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# Healthcare resource utilization among patients receiving non-invasive testing for coronary artery disease in an outpatient setting: A cohort study reflecting daily practice trends

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**Background.** Accurate, early diagnosis and the initiation of appropriate treatment is central to reducing the clinical burden of coronary artery disease (CAD); however, real-world evidence characterizing healthcare resource utilization (HCRU) associated with testing for CAD is lacking.

**Methods and Results.** Using a non-interventional, retrospective, secondary database analysis, patients aged  $\geq 18$  years who underwent outpatient non-invasive cardiac diagnostic testing were identified. The primary objective was to gain an understanding of pre- and post-assessment care pathways and the associated interventions for patients who underwent non-invasive testing for CAD in either an outpatient or emergency department setting. Overall, chest pain was the primary reason for the index visit (54.8%), followed by shortness of breath (23.7%), myocardial infarction (MI), coronary artery disease (CAD) or congestive heart failure (CHF) (3.8%), and other (46.8%); 3.0% of patients had no apparent reason for testing in the last 45 days. Single-photon emission computed tomography (SPECT) was the dominant diagnostic testing modality (40.3%). During the 90-day follow-up, 7.3% ( $n = 22,083$ ) of patients were diagnosed with CAD; among these patients, 19.4% had repeat diagnostic testing, 26.0% of patients had a revascularization procedure, and 65.6% underwent cardiac catheterization. These rates varied by testing modality.

**Conclusions.** In this study of a large real-world data sample, variability in the use of non-invasive tests and HCRU were evident. These results may assist efforts to optimize system-wide care/diagnostic pathways and value-based treatment decisions for patients. (J Nucl Cardiol 2021)

**Key Words:** CAD < diseases/processes • SPECT < modalities • ETT < tests • Diagnostic and prognostic application < outcomes

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s12350-021-02549-2>.

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## INTRODUCTION

In the United States (US), cardiovascular disease is responsible for one in 3 deaths annually with coronary artery disease (CAD) resulting in one in 7 all-cause deaths.<sup>1,2</sup> Consequently, evaluations for suspected CAD account for a substantial percentage of ambulatory health care visits as early diagnosis and treatment are critical to minimizing the clinical burden associated with CAD.<sup>3</sup> Accordingly, various non-invasive tests are widely available for diagnosing CAD, including coronary artery calcium (CAC) for identifying early coronary atherosclerosis; exercise treadmill testing (ETT), stress echocardiography (SE), single-photon emission computed tomography (SPECT), positron emission tomography (PET), and stress magnetic resonance imaging (MRI) for evaluating functional aspects of ischemia; and coronary computed tomography angiography (CTA) and invasive angiography to identify anatomic evidence of ischemia.<sup>4</sup> Locally available resources and expertise are the primary factors that influence which non-invasive testing modality is used, and indications for testing are adopted using published appropriate use criteria and clinical practice guidelines.<sup>5</sup>

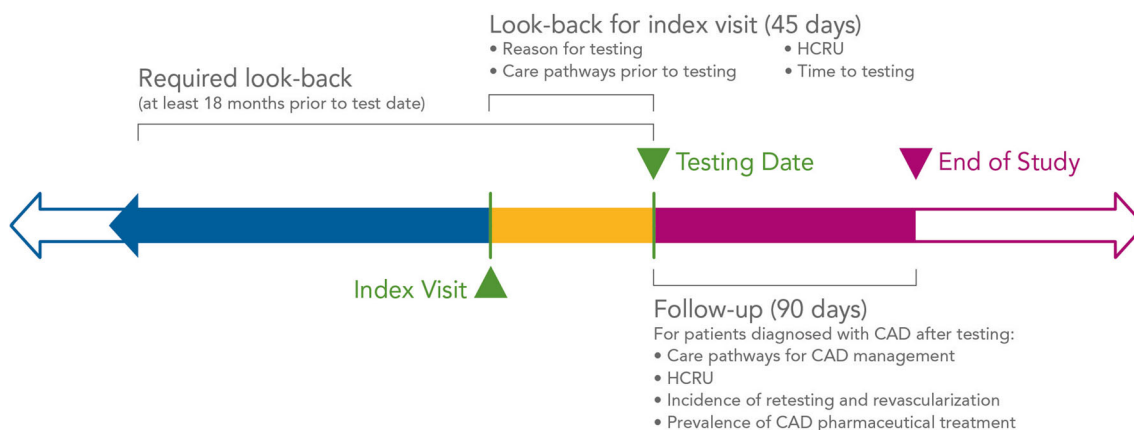
One of the biggest challenges that healthcare systems face is ensuring efficient delivery of care.<sup>6-9</sup> Each year, an estimated \$700 billion is wasted in the US healthcare system as a result of overuse, underuse, and misuse of healthcare services.<sup>6</sup> For CAD, inefficient diagnoses of treatable disease can result in negative and costly consequences (eg, missing significant disease, unnecessary downstream testing) that can impact patients (eg, unnecessary testing, delayed diagnosis and care, worsened outcomes), providers (eg, stress, overload), and healthcare systems (eg, reduced quality, sustainability).<sup>10</sup> The consequences and associated costs partially depend on the role of a test in the diagnostic

pathway and its convenience and availability.<sup>9</sup> However, studies evaluating healthcare resource utilization (HCRU) incident to the choice of a test applied or the factors that impact the quality and timely care of these patients are lacking. Therefore, the purpose of this study was to gain an understanding of HCRU and interventions associated with non-invasive testing for CAD in either an outpatient or emergency department setting; the current report is focused on observations in the outpatient setting only.

