

Trends and predictions of metabolic risk factors for acute myocardial infarction: findings from a multiethnic nationwide cohort

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Summary

Background Understanding the trajectories of metabolic risk factors for acute myocardial infarction (AMI) is necessary for healthcare policymaking. We estimated future projections of the incidence of metabolic diseases in a multi-ethnic population with AMI.

Methods The incidence and mortality contributed by metabolic risk factors in the population with AMI (diabetes mellitus [T2DM], hypertension, hyperlipidemia, overweight/obesity, active/previous smokers) were projected up to year 2050, using linear and Poisson regression models based on the Singapore Myocardial Infarction Registry from 2007 to 2018. Forecast analysis was stratified based on age, sex and ethnicity.

Findings From 2025 to 2050, the incidence of AMI is predicted to rise by 194.4% from 482 to 1418 per 100,000 population. The largest percentage increase in metabolic risk factors within the population with AMI is projected to be overweight/obesity (880.0% increase), followed by hypertension (248.7% increase), T2DM (215.7% increase), hyperlipidemia (205.0% increase), and active/previous smoking (164.8% increase). The number of AMI-related deaths is expected to increase by 294.7% in individuals with overweight/obesity, while mortality is predicted to decrease by 11.7% in hyperlipidemia, 29.9% in hypertension, 32.7% in T2DM and 49.6% in active/previous smokers, from 2025 to 2050. Compared with Chinese individuals, Indian and Malay individuals bear a disproportionate burden of overweight/obesity incidence and AMI-related mortality.

Interpretation The incidence of AMI is projected to continue rising in the coming decades. Overweight/obesity will emerge as fastest-growing metabolic risk factor and the leading risk factor for AMI-related mortality.

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Research in context

Evidence before this study

The influence of metabolic risk factors such as type 2 diabetes mellitus, hypertension, hyperlipidaemia, overweight/obesity and cigarette smoking in the development of cardiovascular disease has been well-established. However, while existing studies have explored the metabolic burden among individuals with acute myocardial infarction (AMI), there is a lack of research projecting the trends and patterns of metabolic disease in this population into the coming decades.

Added value of this study

This study makes use of data from the Singapore Myocardial Infarction Registry (SMIR) from January 2007 to December 2018 to forecast trends of metabolic diseases in the population with AMI. The prevalence of type 2 diabetes mellitus, hypertension, hyperlipidaemia, overweight/obesity and cigarette smoking among AMI-incident and AMI-related mortality populations was projected from 2025 to 2050, and stratified by age-group, sex, and ethnicity. The incidence of AMI is projected to continue its steep upward trends,

paralleled by the rising prevalence of metabolic disease. Overweight/obesity is set to overtake hypertension and hyperlipidemia as the main metabolic risk factors underlying AMI by 2050, thus emerging as the fastest-growing driver of AMI. The rise in the prevalence of obesity is especially pronounced in younger populations with AMI that are of Malay ethnicity.

Implications of all the available evidence

This multi-ethnic nationwide study offers insights not only to overall trends in metabolic diseases, but the varied distribution of metabolic disease across different age-groups, sexes, and ethnic groups. This granularity in data is vital in easing the shift from 'one-size-fits-all' public health models to targeted measures that adapt to the individualised challenges faced by different parts of society. Moreover, Singapore's rapid socioeconomic development, coupled with its multi-ethnic and ageing population allows it to act as a leading indicator of emerging trends worldwide, informing strategies in primary and secondary AMI prevention.

Introduction

The rapid rise in the incidence of cardiovascular disease (CVD) over the past 30 years has brought major challenges for healthcare systems around the world.¹ In Asia, CVD currently accounts for 35% of all deaths and is expected to be the leading cause of death exerting a profound impact on health systems in this region over the coming decades.^{2,3} Treatment advances have lessened the impact of CVD on public health⁴⁻⁶; however, advances in therapeutic interventions are being offset by the epidemic of metabolic disease driven by the increasingly obesogenic and sedentary living environments.⁷⁻⁹ Metabolic risk factors such as type 2 diabetes mellitus (T2DM), hypertension, hyperlipidemia, overweight/obesity and cigarette smoking often exist in tandem,¹⁰ sharing common pathobiological pathways and underlying societal drivers that collectively accelerate atherosclerosis and eventually lead to acute myocardial infarction (AMI).¹¹⁻¹⁴

While existing studies have explored the metabolic burden among individuals with AMI,^{11,15} there is limited data on the projected trends of metabolic diseases in the population with AMI in the decades ahead. This multi-

ethnic nationwide study offers a valuable construct of the trends of all metabolic diseases and risk factors forecasted up to year 2050. Incidence and AMI-related mortality of each metabolic disease were examined and stratified across age groups, sex and ethnicity. As Singapore is a major hub city with a multi-ethnic Asian population, future projections of metabolic risk factors in a population with AMI may potentially inform strategies to reduce metabolic drivers of AMI risk within Asia, and worldwide.

Methods

Study population

Estimates of AMI incidence and mortality based on all patients presenting with AMI and captured by the Singapore Myocardial Infarction Registry (SMIR) from January 2007 to December 2018 were retrieved.¹⁶ The SMIR is a national registry of all patients diagnosed with AMI who present at public and private hospitals in Singapore.¹⁷ AMI cases are identified from hospital discharge records, reimbursement claims, and the national death registry. Additionally, cases of AMI are

identified from screening of cases with troponin levels elevated above the 99th percentile of each laboratory; this laboratory-based screening approach gives the SMIR possibly the most comprehensive coverage compared with any other national AMI registry. All cases of AMI undergo central verification by trained personnel at the SMIR. Trained research personnel collect information on patient demographics, clinical characteristics, and outcomes using standardized data elements from the SMIR notification forms. The International Classification of Diseases 9th Revision (ICD-9) Clinical Modification code 410 was used to identify AMI cases from the data sources prior to 2012, while the ICD-10 Australian Modification codes I21 and I22 were used for AMI cases diagnosed from 2012 onwards. Prior publications have regular internal audits to assess the quality of the data and results from the audits showed that the registry achieved high inter-rater reliability and logic check (>95%) for all data items.^{18,19} SMIR data is combined with mortality data from the Registry of Births and Deaths to obtain mortality outcomes. The reporting of deaths in Singapore is mandated.¹⁶ The study received a waiver for informed consent from patients as it used de-identified data, and was approved by the SingHealth CIRB (Reference No. 2016/2480).

