

Are Mental Health and Substance Use Disorders Risk Factors for Missed Acute Myocardial Infarction Diagnoses Among Chest Pain or Dyspnea Encounters in the Emergency Department?

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Study objective: To assess if having a mental health and/or substance use disorder is associated with a missed acute myocardial infarction diagnosis in the emergency department (ED).

Methods: This was a retrospective cohort analysis (2009 to 2017) of adult ED encounters at Kaiser Permanente Southern California. We used the validated symptom-disease pair analysis of diagnostic error methodological approach to “look back” and “look forward” and identify missed acute myocardial infarctions within 30 days of a treat-and-release ED visit. We use adjusted logistic regression to report the odds of missed acute myocardial infarction among patients with a history of mental health and/or substance use disorders.

Results: The look-back analysis identified 44,473 acute myocardial infarction hospital encounters; 574 (1.3%) diagnoses were missed. The odds of missed diagnoses were higher in patients with mental health disorders (odds ratio [OR] 1.48, 95% confidence interval [CI] 1.23 to 1.77) but not in those with substance abuse disorders (OR 1.22, 95% CI 0.91 to 1.62). The highest risk was observed in those with co-occurring disorders (OR 1.90, 95% CI 1.30 to 2.76). The look-forward analysis identified 325,088 chest pain/dyspnea ED encounters; 508 (0.2%) were missed acute myocardial infarctions. No significant associations of missed acute myocardial infarction were revealed in either group (mental health disorder: OR 0.92, 95% CI 0.71 to 1.18; substance use disorder: OR 1.22, 95% CI 0.80 to 1.85).

Conclusion: The look-back analysis identified patients with mental illness at increased risk of missed acute myocardial infarction diagnosis, with the highest risk observed in those with a history of comorbid substance abuse. Having substance use disorders alone did not increase this risk in either cohort. The look-forward analysis revealed challenges in prospectively identifying high-risk patients to target for improvement. [Ann Emerg Med. 2021;■:1-9.]

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INTRODUCTION

Background

Diagnostic error, as described by the National Academy of Medicine, is a serious public health and patient safety problem.¹ In emergency departments (EDs), missed diagnosis of acute myocardial infarction is an important concern. Symptoms of suspected acute myocardial infarction, such as chest pain, result in millions of ED visits annually.^{2,3} Missed acute myocardial infarction diagnoses are associated with increased mortality and are the leading cause for ED medical malpractice litigation.⁴⁻⁶ Thus, reducing miss

rates for acute myocardial infarction remains a top priority of research and quality improvement efforts.

Recent studies have shown that rates of missed acute myocardial infarction are low (approximately 2% or less); however, there is growing evidence that some populations are at higher risk of cardiovascular disease and have worse health care outcomes and excess mortality. People with mental illnesses (eg, schizophrenia, bipolar disorder, or major depressive disorder) have increased cardiovascular-related mortality relative to the general population.^{4,7-16} Similarly, the risk of cardiometabolic disease is higher among people with substance use disorders.¹⁶

Editor's Capsule Summary*What is already known on this topic*

Patients with mental health and substance use disorders have worse cardiovascular outcomes.

What question this study addressed

Are mental health and substance use disorders associated with missed myocardial infarction?

What this study adds to our knowledge

In this database study of more than 350,000 patients, missed myocardial infarction was more common in patients with mental health disorders and combined mental health/substance use disorders but not among those with substance use alone. Among all emergency department patients, mental health and substance abuse were not useful predictors of missed myocardial infarction.

How this is relevant to clinical practice

This study will not change practice but suggests more research is needed on how to improve cardiovascular outcomes in these vulnerable populations.

Importance

There is evidence that poorer outcomes are related to inequities in the health care system.¹⁷ Patients with mental illness and substance use disorder have similar or more frequent contact with the health system, yet their cardiovascular care is suboptimal relative to the general population.¹⁸⁻²¹ National data show that patients who present to the ED with chest pain and comorbid chronic mental illness or substance use disorder are less likely to be hospitalized for their high-risk cardiovascular symptoms, despite their increased risk. The few small studies that have measured rates of missed acute myocardial infarction among ED patients^{11,12,15,22,23} suggest that patients with mental health or substance use disorders have less favorable outcomes than the general population, calling for more research on this topic. Efforts to improve acute myocardial infarction diagnosis for these vulnerable populations will be an important target for meaningful quality improvement.