## METHODS

### Study Design

This study was a non-interventional, retrospective, secondary database cohort analysis of IBM MarketScan commercial and Medicare claims data (Figure 1). The MarketScan Commercial Database is largely an employer-based administrative database that contains the health insurance claims from inpatient, outpatient, and outpatient prescription drug encounters for employees and their dependents since 1995. Coverage for beneficiaries fall under a variety of fee-for-service and managed care health plans, including Exclusive Provider Organizations (EPOs), Preferred Provider Organizations (PPOs), Point of Service Plans (POS), indemnity plans, and Health Maintenance Organizations (HMOs). Similarly, the MarketScan Medicare Supplemental Database contains the healthcare insurance claims (both medical and pharmacy) for approximately 13.8 million retirees with Medicare supplemental insurance paid for by employers since 1995 and through 2016. Both the Medicare-covered portion of payment and the employer-paid portion are included in this database. Both the MarketScan Commercial and Medicare Databases



**Fig. 1.** Study schematic diagram. CAD coronary artery disease; HCRU healthcare resource use.

provide detailed cost, use, and outcomes data for healthcare services performed in both inpatient and outpatient settings. Medical claims are linked to outpatient prescription drug claims and person-level enrollment data through unique enrollee identifiers.

The primary study objectives were to (1) describe the clinical and demographic characteristics of the patient population presenting with symptoms suspicious for CAD who received non-invasive cardiac testing in the OP setting and (2) characterize the HCRU of the patient population in the 45 days prior to undergoing testing. The secondary objectives were to (1) assess factors associated with the time from presentation of symptoms suspicious for CAD to non-invasive diagnostic testing and (2) describe treatment patterns, cardiac-related clinical outcomes and interventions, and HCRU in patients diagnosed with CAD post-testing in the 90 days following CAD diagnosis.

Patients who received non-invasive CAD diagnostic testing between March 1, 2014 and December 31, 2017 in an OP setting were identified (Figure 1). The time frame for identifying the index visit was up to 45 days prior to and including the testing date or the first healthcare encounter that included a claimed precipitating reason for testing. Post-assessment interventions were evaluated for up to 90 days after the test date in patients who were diagnosed with CAD based on the index diagnostic testing.

### Selection of the Study Population

Included patients were aged  $\geq 18$  years who underwent non-invasive cardiac diagnostic testing (ETT, SE, SPECT, CTA, CAC, stress MRI, and PET) on or after March 1, 2014 in an OP setting (eg, physician office, OP lab) with  $\geq 18$  months of continuous enrollment in the health plan prior to testing. Patients were excluded if they had record of the following prior to testing: a non-invasive cardiac diagnostic test; a diagnosis or claim for revascularization, heart transplant, or heart valve surgery; or myocardial infarction (MI) or congestive heart failure (CHF) more than 45 days before testing. Patients who had a preoperative examination, exercise prescription, or cardiac rehabilitation in the 45 days prior to the testing date were also excluded. Of note, patients with MI, CAD, or CHF were allowed in the study if their *first diagnoses* for any of these conditions occurred in the 45 days prior to testing since these diagnoses are indications for testing.

### Analysis

All analyses were stratified by testing modality. Time to testing was modeled using a zero-inflated

negative binomial regression model that included baseline covariates (age, gender, setting, precipitating reason for index visit, and medication history) and testing modality as predictors of time to testing; relative to the reference group (patients who underwent SE), a RR  $< 1.0$  indicated a shorter time from index visit to testing. Variables included in the adjusted model were based on a review of univariate effects and clinical input. To understand associations between baseline variables and the rate of repeat diagnostic testing and revascularization, Andersen-Gill models that included baseline covariates and testing modality as predictors were constructed.

## RESULTS

### All Screened Patients

**Baseline sociodemographic and clinical characteristics** The study population included 303,052 patients; the median age was 56 years, ranging from 52 to 59 years across testing modalities, and gender proportions differed by testing modality (Table 1; baseline data for patients with CAD post-testing are shown in Table S1). Chest pain was the primary precipitating reason for the index visit (54.8%), followed by shortness of breath (23.7%); an MI, CAD, or CHF (3.8%) diagnosis; and other (46.8%); 3.0% of patients had no apparent reason for testing in the last 45 days. Dyslipidemia and hypertension were the most common comorbidities (Table 1), and SPECT was the dominant testing modality (40.3%).

**HCRU within 45 days prior to and including testing date** HCRU differed by testing modality in the 45 days prior to testing. Fewer cardiac-related OP visits in patients undergoing CAC (mean of 3.5 for CAC vs 3.8 for ETT and 4.0-4.8 for the other modalities) and fewer unique OP medications in patients undergoing CAC or ETT (mean of 2.0 for each vs 2.3-3.6 for the other modalities; Table 2). Initiation of new cardiac-related medications during this time was uncommon, with the highest rate ( $< 5\%$ ) being for antihypertensive/antianginal medications. The most common pattern of patient encounters with healthcare providers within 45 days prior to testing was the patient initially presenting in an outpatient “other” (eg, family medicine, internal medicine, or obstetrician-gynecology practice) setting followed by an encounter in an outpatient cardiology/outpatient “other” setting for testing. A few (10%) patients who underwent CTA initially presented in an OP cardiology setting, followed by testing in an OP “other” setting.