Metabolic disease definitions

Patients with AMI included those with ST-elevation myocardial infarction (STEMI) or non-ST elevation myocardial infarction (NSTEMI). Individuals were diagnosed with AMI by the attending cardiologists based on clinical evidence.²⁰ The presence of T2DM was defined by either a) fasting blood glucose ≥ 7.0 mmol/L or random glucose ≥ 11.1 mmol/L during the index admission, b) a past diagnosis of T2DM, or c) the consumption of glucose-lowering medications.^{21,22} Hypertension was based on a) systolic blood pressure >130 mmHg and/or diastolic blood pressure >85 mmHg during the index admission, b) a past diagnosis of hypertension, or 3) the background use of anti-hypertensive medications.^{22–24} Hyperlipidemia was defined by 1) total cholesterol >6.2 mmol/L, low-density lipoprotein cholesterol >4.1 mmol/L, or triglyceride >1.7 mmol/L, 2) previous diagnosis of hyperlipidemia, or 3) on background lipid-lowering therapy.^{22,25,26} Overweight/obesity was defined as a body mass index of ≥ 23 kg/m², the cut-off value used for Asian populations.^{27,28} Smoking included both active and previous smokers. AMI-specific mortality was determined by identifying death attributable to AMI (410 for ICD-9; I21 and I22 for ICD-10).

Statistical analysis

To predict the crude incidence rate of AMI and metabolic diseases from 2025 to 2050, historical data from 2007 to 2018 were used. Historical data from SMIR were used to obtain the number of AMI cases and AMI

cases with metabolic disease. Taken together, they were used to calculate the crude incidence rate of AMI in each year between 2007 and 2018. The prediction model for incidence of AMI was performed using Poisson regression, with AMI onset year as independent variable and AMI incidence (i.e. number of AMI cases in a year) as dependent variable. The prediction model for crude incidence rate of AMI cases was built using linear regression and log transformation,^{29,30} with the year of AMI onset as independent variable and crude incidence rate of AMI (e.g. number of AMI cases with diabetes in a year divided by the number of Singapore residents in the same year) as dependent variable. These prediction models were generated for the individual metabolic diseases (T2DM, hypertension, hyperlipidemia, overweight/obesity) associated with AMI; and subgroup analyses were conducted for males, females, young adults aged 15–39 years, middle-aged adults aged 40–64 years, older adults aged ≥ 65 years, Chinese, Malays and Indians. The 95% confidence intervals (CI) of the estimated incidence rates were calculated using the delta method.³¹

The same approach was applied for predicting the number of AMI-specific deaths as well as death rates, with separate models for each of the metabolic diseases. All statistical analyses were performed using Stata version 17.0 (College Station, TX).

Role of the funding source

No additional support from organisations beyond the authors' academic institutions was received for this research. As such, no funders had any role in the study design, data collection, data analyses, data interpretation, or writing of the report.

Results

Study population

In 2018, the overall incidence of AMI was 352 per 100,000 population (66.7% males). The population with AMI comprised mainly of Chinese (67.9%), Malay (19.1%), and Indian (13.0%) individuals. The AMI population had a median haemoglobin value of 12.7 g/dL (interquartile range [IQR]: 10.6–14.5) and median creatinine value of 100.0 μ mol/L (IQR: 77.0–168.0). There was a higher incidence of AMI in males (483 per 100,000 population) compared to females (228 per 100,000 population). The highest incidence of AMI was among Indians (523 per 100,000 population), followed by Malays (521 per 100,000 population), then Chinese (313 per 100,000 population). The largest proportion of AMI occurred in the ≥ 65 years group (1380 per 100,000 population), followed by 40–64 (286 per 100,000 population), and 15–39 years (11 per 100,000 population). The largest contributing metabolic risk factor in the overall AMI burden in 2018 was hypertension (259 per 100,000 population), followed by hyperlipidemia (251

per 100,000 population), overweight/obesity (177 per 100,000 population), T2DM (174 per 100,000 population), and active/previous smoking (149 per 100,000 population).

AMI projections

From 2025 to 2050, the overall incidence of AMI is predicted to rise by 194.4% from 482 to 1418 per 100,000 population (Supplementary Tables S1 and S2). AMI incidence is projected to increase in males by 211.9% (663–2069 per 100,000 population) and in females by 169.5% (312–841 per 100,000 population). The Malay population is predicted to have the highest AMI incidence from 2025 to 2050 (216.4% increase; 755–2388 per 100,000 population), followed by Indians (147.4% increase; 658–1628 per 100,000 population), and Chinese (202.8% increase; 429–1300 per 100,000 population). Individuals ≥ 65 years old will observe a 28.3% (1507–1934 per 100,000 population) increase in AMI incidence, those aged 40–64 years will have a 114.0% (362–776 per 100,000 population) increase, and those aged 15–39 years will have a 93.2% (15–28 per 100,000 population) increase. Overweight/obesity is predicted to remain the most prevalent risk factor underlying AMI in all age groups in 2050 (Supplementary Fig. S1), with the largest increase in overweight/obesity from 2025 to 2050 expected to occur in those aged 65 and above (Supplementary Fig. S2). This age group is predicted to bear the highest burden of all metabolic diseases across time. The incidence of AMI counts is found in Supplementary Tables S3 and S4.