Goals of This Investigation

The aim of this study was to assess whether having a mental health and/or substance use disorder was associated with a missed acute myocardial infarction diagnosis in EDs using the symptom-disease pair analysis of diagnostic error

(SPADE) methodological approach, a previously validated strategy to identify missed acute myocardial infarction diagnoses in the ED.

MATERIALS AND METHODS**Study Design and Setting**

We conducted a retrospective, descriptive analysis using the validated 2-step look-back and look-forward SPADE approach to identify probable missed acute myocardial infarction diagnoses among adults presenting to the ED with nonspecific chest pain or dyspnea across 14 medical centers in the Kaiser Permanente Southern California (KPSC) region. KPSC is an integrated health care delivery system serving more than 4.6 million racially and socioeconomically diverse members.⁷ Health care at KPSC is coordinated through an integrated electronic health record system that captures comprehensive information on the care members receive at KPSC-owned and contracting facilities. KPSC also obtains claims data on any out-of-network care that members receive. This comprehensive data set allows for more accurate capture of comorbidities and other clinically relevant patient variables among our discharged ED patients than most ED studies.

Selection of Participants

We previously described the details of the SPADE look-back and look-forward strategy used to classify acute myocardial infarction misdiagnosis-related harms in EDs.⁷ In brief, we searched the electronic health record (in network) and claims data (out of network) for all KPSC health plan members 18 years or older hospitalized with an acute myocardial infarction between January 1, 2009, and December 1, 2017, and enrolled in the health plan at least 30 days prior to the hospitalization. In the look-back analysis, we began with a study sample of patients hospitalized with a primary acute myocardial infarction diagnosis using International Classification of Diseases (ICD) codes and looked back 30 days to identify any treat-and-release ED encounters with a principal diagnosis of chest pain or dyspnea (Appendix E1, available at <http://www.annemergmed.com>). Treat and release was defined as patients discharged home after an ED visit and excluded those who were admitted or transferred to another hospital and who left against medical advice. If a patient had more than one encounter, only the first was included in our analysis. In the look-forward analysis, we identified patients with a treat-and-release ED visit with a principal diagnosis of chest pain or dyspnea per ICD code and followed the patients for 30 days to assess for a subsequent acute myocardial infarction hospitalization. We defined

treat-and-release ED visits as encounters that resulted in a discharge from the ED and excluded encounters that resulted in hospital admission, death, or an acute myocardial infarction diagnosis.

Main Outcomes and Measurements

In the look-back analysis, patients with a treat-and-release ED diagnosis of nonspecific chest pain or dyspnea in the 30 days prior to an acute myocardial infarction hospitalization were considered a “missed acute myocardial infarction” case. In the look-forward analysis, patients with treat-and-release ED encounters with a principal diagnosis of nonspecific chest pain or dyspnea were followed for 30 days to identify acute myocardial infarction hospitalizations after their ED visit (adverse events after a probable missed diagnosis). Similarly, in this look-forward cohort, the primary outcome of interest was an acute myocardial infarction hospitalization preceded by an ED visit for chest pain or dyspnea.

The primary discharge diagnosis of acute myocardial infarction (ST-elevation myocardial infarction or nonST-elevation myocardial infarction) hospitalization was identified using ICD-9 and ICD-10 codes for KPSC and out-of-network (claims) admissions (Appendix E2, available at <http://www.annemergmed.com>) and was derived from a previously published list of validated codes for acute myocardial infarction.²⁴ Patients with mental health disorders and/or substance use disorders were identified as the cohort of interest to better understand how these comorbidities are associated with acute myocardial infarction diagnosis. Mental health and substance use disorders were categorized using ICD codes from the following Healthcare Cost and Utilization Project clinical classification software categorization schemes: 651 (anxiety-related disorders), 657 (mood-related disorders), 659 (schizophrenia-related disorders), 660 (alcohol-related disorders), and 661 (substance use-related disorders).²⁵ Patients were classified as having a pre-existing mental health or substance use disorder if they received any of the aforementioned diagnoses by a provider at any encounter in the year prior to or during their treat-and-release ED visit. A binary classifier variable (present vs absent) summing across all mental health disorders was created from anxiety disorders, mood disorders, and schizophrenia; a similar classifier variable was created for alcohol abuse disorders and substance use disorders.