**Factors associated with time to testing** Median time to testing was  $> 10$  days across all

**Table 1.** Baseline patient characteristics

	ETT	SE	SPECT	CTA	CAC	PET	Stress MRI	Total
N	91,859	77,708	122,233	5,337	3,650	1,902	363	303,052
Female, <i>n</i> (%)	44,768 (48.7)	42,619 (54.8)	64,560 (52.8)	2,641 (49.5)	1,842 (50.5)	1,113 (58.5)	193 (53.2)	157,736 (52.0)
Age, median (Q1, Q3)	52 (44, 59)	55 (47, 62)	59 (52, 64)	54 (45, 61)	57 (50, 62)	59 (52, 65)	52 (40, 59)	56 (48, 62)
Comorbidities, <i>n</i> (%)								
Diabetes with complications	3,044 (3.3)	3,424 (4.4)	11,095 (9.1)	215 (4.0)	107 (2.9)	252 (13.2)	19 (5.2)	18,156 (6.0)
Diabetes without complications	13,569 (14.8)	13,339 (17.2)	35,339 (28.9)	1,035 (19.4)	525 (14.4)	713 (37.5)	66 (18.2)	64,586 (21.3)
Mild CKD	837 (0.9)	885 (1.1)	2,262 (1.9)	60 (1.1)	41 (1.1)	60 (3.2)	3 (0.8)	4,148 (1.4)
Moderate or severe CKD	1,215 (1.3)	1,533 (2.0)	4,521 (3.7)	59 (1.1)	55 (1.5)	113 (5.9)	10 (2.8)	7,506 (2.5)
Dyslipidemia	52,180 (56.8)	47,584 (61.2)	89,686 (73.4)	3,568 (66.9)	2,729 (74.8)	1,442 (75.8)	184 (50.7)	197,373 (65.1)
Gastroesophageal reflux disease	27,739 (30.2)	24,692 (31.8)	46,495 (38.0)	1,883 (35.3)	1,035 (28.4)	763 (40.1)	117 (32.2)	102,724 (33.9)
Hypertension	46,783 (50.9)	42,550 (54.8)	89,179 (73.0)	3,144 (58.9)	1,847 (50.6)	1,530 (80.4)	193 (53.2)	185,226 (61.1)
Cardiac rhythm disorders	25,947 (28.2)	22,888 (29.5)	38,985 (31.9)	1,813 (34.0)	591 (16.2)	711 (37.4)	186 (51.2)	91,121 (30.1)
Medication history, <i>n</i> (%)								
Cholesterol-lowering medications	28,841 (31.4)	27,380 (35.2)	57,101 (46.7)	2,075 (38.9)	1,412 (38.7)	940 (49.4)	122 (33.6)	117,871 (38.9)
Antihypertensive/antianginal medications	23,860 (26.0)	23,043 (29.7)	50,302 (41.2)	2,670 (50.0)	852 (23.3)	976 (51.3)	162 (44.6)	101,865 (33.6)
Antiplatelet therapy	634 (0.7)	700 (0.9)	2,648 (2.2)	68 (1.3)	20 (0.5)	53 (2.8)	3 (0.8)	4,126 (1.4)
Antihypertensive medications	33,266 (36.2)	31,318 (40.3)	66,656 (54.5)	2,150 (40.3)	1,262 (34.6)	1,215 (63.9)	165 (45.5)	136,032 (44.9)
Medications to treat diabetes	9,711 (10.6)	9,695 (12.5)	25,430 (20.8)	670 (12.6)	362 (9.9)	529 (27.8)	56 (15.4)	46,453 (15.3)
Antianginal medications	2,179 (2.4)	2,122 (2.7)	6,472 (5.3)	315 (5.9)	44 (1.2)	102 (5.4)	11 (3.0)	11,245 (3.7)

CAC coronary artery calcium; CKD chronic kidney disease; CTA computed tomography angiography; ETT exercise treadmill testing; MRI magnetic resonance imaging; PET positron emission tomography; SE stress echocardiogram; SPECT single-photon emission computerized tomography

testing groups; median (Q1-Q3) times to testing were 11 days (3-24) for ETT, 12 days for SE (3-24) and CAC (0-28), 13 days (4-25) for SPECT, 17 days (7-30) for PET, 21 days (8-34) for CTA, and 25 days (7-36) for stress MRI (Table 3). Chest pain (relative risk [RR] = 0.73) and shortness of breath (RR = 0.90) were associated with a shorter time to testing; presence (vs absence) of

CHF diagnosis in the 45 days prior to testing was typically associated with a longer time to testing (RR = 1.1), while the presence (vs absence) of a MI diagnosis in the 45 days prior to testing was associated with shorter times to testing (RR = 0.91). With regards to testing modality, patients undergoing ETT (RR = 0.98) or SPECT (RR = 0.989) experienced a shorter time to