The overall number of AMI-related deaths is projected to fall by 43.9% from 2025 to 2050 (Supplementary Tables S7 and S8). Males are expected to observe a greater decrease in AMI-related mortality (47.1% decrease; 411–217) than females (39.6% decrease; 311–188). The projected mortality rates can be found in Supplementary Tables S5 and S6.

T2DM projections

The incidence of T2DM in patients with AMI is projected to increase by 215.7% (245–772 per 100,000 population) from 2025 to 2050 (Fig. 1; Supplementary Fig. S3). The total number of AMI-related deaths in the T2DM group is projected to decrease by 32.7% (from 334 to 225) within the same time frame (Supplementary Tables S7 and S8; Fig. 2).

The incidence of T2DM in patients with AMI from 2025 to 2050 is expected to rise more in males (274.7% increase; 327–1226 per 100,000 population) than in females (146.2% increase; 169–416 per 100,000 population) (Supplementary Tables S1 and S2; Fig. 3; Supplementary Fig. S3). Females with T2DM are projected to observe a larger decrease in the number of AMI-related deaths (42.3% decrease; 145–84) compared to males (25.4% decrease; 189–141) (Supplementary Tables S7 and S8). The ethnic-specific incidence of

T2DM in patients with AMI is projected to be the highest in Malays (269.7% increase; 455–1681 per 100,000 population) and Indians (182.1% increase; 442–1246 per 100,000 population), with lower incidence in Chinese (209.7% increase; 193–599 per 100,000 population) from 2025 to 2050 (Fig. 4; Supplementary Fig. S3). The AMI-related mortality decreased by 37.7% in Chinese, 32.5% in Malays, and 13.0% in the Indian population from 2025 to 2050.

Hypertension projections

The incidence of hypertension in patients with AMI is forecasted to rise by 248.7% (379–1321 per 100,000 population) from 2025 to 2050 (Fig. 1; Supplementary Fig. S3) whereas the total number of deaths is projected to fall by 29.9% (from 510 to 358) (Fig. 2).

From 2025 to 2050, the incidence of hypertension in patients with AMI is predicted to have a greater increase in males (296.4% increase; 502–1988 per 100,000 population) than in females (189.4% increase; 265–767 per 100,000 population) (Fig. 3; Supplementary Fig. S3). Females with hypertension are set to observe greater reductions in AMI-related deaths (34.9% decrease; 234–152) compared to males (25.7% decrease; 277–205). From 2025 to 2050, Malays with hypertension are expected to have the highest incidence of AMI (264.9% increase; 568–2071 per 100,000 population), followed by Indians (207.1% increase; 518–1591 per 100,000 population) and Chinese (257.7% increase; 342–1223 per 100,000 population) (Fig. 4; Supplementary Fig. S3). Malays and Chinese will have the largest reductions in AMI-related mortality by 27.7% and 32.5% respectively, with a fall of 18.0% for Indians from 2025 to 2050.

Hyperlipidemia projections

AMI incidence in patients with hyperlipidemia is projected to increase by 205.0% from 2025 to 2050, from 341 to 1041 per 100,000 population (Fig. 1; Supplementary Fig. S3), while AMI-related mortality is predicted to fall by 11.7% (from 466 to 412) (Fig. S2).

A larger rise in the incidence of AMI with hyperlipidemia is expected in males (211.1% increase; 456–1418 per 100,000 population) as compared to females (200.3% increase; 234–703 per 100,000 population) (Fig. 3; Supplementary Fig. S3). However, females with hyperlipidemia will have a larger decrease in AMI-related deaths (16.1% decrease; 203–170) than males (8.4% decrease; 264–242). The incidence of AMI in individuals with hyperlipidemia will likely be highest in Malays (211.0% increase; 545–1694 per 100,000 population) and Indians (156.7% increase; 508–1304 per 100,000 population), followed by Chinese (220.5% increase; 298–956 per 100,000 population) (Fig. 4; Supplementary Fig. S3). AMI-related mortality in individuals with hyperlipidemia is forecasted to rise by 11.8% in Indians, but fall by 13.9% in Chinese and 19.0% in Malays from 2025 to 2050.