Statistical Analysis

We calculated descriptive statistics, including counts, proportions, and means, as appropriate, for both look-back and look-forward analyses. We compared patient sociodemographics, vascular risk factors, and comorbidities

(including the proportion of patients with an Elixhauser comorbidity index score of more than 3) across the key comparison groups.⁹ A sensitivity analysis was conducted in a subgroup of the look-forward analysis, focusing on patients at higher risk of acute myocardial infarction, defined as adults older than 50 years with at least 1 cardiovascular risk factor (ie, coronary artery disease, hypertension, hyperlipidemia, diabetes, current smoker, or body mass index 30 or higher) in the year prior to the ED encounter. This subgroup analysis was done to understand if a population among ED patient encounters at higher risk of acute myocardial infarction than the general ED chest pain/dyspnea group had a stronger/weaker association of mental health or substance abuse disorders and missed acute myocardial infarction. We used logistic regression to calculate the odds of having a “missed” acute myocardial infarction in the look-back and look-forward analyses. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Proportions of missed acute myocardial infarctions were presented for patients with history of each disorder (ie, anxiety, mood disorder, schizophrenia, alcohol abuse, and substance abuse) as well as for binary classifiers (ie, mental health disorders, alcohol, and substance abuse disorders) (Table 1). Logistic regressions adjusting for age, sex, race, history of coronary artery disease, hypertension, diabetes, hyperlipidemia, stroke, peripheral vascular disease, and medical center were conducted for the binary classifiers of mental health disorders and alcohol/substance abuse disorders as well as the combination of both (Table 2). Due to historical disparities in the care of some racial and ethnic groups, we included these patient variables to understand any potential association with missed diagnoses in the models. A description of the definitions used to determine race and ethnicity in our data set, along with the accuracy of these designations, has been previously reported.²⁶ Clinical variables were dropped from the model if they did not impact OR or improve fit statistics. For quantitative comparisons, all *P* values were 2-sided, with α (type I) error set to equal 0.05. All analyses were conducted in SAS Enterprise Guide 7.1. This manuscript follows EQUATOR (STROBE) reporting guidelines for observational studies in epidemiology.²⁰ This study was approved by the KPSC Institutional Review Board.

RESULTS

Patient Characteristics or Demographics Representing High Risk

The look-back cohort included only patients with acute myocardial infarction hospitalizations and was a relatively

Table 1. Proportion of missed acute myocardial infarction among patients with mental health and substance abuse disorders in the look-back and look-forward cohorts.

Mental Health or Substance Use Disorder Diagnosis	Look Back (N = 44,473)				Look Forward (N = 325,088)			
	Proportion of Missed AMI* (N = 574)		Difference in Proportions (95% CI) ‡		Proportion of Missed AMI† (N = 508)		Difference in Proportions (95% CI) ‡	
	Patients With the Disorder	Patients Without the Disorder	Total (% of Look Back)		Patients With the Disorder	Patients Without the Disorder	Total (% of Look Forward)	
Mental health disorders	191 (1.8%)	383 (1.1%)	10593 (23.8%)	0.7% (0.4 to 1.0)	80 (0.2%)	428 (0.2%)	42807 (13.2%)	0.0% (-0.0 to 0.1)
Anxiety disorder	102 (1.9%)	472 (1.2%)	5333 (12.0%)	0.7% (0.4 to 1.1)	39 (0.2%)	469 (0.2%)	25678 (7.9%)	0.0% (-0.1 to 0.1)
Mood disorder	143 (1.8%)	431 (1.2%)	7985 (18.0%)	0.6% (0.3 to 1.0)	56 (0.2%)	452 (0.2%)	30173 (9.3%)	0.0% (-0.0 to 0.1)
Schizophrenia	11 (2.3%)	563 (1.3%)	479 (1.1%)	1.0% (-0.1 to 2.9)	3 (0.2%)	505 (0.2%)	1384 (0.4%)	0.1% (-0.1 to 0.5)
Alcohol and substance abuse disorders	54 (1.5%)	520 (1.3%)	3545 (8.0%)	0.3% (-0.1 to 0.7)	24 (0.2%)	484 (0.2%)	11101 (3.4%)	0.1% (-0.0 to 0.2)
Alcohol abuse disorder	19 (1.3%)	555 (1.3%)	1488 (3.3%)	0.0% (-0.5 to 0.7)	9 (0.2%)	499 (0.2%)	4862 (1.5%)	0.0% (-0.1 to 0.2)
Substance abuse disorders	42 (1.7%)	532 (1.3%)	2427 (5.5%)	0.5% (-0.0 to 1.1)	16 (0.2%)	492 (0.2%)	7884 (2.4%)	0.0% (-0.0 to 0.2)

