70–79 years.

with smoking across various age groups. A recent study explored the OR of being a smoker in those who presented with STEMI across different age groups.[12] Those in the youngest age group were the most likely to be smokers (OR 11.4, 95% CI 10.0 to 12.8), compared to those aged over 65 whose OR peaked at only 3.4 (95% CI 3.3 to 3.4). Our study examined this trend from a different angle, using current, ex- and never smokers as the starting points, and using incidence analysis to calculate their risk of STEMI across different age groups conferred by their smoking.

From this analysis, we found that those who were under the age of 50 years had the highest likelihood of acute STEMI attributable to their smoking, compared to their age matched ex- and never smokers. Indeed, this group was over eight times more likely to suffer an acute STEMI. The older age groups did not appear to confer such a high risk from their smoking when compared to age-matched ex- and never smokers. Those aged 50–65 years were over five times more likely to suffer an acute STEMI and those aged over 65 years were over three times more likely. The MONICA trials found similar results: those who were young and smoked were more at risk and that the relative risk associated with smoking decreased with the ageing groups, a trend mirrored in our data.[6] The INTERHEART study also looked at the risk profiles across age groups and reported that younger smokers compared with age matched never smokers experienced a larger effect from current smoking (OR 3.53, 95% CI 3.23 to 3.86) with respect to increased risk to AMI than older individuals. However, these studies predated the newer AMI classification and did not identify acute STEMI patients in particular.

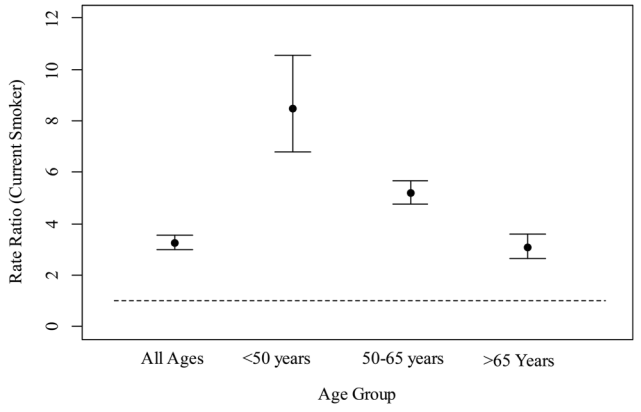

Figure 3 Rate ratios of smokers compared to ex- and never smokers for the incidence of acute ST-segment elevation myocardial infarction (STEMI) by age group, calculated using patient time from the Office of National Statistics Integrated Household Survey (ONS-IHS) and a cohort of patients presenting with STEMI. Those in the youngest age group <50 years had the highest likelihood of an acute STEMI conferred by smoking (RR 8.47). The risk conferred by smoking on acute STEMI was lowest in the oldest age groups.

From our data alone, it is difficult to explain the much higher risk of acute STEMI imparted by smoking on the youngest patients and raises important questions as to why this should occur. It is recognised that the youngest populations tend to demonstrate fewer risk factors such as hypertension, hyperlipidaemia or diabetes and this has been demonstrated in young STEMI patients who smoke.[15] Therefore, smoking appears to be a much more potent risk of STEMI in the young, as it is one of the very few risk factors present in this group. The GRACE registry reported that smokers presented with acute coronary syndrome with a much more favourable risk profile, and because smokers were on average around 10 years younger than non-smokers, this may support the above theory.[8] While other studies concur that smoking prevalence is higher in younger age groups with myocardial infarction, other risk factors have also been identified as being more prevalent in younger age groups, such as a family history of coronary artery disease and hyperlipidaemia.[5 16–18]

The high RR seen in the youngest smokers may indicate that smoking is perhaps the most powerful of all risk factors, exerting its effect much sooner than any other. This is supported by other studies which identified smoking as not only the most prevalent risk factor, but also one of the most important in the young.[16]

Recent evidence suggests that the histological composition of plaque differs between smokers and non-smokers.[19] Cigarette smokers appear to be more vulnerable to arterial plaque rupture due to the higher burden of a necrotic core (20.7% vs 17.2% in non-smokers; p=0.04). This suggests that smoking may induce plaque instability. In addition, a recent study has demonstrated an unexpected finding that post-STEMI smokers have not demonstrated a significant reduction in the risk of all-cause mortality,[15] despite receiving evidence-based therapies. This strengthens the argument for a focus on prevention of smoking in the youngest age groups.