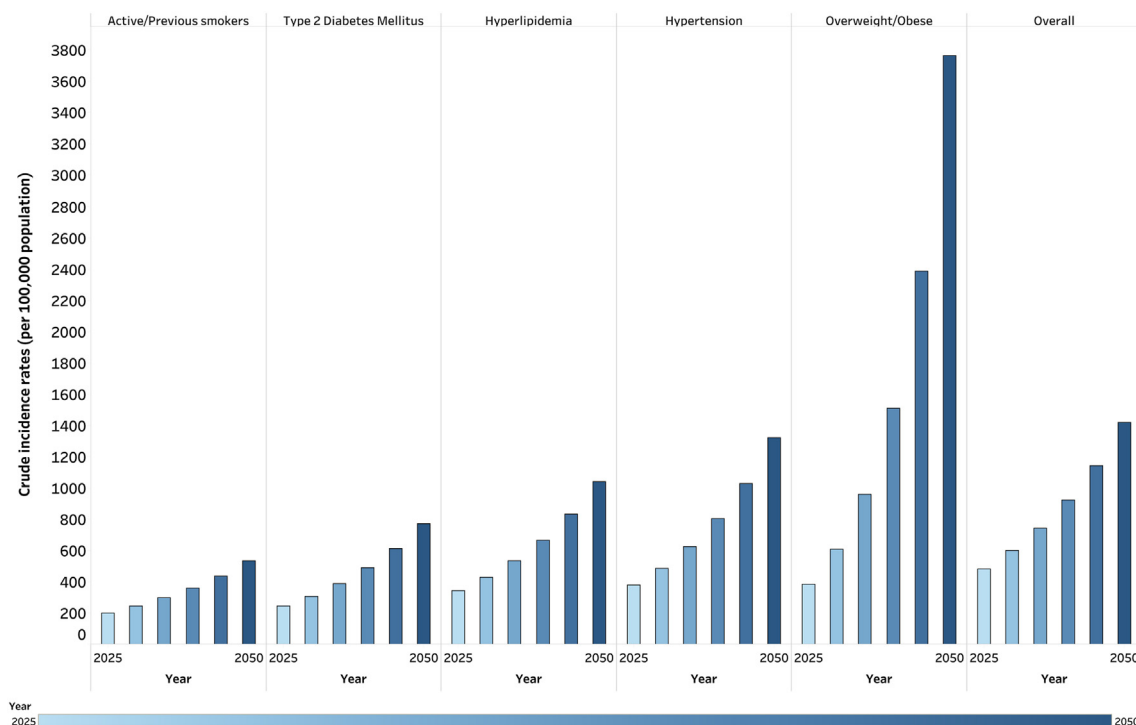


Fig. 1: Projected incidence of acute myocardial infarction with concomitant metabolic diseases and risk factors in the Singapore population from 2025 to 2050. Incidence is presented per 100,000 population.

Active/previous smoking projections

From 2025 to 2050, the incidence of patients with AMI who are active or previous smokers is projected to increase by 164.8% (201–532 per 100,000 population) (Fig. 1; Supplementary Fig. S3), while mortality projected to decrease by 49.6% (from 187 to 95) (Fig. 2).

Between 2025 and 2050, the incidence of males with AMI who are active/previous smokers is predicted to rise by 188.6% (394–1136 per 100,000 population) while incidence in females rose 30.2% (23–30 per 100,000 population) (Fig. 3; Supplementary Fig. S3). Females who are active/previous smokers are also expected to experience a larger decline in AMI-related deaths (83.3% decrease) compared to males (47.1% decrease). Ethnicity-specific analysis revealed that the incidence of patients with AMI who are active/previous smokers is predicted to remain the highest in Malays (240.9% increase; 388–1321 per 100,000 population), followed by Indians (137.8% increase; 295–701 per 100,000 population) and Chinese (153.3% increase; 165–418 per 100,000 population) (Fig. 4; Supplementary Fig. S3). The largest decrease in AMI-related mortality was found in Chinese (80.9% decrease), followed by Indians (29.3% decrease) and Malays (17.0% decrease).

Overweight/obesity projections

There will be a projected rise of 880.0% in the incidence of patients with AMI who are overweight or obese by

2050 (384–3764 per 100,000 population) (Fig. 1; Supplementary Fig. S3), and total AMI-related mortality is expected to see a 294.7% increase (from 433 to 1711) (Fig. 2).

A larger rise in incidence can be observed in females (1204.7% increase; 243–3173 per 100,000 population) than males who are overweight/obese (791.5% increase; 539–4805 per 100,000 population) in the AMI cohort by 2050 (Fig. 3; Supplementary Fig. S3). Females are projected to have a larger increase in AMI-related deaths (295.3% increase) compared to males (294.3% increase). Between 2025 and 2050, a higher incidence of patients with AMI who are overweight/obese is expected among Malays (1191.9% increase; 803–10,372 per 100,000 population) followed by Indians (609.1% increase; 601–4261 per 100,000 population) and Chinese (865.4% increase; 299–2887 per 100,000 population) (Fig. 4; Supplementary Fig. S3). The largest rise in AMI-related mortality over time is predicted in Malays (419.3% increase), followed by Indians (253.5% increase), and Chinese (211.5% increase).

Discussion

AMI incidence is expected to rise sharply in Asia in the coming decades, paralleling the shift in deleterious lifestyle practices and the growing metabolic burden across this populous region.³² In this study of 3 Asian