**Table 2.** HCRU within 45 days prior to and including testing date

Testing modality	OP encounters, mean (SD)	Cardiac-related OP encounters <sup>a</sup> , mean (SD)	Unique OP medications <sup>b</sup> , mean (SD)
ETT (N = 91,859)	3.8 (2.4)	2.2 (1.2)	2.0 (2.4)
SE (N = 77,708)	4.0 (2.5)	2.2 (1.1)	2.3 (2.5)
SPECT (N = 122,233)	4.4 (2.8)	2.4 (1.2)	3.0 (3.0)
CTA (N = 5,337)	4.7 (2.9)	2.8 (1.6)	2.6 (2.8)
CAC (N = 3,650)	3.5 (2.4)	1.0 (1.2)	2.0 (2.4)
PET (N = 1,902)	4.8 (3.0)	2.6 (1.4)	3.6 (3.3)
Stress MRI (N = 363)	4.8 (3.2)	2.5 (1.9)	3.0 (3.2)
Total (N = 303,052)	4.1 (2.6)	2.3 (1.2)	2.5 (2.7)

CAC coronary artery calcium; CTA computed tomography angiography; ETT exercise treadmill testing; MRI magnetic resonance imaging; OP outpatient; PET positron emission tomography; SE stress echocardiogram; SPECT single-photon emission computerized tomography

<sup>a</sup>Based on a diagnosis of chest pain, shortness of breath, MI, CAD, CHF or other

<sup>b</sup>The counts of unique OP medications are based on the generic names field in Red Book

testing compared to patients undergoing other testing modalities (RR >1, using SE as the reference testing modality). Furthermore, a record of a cardiologist visit prior to or including testing date increased time to testing.

### CAD Patients With 90-Day Follow-up

**Rates of repeat diagnostic testing, cardiac catheterization, and revascularization ≤90 days post-CAD diagnostic testing among patients diagnosed with CAD** After initial testing, 7.3% ( $n = 22,083$ ) of patients (range, 4.2% [ETT patients]—20.1% [CTA patients]) were diagnosed with CAD, the majority (63.3%) of which were males (Table 4). Overall, 19.4% had repeat diagnostic testing in 90 days after initial testing, 65.6% of patients diagnosed with CAD underwent cardiac catheterization, and 26.0% underwent a coronary revascularization procedure. Among patients who received repeat diagnostic testing within 90 days post-index ( $n = 4,200$ ), the testing modalities most frequently associated with repeat testing were CAC (90-day cumulative incidence, 51.6%) and ETT (36.7%), while patients who underwent PET, SPECT, or CTA were less likely to undergo repeat testing (Table 4 and Figure 2). Consistent with the results of the 90-day cumulative incidence, patients who underwent CAC (HR = 2.866) or ETT (HR = 2.121) testing had significantly higher rates of repeat diagnostic testing, while patients who underwent PET (HR=0.587), SPECT (HR = 0.824), or CTA (HR = 0.817) had significantly lower rates of repeat testing using SE as the reference group. Revascularization rates were similar in

patients who underwent ETT, SE, or SPECT, while revascularization rates were lower for CTA (HR = 0.727) and CAC (HR = 0.370) (Table 4).

Per the multivariate model, other baseline characteristics apart from testing modalities were also found to be associated with rates of repeated diagnostic testing and revascularization. Using 40-59 years as the reference age group, the 80+ years age group had a lower rate of repeat diagnostic testing (HR = 0.753) and catheterization procedures (HR = 0.919); revascularization rates were higher in patients 60+ years (HR = 1.241 for 60-79 years, HR = 1.331 for 80+ years) and lower in patients <40 years (HR = 0.525), who also had a lower rate of catheterization in (HR = 0.744). This finding is expected given lower likelihood of CAD in patients <40 years ago. Females had a higher rate of repeat diagnostic testing (HR = 1.065) and lower rates of revascularization (HR = 0.555) and catheterization (HR = 0.913) than males. These constellations of findings are explained by the challenges of non-invasive testing in women, leading to more repetitive testing along with higher likelihood of nonobstructive or microvascular disease in women presenting with chest pain.<sup>11</sup>

For co-morbidities and medication history, the reference group was those without that condition or medication history. Patients who had history of being on antianginal medications had lower rates of repeat diagnostic testing (HR=0.824) and high rates of revascularization (HR = 1.333) and catheterization (HR = 1.117). Catheterization rates were lower in patients with chronic kidney disease (HR = 0.923) or dyslipidemia (HR = 0.973), but higher in patients with diabetes with complications (HR = 1.084) or hypertension (HR =