Older age groups experience less risk from smoking

While an increased risk of acute STEMI persisted in older current smokers (RR 3.10), it was much lower than what is seen in the younger age groups (RR 8.47). The epidemiological landscape of risk factors in older patients is more complex, and cardiac risk factors are more prevalent. Therefore, it may be expected that the incidence of STEMI across the whole population would increase similarly for the ex-, never and current smokers, thus diluting the detrimental effect of smoking seen in the youngest age group. This can be demonstrated by the steadily increasing incidence rate of acute STEMI of ex- and never

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smokers with age (figure 2) and the subsequent lower RR in the oldest age groups.

Interestingly, the incidence of STEMI in current smokers decreases notably between the ages of 70–79 years, which contributed to the smaller RR seen in the older current smokers. There may be a few reasons for this decrease. Firstly, there may be some element of survival bias. Those who were current smokers may have died, decreasing the incidence of acute STEMI in this group and resulting in a distorted representation of this outcome. Secondly, it may be that plaque composition changes, which occur over time, may have a direct bearing on the incidence of acute STEMI, as the plaques become more calcified and less vulnerable in older patients.

Study strengths

This study accurately determined the incidence of STEMI in South Yorkshire using data on smoking prevalence within this region. By comparing the smoking habits of patients with an acute STEMI to that of the general population of the area we have not only reported an increased smoking prevalence in the young, but also quantified the risk this habit imparts upon them. This can guide health policy on targeting the most important groups to promote preventative measures. This study may also help to tackle the misconception by young smokers that acute STEMI is a disease of the elderly, by showing that this group is very vulnerable and has the highest risk from their smoking.

Study limitations

This study is based on retrospective analysis of prospectively collected data. While the inclusion criteria for this study are broad, only those suffering an acute STEMI who underwent PCI at the South Yorkshire Cardiothoracic Centre were studied. Patients who died before admission or who were deemed unsuitable for PCI were not included in the analysis. Although we do not have exact data, we would highlight that the well-established and monitored primary PCI service in South Yorkshire successfully identifies and refers nearly all patients with acute STEMI to the South Yorkshire Cardiothoracic Centre. It is rare for a patient to be excluded from such proven treatment and the alternative (and less effective) thrombolytic therapy has now been largely forgotten. It is also rare for a patient, who may be experiencing severe chest pain and feeling very unwell, to refuse to give their consent to undergo primary PCI. We estimate that <1% of patients would be excluded for these reasons.

Key messages

What is already known on this subject?
Smoking is a recognised and important cardiovascular risk factor that has not yet been quantified using incidence rate ratio analysis in different age groups.

What might this study add?
This study specifically looks at incidence rate ratios of acute ST-segment elevation myocardial infarction (STEMI) and shows that smoking is associated with an increased incidence in acute STEMI for all ages, but this is greatest in the youngest smokers compared to their age-matched non-smoking counterparts.

How might this impact on clinical practice?
The cause of the differing risks from cigarette smoking on younger and older smokers remains unclear. All current smokers must be encouraged into smoking cessation therapy to reduce their risk of acute STEMI, with a focus on the youngest smokers whose increased risk is often unrecognised.

CONCLUSIONS

This is the first study to use population data combined with case data to conclusively show that rate ratios are much higher in younger smokers compared with older smokers in acute STEMI. The difference between the ages is striking: young smokers are over eight times more likely to suffer acute STEMI compared with their age matched counterparts, whereas those aged 50–65 are just five times more likely, and those aged ≥65 only three times more likely.

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Contributors Study concept and design: AL, LS, JF, AS, JI, MDT and EDG. Acquisition of data: AL, LS, JF, AS and JI. Analysis and interpretation of data: AL, LS, JF, JI, MDT and EDG. Drafting of the manuscript: AL, LS, JF, AS, JI and EDG. Critical revision of the manuscript for important intellectual content: AL, LS, JF, AS, JI and EDG. Statistical analysis: AL and JF. Administrative, technical, or material support: AS, JI and EDG. Study supervision: EDG.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement We are unable to release any data obtained from the Office for National Statistics or Myocardial Ischaemia National Audit Project and this was released to us solely for internal validation and data calculations.

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