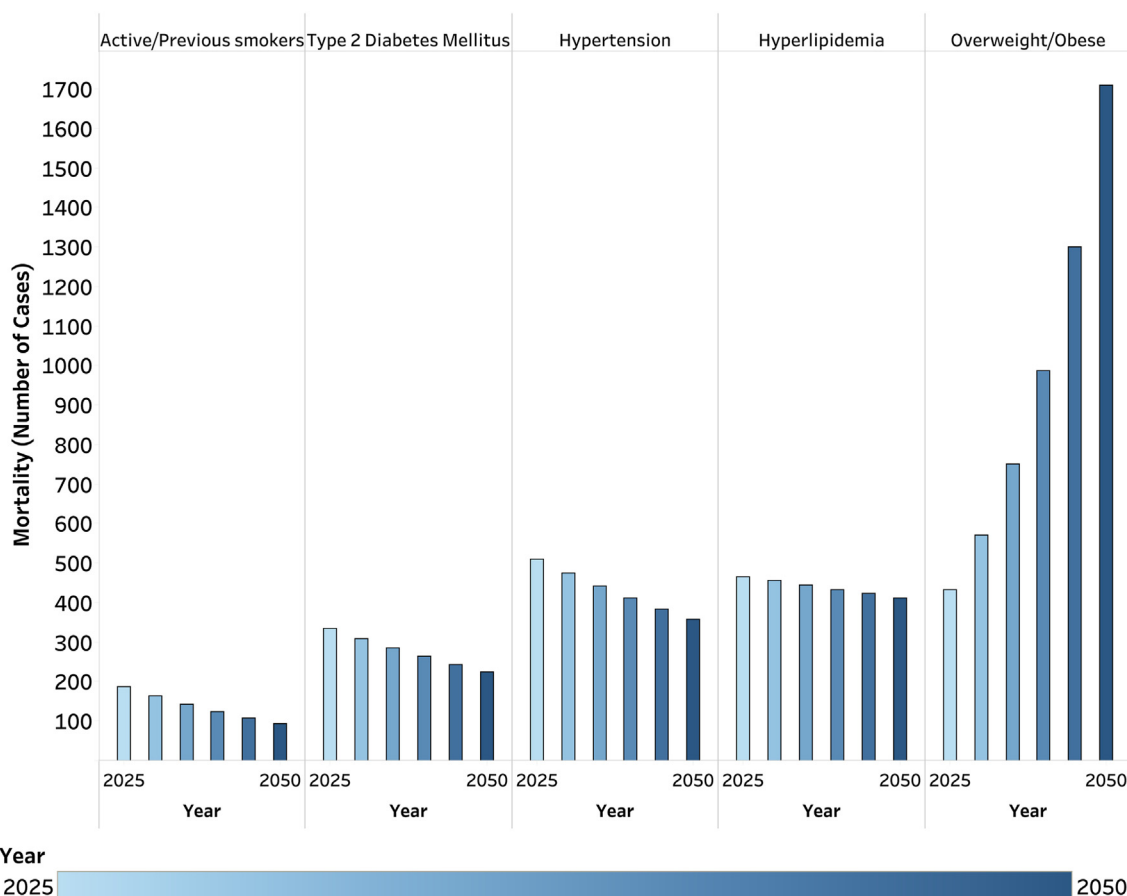


Fig. 2: Projected mortality associated with acute myocardial infarction and its concomitant metabolic diseases and risk factors in the Singapore population from 2025 to 2050.

ethnicities with AMI, overweight/obesity is projected to be the leading metabolic risk factor contributing to AMI up to 2050, followed by hypertension, hyperlipidemia, T2DM, and active/previous smoking. The metabolic risk factor with the fastest-growing incidence among the AMI cohort is predicted to be overweight/obesity over the next 25 years. The other metabolic risk factors are also expected to rise in incidence, albeit at a slower pace, with hypertension observing the second largest increase, followed by T2DM, hyperlipidemia and active/previous smoking by 2050. Overweight/obesity is also predicted to be the main metabolic risk factor underlying AMI-related deaths in the years to come, while other risk factors (T2DM, hypertension and active/previous smoking) will observe a decline in associated AMI-related mortality (*Central Illustration*). Indian and Malay male patients are likely to disproportionately bear the brunt of this overweight-obesity metabolic burden in the future.

Overweight/obesity share close and bidirectional associations with other metabolic disorders, with visceral

adiposity contributing to lipotoxicity, insulin resistance, pro-inflammatory processes that contribute to adverse metabolic sequelae and adverse cardiovascular prognosis.³³ On the other hand, studies have described that the ‘obesity paradox’ portends favourable outcomes in patients with heart failure,³⁴ AMI,^{35,36} and aortic stenosis,³⁷ possibly related to greater metabolic reserves, protective cytokines and the altered response to renin-angiotensin-aldosterone system.³⁸ However, evidence has shown that the presence of concomitant metabolic dysfunction in individuals with obesity has a more deleterious impact on survival following AMI, that can undermine the potential protective effects observed in metabolically healthy obesity.³⁶ In fact, there is ongoing debate on whether metabolically healthy obesity is a permanent state, given its decline in prevalence and its high tendency for transiting from the metabolically healthy to unhealthy phenotype.³⁶ Hence, this complex interplay between obesity and metabolic health suggests that the forecasted increase of overweight/obesity-related deaths following AMI may be driven, in part,