AMI, Acute myocardial infarction; CL, confidence limit; ED, emergency department.

Bolded numbers represent statistically significant results.

*Probable Missed AMI: Principal diagnosis of nonspecific chest pain or dyspnea at ED treat-and-release visit in 30 days prior to AMI.

†Probable Missed AMI: ED treat-and-release encounter for chest pain or dyspnea discharged from ED with a subsequent AMI within 30 days of discharge.

‡95% Newcombe confidence limits.

homogeneous group in terms of age and vascular risk factors, with small differences between those with presumably missed acute myocardial infarctions and those without missed diagnoses. The look-forward analysis revealed large differences in vascular risk profiles of ED patients seen and discharged with chest pain or dyspnea who went on to have subsequent acute myocardial infarction hospitalizations relative to patients who did not (Table 3). For example, in the look-back cohort, patients with missed acute myocardial infarctions were slightly more likely to have Elixhauser comorbidity scores of more than 3 compared with acute myocardial infarction patients who were not considered missed (69.5% vs 63.7%). By contrast, in the look-forward cohort, 40.2% of patients seen at the ED who went on to have an acute myocardial infarction had Elixhauser comorbidity score of more than 3, while only 15.5% of patients who did not go on to have an acute myocardial infarction had a score of more than 3. Vascular risk factors were more common among patients who had an acute myocardial infarction compared with those who did not have 30-day acute myocardial infarction in the look-forward cohort, including active smokers (12.4% vs 8.3%), hypertension (65.7% vs 34.5%), diabetes (35.2% vs 15%), and lipid disorder (54.5% vs 27.6%). Although women were more likely to have missed acute myocardial infarction in the look-back cohort (43.4% missed were women vs 36.6% of those not missed), they were less likely to have missed 30-day acute myocardial infarction after treat-and-release ED visits in the look-forward cohort (57.2% women in the not-missed group vs 40.6% in the missed acute myocardial infarction group), reflecting, respectively, the challenges in addressing disparities in missed diagnoses for women due to the higher lifelong risk of myocardial infarction in men.²⁷

Main Results or Outcomes

The look-back analysis identified 44,473 acute myocardial infarction hospitalizations, and of these, 574 (1.3%) were associated with a treat-and-release ED visit in the 30 days prior for nonspecific chest pain or dyspnea (ie, “missed diagnoses”). Of the look-back cohort, 10,593 (23.8%) had a history of mental health disorders, while 3,545 (8.0%) had history of alcohol or substance abuse disorders. Of the patients with history of mental health or alcohol/substance abuse disorders, 1,395 had history of both. Patients with mental health disorders were more likely to have missed acute myocardial infarction (1.8% vs 1.1%; difference in proportions 0.7%; 95% CI 0.4 to 1.0), but patients with alcohol/substance use disorders did not have a

Table 2. Adjusted logistic regression in look-back and look-forward cohorts.