**Table 3.** Time to testing according to testing modality, precipitating reason for index visit, and comorbidities

	<b>Median (Q1-Q3)</b>	<b>Crude RR</b>	<b>(95%CI)</b>	<b>Adjusted RR</b>	<b>(95% CI)</b>
Testing modality					
ETT	11 (3-24)	0.992	(0.983-1.000)	0.98 <sup>a</sup>	(0.976-0.992)
SE	12 (3-24)	Ref.	(Ref.-Ref.)	Ref.	(Ref.-Ref.)
SPECT	13 (4-25)	0.994	(0.987-1.002)	0.989 <sup>a</sup>	(0.982-0.997)
CTA	21 (8-34)	1.345 <sup>a</sup>	(1.315-1.376)	1.335 <sup>a</sup>	(1.306-1.366)
CAC	12 (0-28)	1.203 <sup>a</sup>	(1.167-1.240)	1.056 <sup>a</sup>	(1.025-1.087)
PET	17 (7-30)	1.18 <sup>a</sup>	(1.137-1.225)	1.144 <sup>a</sup>	(1.104-1.186)
MRI	25 (7-36)	1.498 <sup>a</sup>	(1.374-1.632)	1.361 <sup>a</sup>	(1.252-1.479)
Any cardiologist visit pre-testing	12 (3-25)	0.999	(0.992-1.005)	0.992 <sup>a</sup>	(0.986-0.998)
Precipitating reason for index visit					
Chest Pain	10 (3-21)	0.732 <sup>a</sup>	(0.728-0.737)	0.73 <sup>a</sup>	(0.725-0.734)
Shortness of breath	11 (3-23)	0.953 <sup>a</sup>	(0.946-0.960)	0.902 <sup>a</sup>	(0.895-0.908)
MI, CAD, or CHF	14 (4-28)	1.135 <sup>a</sup>	(1.122-1.148)	1.043 <sup>a</sup>	(1.030-1.057)
Comorbidities					
Myocardial infarction	15 (5-28)	1.049 <sup>a</sup>	(1.003-1.098)	0.912 <sup>a</sup>	(0.871-0.954)
Congestive heart failure	21 (9-34)	1.275 <sup>a</sup>	(1.243-1.308)	1.103 <sup>a</sup>	(1.074-1.134)

CAC coronary artery calcium; CAD coronary artery disease; CHF congestive heart failure; CI confidence interval; CTA computed tomography angiography; ETT exercise treadmill test; MI myocardial infarction; MRI magnetic resonance imaging; PET positron emission tomography; RR relative risk; SE stress echocardiogram; SPECT single-photon emission computerized tomography  
<sup>a</sup>Significant adjusted HR

1.055). Additionally, patients who had chest pain (HR = 1.50) and shortness of breath (HR = 1.116) as precipitating reason for index visit and those with comorbidities such as diabetes (HR = 1.311), hypertension (HR = 1.09) or dyslipidemia (HR = 1.088) had higher rates of revascularization. Furthermore, increases in the number of prescriptions were observed for some medication classes and HCRU differed by testing modality (Table 5).

**HCRU ≤90 days post-CAD diagnostic testing date among patients diagnosed with CAD** Overall, the median number of OP visits were the same (median = 6) across all testing modalities, with slightly fewer median visits seen for CAC (median = 5); the median number of cardiac OP visits was 3 for all modalities except for SPECT and MRI (median = 4, both). For both general and cardiac-related inpatient and ED visits, the median number of days did not differ across all modalities (median = 0). For those patients hospitalized during this 90-day time period for any reason, the median length of stay was 6 days for all modalities except for CTA and CAC (median = 5).

## DISCUSSION

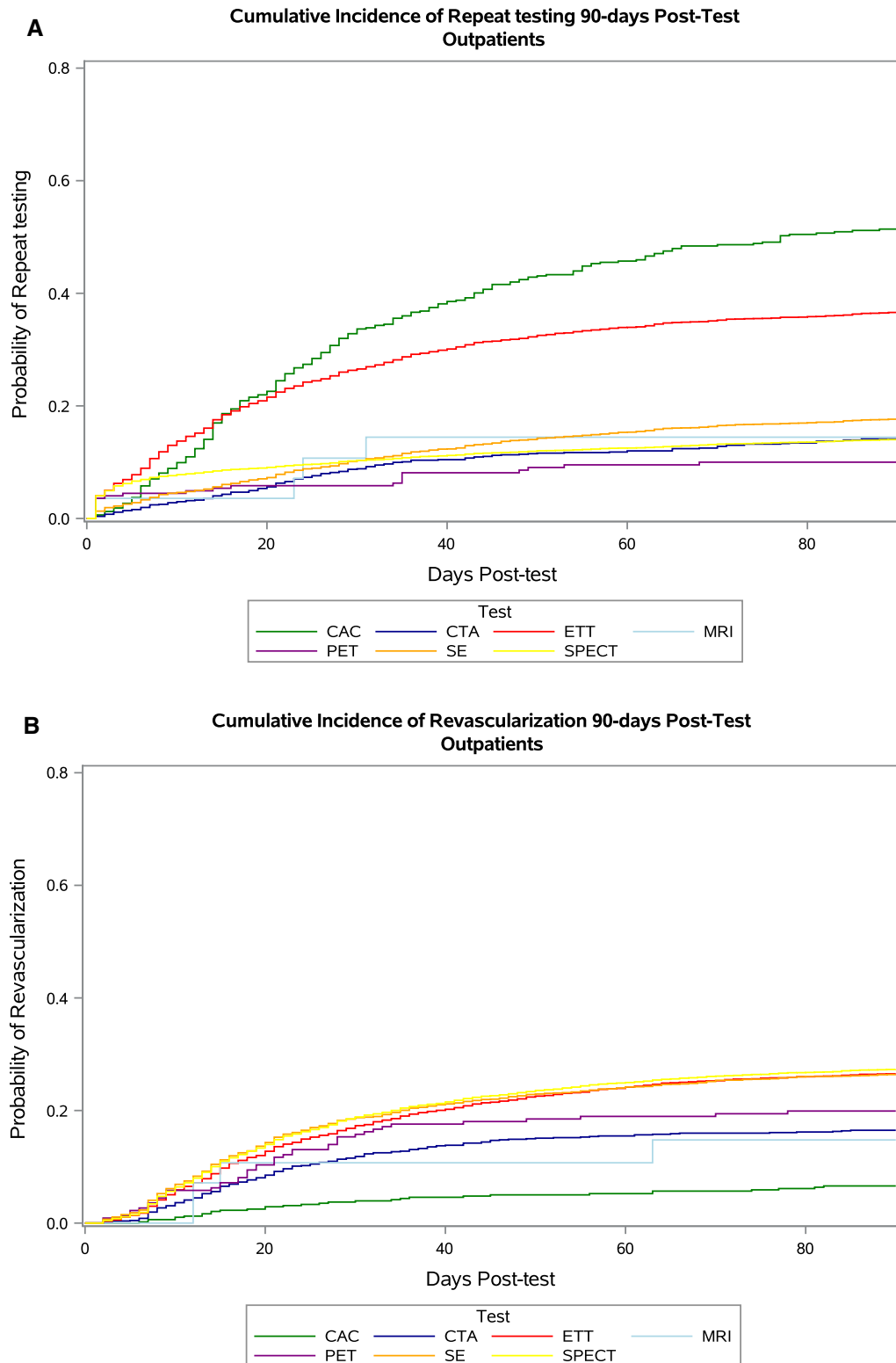
Understanding the value of and optimizing system-wide diagnostic and treatment processes (eg, reducing time from the onset of symptoms to appropriate diagnostic testing, ensuring patients receive appropriate follow-up), present opportunities to improve outcomes and ensure efficient use of healthcare resources. Accordingly, the results of this study suggest that (1) patient characteristics and symptoms drive diagnostic testing decisions; (2) a minority of the study population tested were diagnosed with CAD, potentially highlighting challenges in current diagnostic testing strategies; and (3) HCRU of medications and revascularization based on test results reflect variations in practice. SPECT appears to be the most common modality used for diagnostic testing in CAD, although revascularization rates did not differ among diagnostic modalities. Time to testing differed by test and clinical factors after multivariate adjustment. For example, a longer time to testing for SPECT relative to SE was anticipated based on the known preauthorization in real-world practice; however, time to testing was in fact shorter with a small but potentially meaningful difference. One potential reason for this finding is that SPECT was used in higher-risk