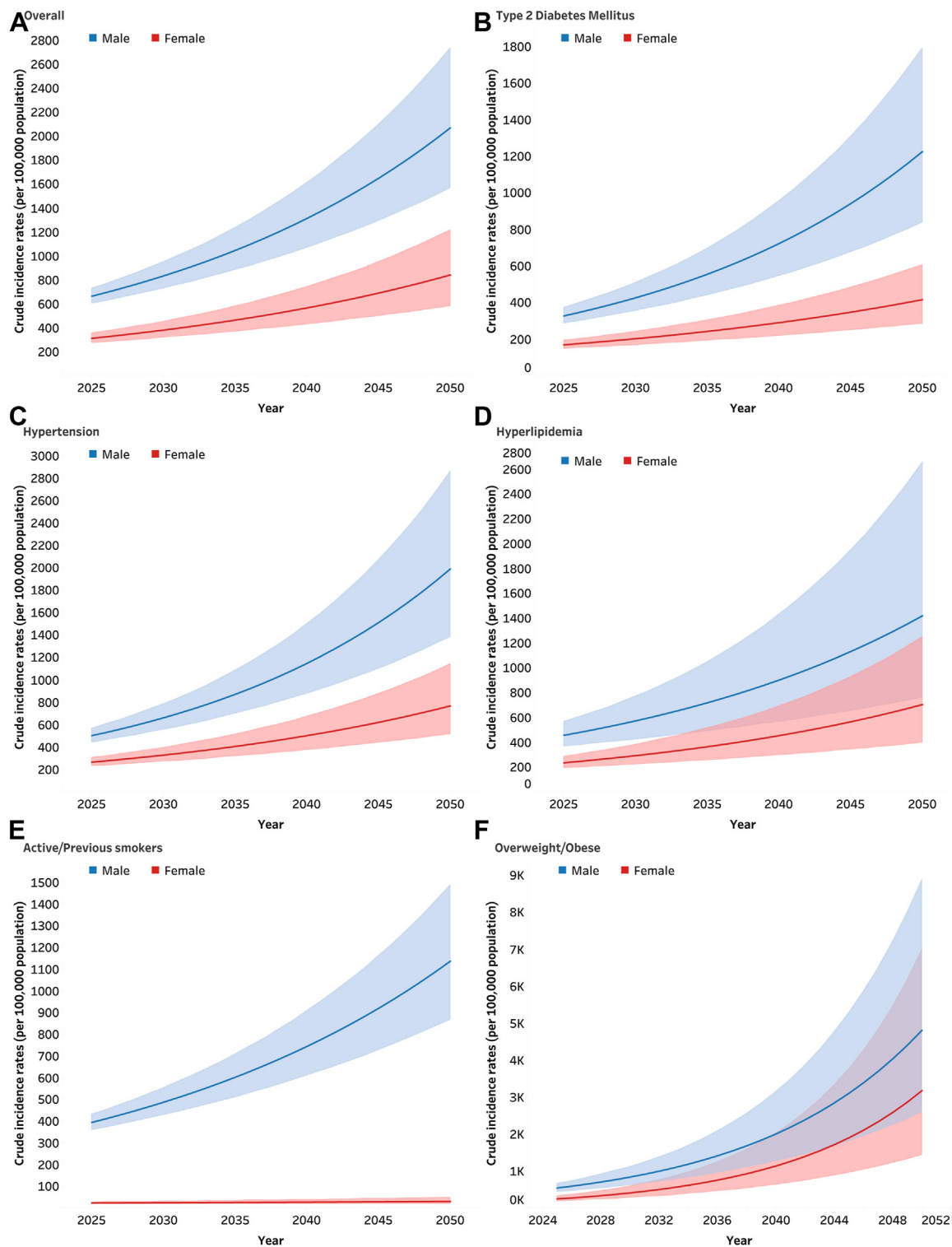


Fig. 3: Projected incidence of acute myocardial infarction with concomitant metabolic diseases and risk factors in the Singapore population from 2025 to 2050, stratified by sex. Incidence is presented per 100,000 population.

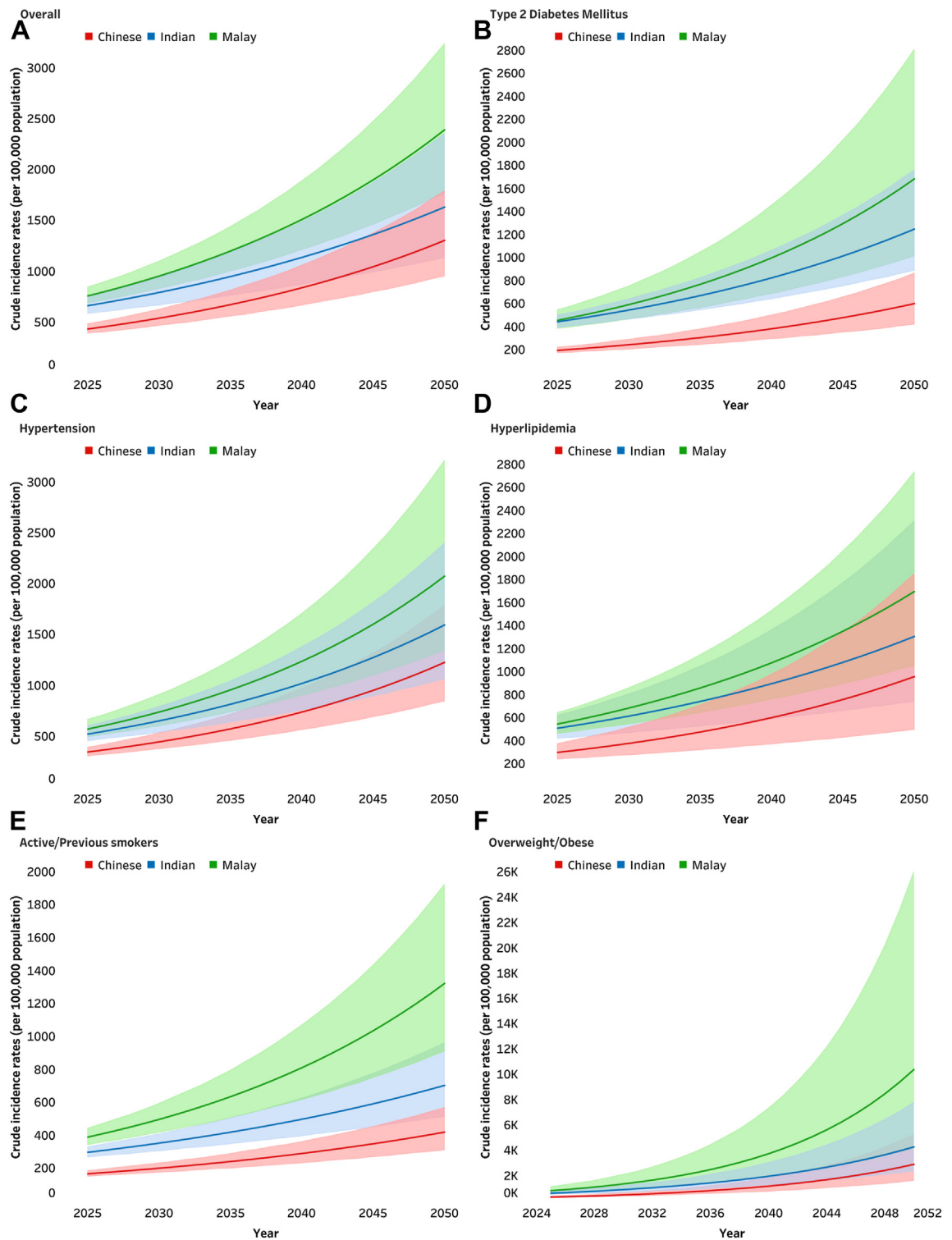
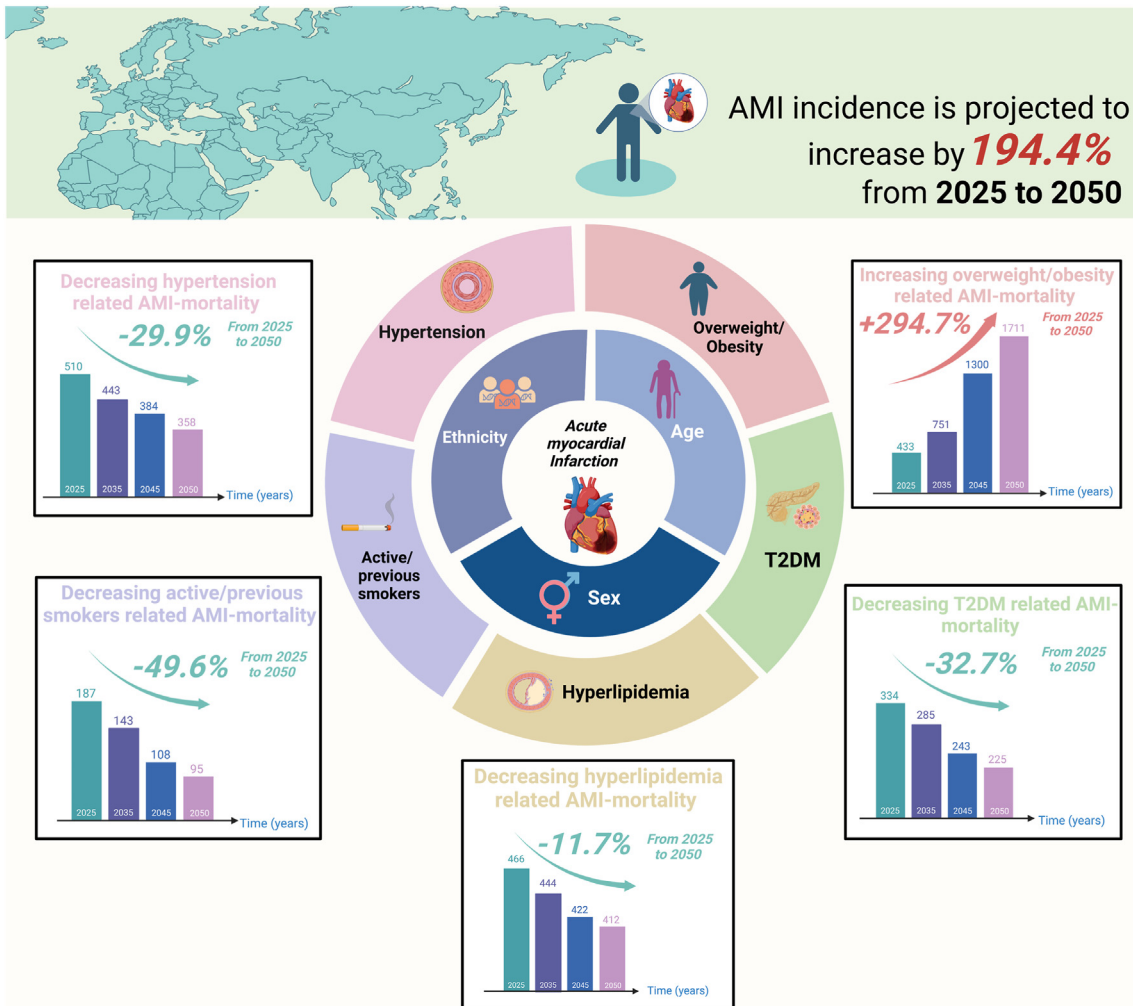