Mental Health or Substance Use Disorder Diagnosis	Look Back	Look Forward
	OR (95% CI)*	OR (95% CI)*
Mental health disorders vs none	1.48 (1.23 to 1.77)	0.92 (0.71 to 1.18)
Substance abuse disorder vs none	1.22 (0.91 to 1.62)	1.22 (0.80 to 1.85)
Mental health and substance abuse disorders vs neither	1.90 (1.30 to 2.76)	1.22 (0.68 to 2.19)

CAD, Coronary artery disease; CI, confidence interval; OR, odds ratio.

Bolded numbers represent statistically significant results.

*OR values are from logistic regression model that adjusted for age, sex, race, CAD hypertension, diabetes, hyperlipidemia, stroke, peripheral vascular disease, and medical center.

significantly higher rate of missed acute myocardial infarction (1.5% vs 1.3%; difference in proportions 0.3%; 95% CI -0.1 to 0.7) compared with patients without alcohol/substance abuse disorders. Among those patients with mental health disorders, patients with anxiety (1.9% vs 1.2%; difference in proportions 0.7%; 95% CI 0.4 to 1.1) or mood disorders (1.8% vs 1.2%; difference in proportions 0.6%; 95% CI 0.3 to 1.0) had higher proportions of missed acute myocardial infarctions. The proportion of missed acute myocardial infarctions did not differ between patients with and without history of alcohol use or substance use disorders. Adjusted results demonstrated higher odds of missed diagnoses for patients with mental health disorders compared with those without (OR 1.48, 95% CI 1.23 to 1.77) and was highest for those with mental health diagnoses and alcohol or substance abuse disorders compared with those with neither disorder (OR 1.90, 95% CI 1.30 to 2.76). The adjusted OR for patients with alcohol/substance use disorders was not statistically significant (OR 1.22, 95% CI 0.91 to 1.62) (Table 2) (full model can be found in Appendix E3, available at <http://www.annemergmed.com>).

The look-forward analysis identified 325,088 ED visits for chest pain/dyspnea during the study period; 508 encounters were associated with a missed acute myocardial infarction diagnosis (rate 0.2%). Of the look-forward cohort, 13.2% had history of mental health disorders ($n=42,807$), 3.4% ($n=11,101$) had history of alcohol or substance abuse disorders, and of these patients, 5,720 had history of both disorders. There was not a significant difference of missed acute myocardial infarction among patients with mental health disorders (0.19% vs 0.15%; difference in proportions 0.04%; 95% CI -0.01 to 0.08) and alcohol or substance abuse disorders (0.22% vs 0.15%; difference in proportions 0.06%; 95% CI -0.01 to 0.17) (Table 1) compared with patients without these disorders. Adjusted binary classifier results (Table 2) (full model can be found in Appendix E3) showed no statistically significant association between each diagnosis group and missed acute myocardial infarction

diagnoses (mental health disorders: OR 0.92; 95% CI 0.71 to 1.18; substance abuse disorders: OR 1.22, 95% CI 0.80 to 1.85) in the look-forward analysis. Similarly, we did not find a statistically significant association when looking at patients with history of both mental health disorders and alcohol or substance abuse disorders compared with patients with neither disorder (OR 1.22, 95% CI 0.68 to 2.19) (Table 2). We performed a subgroup analysis focusing on patients with higher risk of cardiovascular disease in the look-forward cohort (age of at least 50 years with at least 1 cardiovascular risk factor). We found no difference in the proportion of missed acute myocardial infarctions among patients with or without mental health disorders (0.3% vs 0.3%) or alcohol/substance use disorders (0.4% vs 0.3%) in this higher-risk group.

LIMITATIONS

Some limitations should be noted. Those with mental health and substance use disorders may present with atypical symptoms of acute myocardial infarction not captured by the symptom-disease pair used (ie, chest pain or dyspnea-related acute myocardial infarction). Therefore, reports of missed acute myocardial infarction may be underestimating true misdiagnosis and misdiagnosis-related harm. Additionally, reliance on administrative data as source data to accurately reflect diagnoses of acute myocardial infarction, mental health disorders, and substance use disorders without reference data (eg, chart review) for validation can be problematic.²⁸ Our study used the SPADE method to identify likely missed acute myocardial infarction diagnoses, which does not capture missed diagnoses that may result in 30-day death. Future research to include that group of patients will complement our study results. These limitations may have led to misclassification (over- or under-representation) of the diagnoses in each group. Lastly, our study was performed in an integrated health

Table 3. Characteristics of patients with or without missed acute myocardial infarction in the look-back and look-forward cohorts from 2009 to 2017.