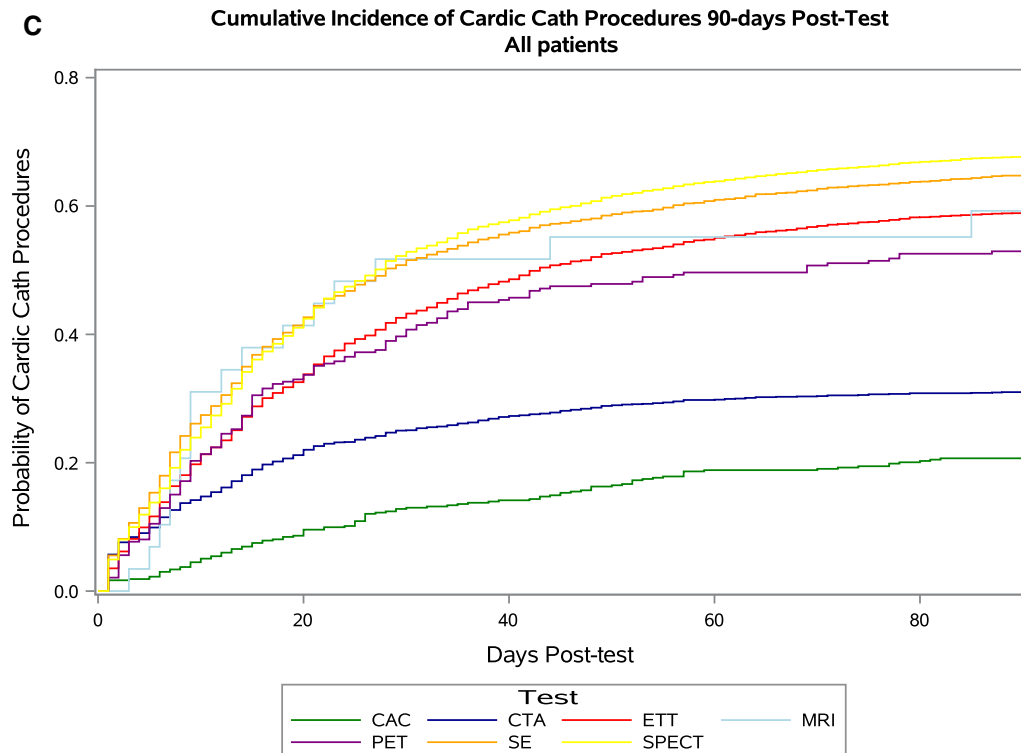
**Table 4.** CAD diagnoses and procedures/interventions up to 90 days post-CAD diagnostic testing among patients diagnosed with CAD