Fig. 4: Projected incidence of acute myocardial infarction with concomitant metabolic diseases and risk factors in the Singapore population from 2025 to 2050, stratified by ethnicity. Incidence is presented per 100,000 population.



Central Illustration: Trends and predictions of acute myocardial infarction and its associated metabolic risk factors from 2025 to 2050.

by the obesity-related metabolic dysfunction. Nevertheless, the epidemic of overweight and obesity remains a major public health concern that has far-reaching implications for the health and well-being of individuals and societies within Asia, and worldwide.^{7,11,37,39,40} Similar to our population estimates, predictions from the general United States (U.S.) population reported that nearly 1 in 2 adults will be obese by 2030, posing concerns regarding future healthcare costs.⁴¹ This highlights the importance of preventive efforts in achieving and maintaining meaningful weight loss. Upstream interventions addressing the underlying obesogenic environments and the promotion of healthier lifestyles to alter this trajectory have been implemented in national programs in Singapore.⁴²

Beyond lifestyle measures, pharmacotherapies to treat hypertension, hyperlipidemia and T2DM have proven to be highly effective in secondary prevention following AMI.⁴³ The high adoption rates of these

pharmacotherapies for secondary prevention, encouraged by national AMI quality-of-care scorecards,⁴⁴ may account for the declines in mortality attributable to hypertension, hyperlipidemia and T2DM. Until recently, there has been no effective pharmacotherapy for obesity/overweight treatment. The glucagon-like peptide-1 receptor agonists (GLP1-RA) have shown not only to reduce weight by as much as 17% in randomised clinical trials but have also demonstrated salutary effects on visceral fat reduction, glycaemic control, and blood pressure lowering effects, offering hope for further reduction in AMI-related mortality attributable to overweight/obesity.⁴⁵ There is a concerted push for the incorporation of exercise or lifestyle programs, including cardiac rehabilitation that focuses on supervised exercise training, as part of the AMI care bundle. The supporting evidence has highlighted the protective effects of cardiac rehabilitation programs on the reduction of morbidity and mortality, improvement

in exercise tolerance, and quality of life in individuals with AMI or heart failure.^{46–48} Nation-wide based programs focusing on the implementation of cardiac rehabilitation, in combination with other strategies such as dietary and medication adherence, through government-based policy establishment, can potentially be a key pillar in altering the trajectory of obesity-related mortality.