Demographic Variable (n [%] Except for Age)	Look Back			Look Forward		
	No Missed AMI	Missed AMI*	Total	No Missed AMI [†]	Missed AMI [†]	Total
	N = 43,899 (98.7%) [‡]	N = 574 (1.3%) [‡]	N = 44,473	N = 324,580 (99.8%) [‡]	N = 508 (0.2%) [‡]	N = 325,088
Mean age (SD)	67.9 (14.0)	68.9 (14.2)	68.0 (14.0)	48.9 (20.7)	68.7 (13.9)	48.9 (20.7)
Female	16,087 (36.6%)	249 (43.4%)	16,336 (36.7%)	185,756 (57.2%)	206 (40.6%)	185,962 (57.2%)
Race/ethnicity						
Asian/Pacific Islander	3,940 (9.0%)	42 (7.3%)	3,982 (9.0%)	23,855 (7.3%)	34 (6.7%)	23,889 (7.3%)
Black	5,028 (11.5%)	83 (14.5%)	5,111 (11.5%)	43,383 (13.4%)	64 (12.6%)	43,447 (13.4%)
Hispanic	10,758 (24.5%)	142 (24.7%)	10,900 (24.5%)	120,003 (37.0%)	129 (25.4%)	120,132 (37.0%)
White	23,251 (53.0%)	291 (50.7%)	23,542 (52.9%)	124,869 (38.5%)	263 (51.8%)	125,132 (38.5%)
Others	922 (2.1%)	16 (2.8%)	938 (2.1%)	922 (2.1%)	16 (2.8%)	938 (2.1%)
Needs an interpreter	3,292 (7.5%)	43 (7.5%)	3,335 (7.5%)	3,292 (7.5%)	43 (7.5%)	3,335 (7.5%)
Married or partnered	25,013 (57.0%)	308 (53.7%)	25,321 (56.9%)	154,315 (47.5%)	282 (55.5%)	154,597 (47.6%)
Median income<45,000	10,697 (24.4%)	159 (27.7%)	10,856 (24.4%)	87,155 (26.9%)	140 (27.6%)	87,295 (26.9%)
Education						
At least some college	58.0 (18.6)	57.2 (17.5)	58.0 (18.56)	56.1 (19.0%)	56.9 (17.7%)	56.1 (19.0)
Active smoker	5,327 (12.1%)	66 (11.5%)	5,393 (12.1%)	27,000 (8.3%)	63 (12.4%)	27,063 (8.3%)
Elixhauser>3	27,973 (63.7%)	399 (69.5%)	28,372 (63.8%)	50,315 (15.5%)	204 (40.2%)	50,519 (15.5%)
CAD	21,445 (48.9%)	360 (62.7%)	21,805 (49.0%)	30,933 (9.5%)	231 (45.5%)	31,164 (9.6%)
Hypertension	34,893 (79.5%)	476 (82.9%)	35,369 (79.5%)	111,902 (34.5%)	334 (65.7%)	112,236 (34.5%)
Diabetes	18,144 (41.3%)	251 (43.7%)	18,395 (41.4%)	48,804 (15.0%)	179 (35.2%)	48,983 (15.1%)
Lipid disorder	34,060 (77.6%)	467 (81.4%)	34,527 (77.6%)	89,448 (27.6%)	277 (54.5%)	89,725 (27.6%)
Stroke	2,692 (6.1%)	30 (5.2%)	2,722 (6.1%)	2,548 (0.8%)	16 (3.1%)	2,564 (0.8%)
Peripheral vascular disorders 1 y prior	16,185 (36.9%)	242 (42.2%)	16,427 (36.9%)	26,674 (8.2%)	143 (28.1%)	26,817 (8.2%)

*Probable Missed AMI: Principal diagnosis of nonspecific chest pain or dyspnea at ED treat-and-release visit in 30 days prior to AMI hospitalization.