Testing modality	Diagnosis of CAD after testing (% of patients)	Repeat diagnostic testing			Revascularization			Cardiac catheterization		
		90-Day cumulative incidence (%)	Adjusted HR	95% CI	90-Day cumulative incidence (%)	Adjusted HR	95% CI	90-Day cumulative incidence (%)	Adjusted HR	95% CI
ETT (N = 3,836)	4.2	36.7	2.121 <sup>a</sup>	1.946, 2.311	1.004	1.004	0.929, 1.086	61.0	0.906 <sup>a</sup>	0.877, 0.936
SE (N = 3,532)	4.5	17.7	Ref.	Ref., Ref.	Ref.	Ref.	Ref., Ref.	66.5	Ref.	Ref., Ref.
SPECT (N = 12,904)	10.6	14.1	0.824 <sup>a</sup>	0.756, 0.898	1.017	1.017	0.953, 1.084	70.7	1.074 <sup>a</sup>	1.048, 1.101
CTA (N = 1,075)	20.1	14.1	0.817 <sup>a</sup>	0.690, 0.968	0.727 <sup>a</sup>	0.727 <sup>a</sup>	0.624, 0.846	40.7	0.716 <sup>a</sup>	0.663, 0.773
CAC (N = 484)	13.3	51.6	2.866 <sup>a</sup>	2.538, 3.236	0.370 <sup>a</sup>	0.370 <sup>a</sup>	0.253, 0.541	18.9	0.321 <sup>a</sup>	0.267, 0.388
PET (N = 224)	11.8	10.0	0.587 <sup>a</sup>	0.392, 0.880	0.817	0.817	0.618, 1.082	56.7	0.925	0.829, 1.032
Stress MRI (N = 28)	7.7	14.4	0.942	0.360, 2.466	0.636	0.636	0.271, 1.495	57.8	0.941	0.683, 1.297

<sup>a</sup> Significant adjusted HR; adjusted HRs were considered significant if the CI did not include 1  
CAC coronary artery calcium; CAD coronary artery disease; CI confidence interval; CTA computed tomography angiography; ETT exercise treadmill test; HR hazard ratio; MRI magnetic resonance imaging; n/a not available; OP outpatient; PET positron emission tomography; SE stress echocardiogram; SPECT single-photon emission computerized tomography



**Fig. 2.** Cumulative incidence function of (A) Repeated diagnostic testing, (B) Revascularization, and (C) cardiac catheterization in the outpatient setting. *CAC* coronary artery calcium; *CTA* computed tomography angiography; *ETT* exercise treadmill test; *MRI* magnetic resonance imaging; *PET* positron emission tomography; *SE* stress echocardiogram; *SPECT* single-photon emission computerized tomography.



**Fig. 2.** continued.

patients in our study, where it would be considered appropriate and thus not require a lengthy preauthorization process.

One noteworthy observation pertains to the use of CAC, which led to more retesting and less revascularization relative to the other testing modalities; this is supported by results from previously conducted studies in asymptomatic populations.<sup>12</sup> Calcium score is a reflection of overall burden of atherosclerosis, and although higher scores may indicate a higher likelihood of obstructive CAD, patients with markedly elevated calcium scores may not necessarily have obstructive disease causing ischemia.<sup>13,14</sup> Accordingly, this test is considered “rarely appropriate” in symptomatic patients according to diagnostic guidelines as detection of non-calcified obstructive disease may be missed in some cases, particularly in younger patients.<sup>15</sup> Clinicians use a low calcium score (<100) to avoid further testing and higher calcium scores >400 to further evaluate for ischemia. Although details of calcium score burden are not available in the dataset for our study, the trend of increased downstream testing reflects the downstream effects of CAC when abnormal. ETT followed the same trend as CAC with respect to repeat diagnostic testing likely due to lower overall sensitivity

and specificity, thus prompting clinicians to order further testing to evaluate for CAD depending on clinical suspicion based on test results. Overall, there was substantial variability between tests with respect to medication change, repeat diagnostic testing, revascularization, and cardiac catheterization rates. Our study suggests that some noninvasive CAD tests, such as ETT and CAC, may lead to further downstream diagnostic evaluations, whereas SPECT, the most commonly used testing modality observed in this study, serve to more efficiently triage patients for invasive testing/revascularization; these findings confirm those of other studies that indicated the incremental benefit of SPECT as a diagnostic strategy in higher risk patients and as a gate keeper to avoid additional downstream testing when SPECT is normal, given its high negative predictive value.<sup>16</sup>

Although the SPECT group had higher catheterization rates than with SE, revascularizations were no different between the 2 groups. Perfusion-based diagnostic tests in general have a higher sensitivity for CAD relative to wall motion-based techniques like SE, but can be abnormal in a multitude of conditions apart from obstructive CAD (leading to lower specificity when compared to invasive angiography). Clinically and