The ethnic gap in AMI and its associated metabolic risk factors is projected to widen further in the years to come. The unfavourable, disparate AMI and metabolic disease incidence was observed among the Malay and Indian ethnic groups, and this is likely driven by a combination of biological and socioeconomic factors. Malays and Indians in Singapore have higher rates of T2DM,⁴⁹ hypertension,⁵⁰ and obesity⁵¹ compared to Chinese. Genetic factors associated with metabolic risk factors and CVD have been described,⁵² with a higher predisposition for Malays and Indians to develop hyperlipidemia⁵³ and T2DM⁵⁴ respectively. Indians and Malays have reportedly lower average income and education levels compared to Chinese in Singapore⁵⁵; this socioeconomic disparity may exacerbate biological underpinnings, with lower socioeconomic status associated with sedentary lifestyle, unfavourable metabolic burden, and AMI outcomes. Similarly, higher prevalence of metabolic diseases have been projected in ethnic minorities and low-income adults in the U.S. population,^{41,56} with the collective findings highlighting the need for greater attention to deeply entrenched socioeconomic barriers to the sustainability of metabolic health.⁵⁷ Despite the ever-changing global landscape, the ethnic composition of the Singapore population has remained stable over the previous years, with the Chinese making up the large majority of the resident population (74.1%), followed by Malays (13.6%) and Indians (9.0%) in 2022.⁵⁸ This racial balance is expected to remain the same in the years to come, preserving social stability and the multiracial character within the country.⁵⁹ Moreover, Singapore has one of the highest immigrants-to-total-population ratios in the world.⁶⁰ This close nexus between immigration and public health has led to a rising burden of cardiovascular diseases in Singapore, that has been unmasked by the increased screening of cardiometabolic risk factors during the coronavirus disease-2019 pandemic among migrant workers.⁶¹ Although this may attenuate the projected trends derived from the current prediction models on AMI incidence and mortality, readers should remain cognizant that the forecast analysis is unable to fully account for the complexities surrounding migrant health and the accessibility to healthcare in Singapore.^{62,63}

A 'one-size-fits-all' public health model may prove insufficient especially with the different public health challenges faced by each age group within the population

with AMI. The younger and middle age groups are predominantly affected by overweight and obesity, especially with the country's rapid development and nutritional transition, promoting sedentary living and easier accessibility to high-calorie foods.⁶⁴ The rapid rise in overweight/obesity as a risk factor in younger people has profound implications for metabolic disease morbidity and mortality among future generations.^{7,11,33,37,39,40} This is in contrast to the older populations with AMI, that is driven by hypertension and hyperlipidemia, which often necessitate earlier utilisation of pharmacological therapy and frequent follow-ups.⁴⁵ As such, the interventions prioritised in different age groups must also reflect this variance.²³

Moving forward, it is crucial to focus on targeting upstream metabolic risk factors to halt the projected AMI trajectory. Sex and ethnic-specific differences in the overall metabolic burden among patients with AMI deserve its due consideration when designing healthcare initiatives. The identification of vulnerable groups can allow for better education, promotion of healthier lifestyles, and early detection and treatment of sub-clinical disease in a targeted manner.³⁵ As part of the global initiatives in advocating for healthcare quality and access across all regions in the world, *The Lancet Regional Health Global Initiative and JACC Asia* are vital in advocating for research and information exchange especially within the Asian community. Singapore's rapid rate of socioeconomic development, together with its multi-ethnic and ageing population has it uniquely positioned as an excellent representation of larger, emerging trends worldwide. While European²⁹ and U.S.⁵⁶ based studies project the ever-growing CVD burden within general populations, the epidemiological insights gleaned from the present population-based analysis can further inform future strategies in primary and secondary prevention of AMI.

Limitations

This study has its limitations. First, the study used BMI as a surrogate measure for obesity. Studies have shown that obesity measures—including waist circumference, waist-to-hip ratio or waist-to-height ratio, are more accurate surrogate markers of central obesity, and are better predictors of cardiovascular outcomes than BMI.^{34,65–67} Excessive fat-free mass from muscle may not equal to fat mass as defined as obesity, and BMI alone does not reflect the different body compositions.³⁴ Additionally, BMI may fail to demonstrate sex-based differences in the context of central adiposity and cardiovascular outcomes. Measures of central obesity, particularly waist-to-hip ratio, have been shown to be more strongly associated with the risk of AMI compared to BMI, especially among females.⁶⁸ However, such granular data on central obesity were lacking in the nationwide database, and future research exploring the predicted trends of central obesity and AMI using

the aforementioned obesity measures will be an important next step. Second, all the projections employed in this study are contingent on the assumption that the trends observed in the analysis of past data will remain consistent moving forward. In reality, the numerous new government initiatives that have been put in place over the past few years, and the interventions still yet to come may attenuate the projected trends. Nevertheless, the methodologies adopted in this study are widely-utilised and have generated robust findings in many other studies of population health.^{41,56} Third, we did not have access to socioeconomic data, which may be a confounder when considering ethnic disparities in metabolic diseases. Fourth, as with all time-series data, there may be autocorrelation for the error terms over time. However, there is no time-series with the Poisson regression model for incidence and mortality counts, that can account for the possibility of autocorrelation. Last, the forecast analysis did not account for AMI incidence during the coronavirus disease-2019 pandemic due to the fluctuations in AMI presentations related to systems and non-system based confounders.⁶⁹⁻⁷²

Conclusion

The incidence of AMI is projected to continue rising sharply in the coming decades and will be paralleled by worsening metabolic disease trends. While hypertension and hyperlipidemia are expected to persist as key metabolic risk factors underlying AMI, overweight/obesity is set to emerge as the fastest-growing and leading metabolic risk factor underlying AMI onset by 2050.

Contributors

All authors approve the final version of the manuscript, including the authorship list and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data sharing statement

All data and code used in analysis and projections are available upon request to the corresponding author.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lanwpc.2023.100803>.

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