[†]Probable Missed AMI: ED treat-and-release encounter for chest pain or dyspnea discharged from ED with a subsequent AMI within 30 days of discharge.

[‡]Percentages in the column headers reflect proportions within that row (ie, denominator is the total in the same row). This is unlike most of the values in the rest of the table, which have as their denominator the total at the head of the respective column.

system with a high likelihood of in-system return visits—it is possible that the results found here may not fully generalize to other health systems. This includes differences in patient characteristics and baseline risks for acute myocardial infarction as well as potentially different rates of substance abuse and mental illness in different settings. Additionally, the use of the HEART score became widely implemented across KPSC EDs in May 2016 through electronic health record best practice advisories and linkage to performance measure incentives. The HEART score is a validated tool to predict 6-week risk of major adverse cardiac event in any patient presenting to the ED with chest pain deemed appropriate for acute coronary syndrome workup. Implementation of the HEART score is associated with decreased missed diagnosis rates through increased detection of acute myocardial infarction during index ED visits, thereby threatening the generalizability of our data to other ED sites with potentially less robust adoption of this prediction tool.²⁹

DISCUSSION

In this study, we used a previously validated SPADE approach to identify missed acute myocardial infarction diagnoses in the ED and evaluated the association of comorbid mental illness and substance use disorders with the risk of a missed diagnosis. Our analyses of 2 different cohorts (look-back and look-forward) each had distinct advantages. The look-back cohort primarily identified nonvascular risk factors among similar patients who had all experienced an acute myocardial infarction; this analysis found a higher odds of mental illness, particularly anxiety disorder, among those with a missed acute myocardial infarction. Additionally, those with substance abuse diagnoses were at slightly higher risk, and those patients with mental health diagnoses and substance abuse diagnoses had the highest risk of a missed acute myocardial infarction. By contrast, the look-forward cohort primarily helped to describe rates of missed events among a large diverse population of patients, offering an opportunity to target a population of patients for improvement (ie, ED patients discharged with a chest pain or dyspnea diagnosis); this analysis showed no substantial risk of misdiagnosis among patients with mental health or substance abuse diagnoses.

These results are consistent, in many ways, with past literature. Most studies looking at missed or delayed diagnoses used a strategy similar to our look-back approach that started with the diagnosis of interest to look back and identify potential risk factors.³⁰⁻³² This is

one reason our results from the look-back cohort are similar to a previous report of high-risk diagnoses missed in the ED that found patients with depression had increased odds (OR 1.32) of a missed acute myocardial infarction.¹¹ The challenge with this approach is that it does not necessarily translate into improved patient care among the prospective cohort of patients that physicians and health systems would target for improvement.^{33,34} This was apparent in our look-forward analysis, which found a misdiagnosis rate of just 0.2%, demonstrating the challenges of finding at-risk patients who may benefit from any practice improvement intervention. Not surprisingly, the look-forward cohort found that known coronary artery disease risk factors (age, diabetes, hypertension, dyslipidemia, etc) were associated with a miss because they are known to be associated with an acute myocardial infarction. We hope that physicians are already aware of these well-documented cardiovascular risks associated with acute myocardial infarction.

There is a need for future research to identify effective ways to improve diagnostic accuracy, specifically targeting vulnerable patient populations, such as those with mental illnesses and substance abuse disorders. As physicians seek to understand ways to improve, there is evidence to support the use of decision support and/or clinical pathways using standard risk assessment to improve care and potentially reduce disparities in outcomes for patients with symptoms like chest pain and dyspnea.³⁵⁻³⁷

In conclusion, our look-back analysis found an increased risk of missed acute myocardial infarction diagnoses among patients with mental health disorders, particularly anxiety disorders, and this risk was the highest among those with a comorbid substance use disorder. However, we found no association of missed acute myocardial infarction among patients with alcohol/substance abuse disorders alone in the adjusted analyses of either cohort. Our look-forward results confirm the challenges in identifying patients at high risk of a missed acute myocardial infarction diagnosis, calling for future research to improve diagnostic accuracy for vulnerable patient populations.

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All authors attest to meeting the four [ICMJE.org](https://www.icmje.org) authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement 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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