**Table 5.** HCRU up to 90 days post-CAD diagnostic testing among patients diagnosed with CAD

Testing modality	Med Management Change (% Increased Post-Testing)							
	OP encounters, mean (SD)	Cardiac-related OP encounters <sup>a</sup> , mean (SD)	Unique OP medications <sup>b</sup> , mean (SD)	Cholesterol-lowering	Antihypertensive or antianginal <sup>c</sup>	Antiplatelet	Antianginal	Antihypertensive
ETT (N = 3,836)	7.9 (6.3)	4.4 (3.9)	5.1 (4.0)	21.0	21.1	21.5	18.2	7.3
SE (N = 3,532)	8.2 (6.6)	4.4 (4.2)	5.4 (4.1)	20.4	21.3	22.6	18.6	7.2
SPECT (N = 12,904)	8.5 (6.6)	4.5 (3.8)	6.1 (4.6)	16.6	18.5	20.9	18.9	5.9
CTA (N = 1,075)	7.2 (6.0)	3.5 (3.3)	4.8 (4.0)	19.9	9.6	15.2	12.0	3.7
CAC (N = 484)	5.9 (4.6)	2.6 (2.0)	4.2 (4.0)	20.8	6.4	5.8	6.8	4.2
PET (N = 224)	7.9 (6.1)	3.6 (3.2)	6.6 (4.7)	10.5	12.1	15.0	20.8	3.7
Stress MRI (N = 28)	8.8 (6.6)	5.6 (6.0)	5.8 (4.2)	15.3	26.4	7.1	18.3	3.6
Total (N = 22,083)	8.3 (6.5)	4.3 (3.8)	5.7 (4.4)	18.2	18.6	20.6	18.1	6.1

CAC coronary artery calcium; CTA computed tomography angiography; ETT exercise treadmill testing; HCRU healthcare resource use; MRI magnetic resonance imaging; OP outpatient; PET positron emission tomography; SE stress echocardiogram; SPECT single-photon emission computerized tomography

<sup>a</sup>Based on a diagnosis of chest pain, shortness of breath, MI, CAD, CHF or other

<sup>b</sup>The counts of unique OP medications are based on the generic names field in Red Book

<sup>c</sup>Antihypertensive/antianginal agents include calcium channel blockers, beta blockers, and combination products

prognostically relevant perfusion abnormalities can be detected even in the absence of CAD (such as diffuse non-obstructive atherosclerosis or microvascular disease secondary to comorbidities such as diabetes and hypertension).<sup>17,18</sup> Hence, it is likely that there is a higher referral bias related to abnormal SPECT for catheterizations, but not necessarily leading to revascularizations.

Our findings also reflect on some management trends following CAD diagnosis, as not all patients are started on cardiac medications or referred for cardiac catheterization when diagnostic studies are abnormal. The reasons for this are multifactorial and cannot be fully gleaned from this study; however, similar trends have been noted in prior publications. For example, the relatively low frequency of referrals for patients with abnormal functional studies has been previously reported according to the SPARC multicenter registry study, which also evaluated multiple noninvasive diagnostic modalities, including SPECT, PET, and CTA.<sup>19</sup> In this study, <50% of patients with significant perfusion abnormalities were referred for cardiac catheterization; furthermore, use of medications following an abnormal scan were suboptimal as <50% of patients were prescribed a medication change. We found that the use of some CAD-related medication classes increased substantially in the 90-day time period following testing, indicating that an objective CAD diagnosis (compared to suspicion) prompted the initiation of treatment. Furthermore, revascularizations, which have been shown to improve quality of life and prevent cardiovascular death,<sup>20</sup> were performed in one quarter of the patients in our study. Another point of interest was the type of healthcare encounters prior to testing and following a CAD diagnosis; few patients had a cardiology OP visit before the testing visit, and the number of cardiology OP visits (median visits = 3) during the 90 days following a CAD diagnosis was lower than the median number of “other” OP visits (median visits = 6). However, further research into patient access to a cardiologist before and after a CAD diagnosis is needed to determine whether these differences impact outcomes. Lastly, considering only ~7% of patients who underwent non-invasive testing in this study received a CAD diagnosis, avoidance of unnecessary testing and/or testing low-risk populations is another factor that should be addressed in improving CAD diagnostic testing pathway efficiency.

A strength of this study is that it was informed by data from the IBM MarketScan® database, which is a large and generalizable US-based claims dataset, making it well-suited for addressing the study objectives. However, there are several limitations that should also

be noted. As with any retrospective database study, the findings may be limited by the availability of data or duration of follow-up of patients within the databases. Additionally, the study was a non-interventional study and was not designed to influence diagnostic procedures. We relied on symptoms (eg, chest pain, dyspnea, etc) presented at the visit as a trigger to order tests. However, the reliability of this approach in calculating the time period between ordering a test and performance is based solely on reasonable clinical expectations. Additionally, since administrative claims data are collected for billing rather than research purposes, typical limitations apply. Specifically, for the IBM MarketScan® Commercial and Medicare Supplemental claims databases, Medicare patients are underrepresented, and no Medicaid beneficiaries are captured. Lastly, while criteria were applied to identify patients only suspected of CAD, it is possible that patients who received a historical CAD diagnosis may have been included in the study. Additionally, the classification of patient records and interventions over a defined time period can be challenging; in our study, the 45-day period prior to testing was informed by clinical expertise; however, it is possible that the work-up to CAD testing began earlier than 45 days prior.

In conclusion, according to this large real-world data sample of patients who received a CAD diagnosis per non-invasive testing modalities in an OP setting, there are opportunities to improve upon and optimize healthcare system-wide HCRU and value-based treatment decisions for patients at risk for CAD.

## NEW KNOWLEDGE GAINED

Large studies of real-world trends in delivery of patient care towards CAD diagnoses are sparse, and this study provides insights into testing modalities adopted as part of diagnosing CAD. It includes evaluation of all modalities of non-invasive testing used for assessment of suspected CAD, time to diagnosis, and subsequent actionable care delivered (including additional testing, invasive evaluation, and medication changes by testing modality).

Our study identifies key trends where more research is needed, such as reevaluation of identifying the right patient population for diagnostic testing as a whole for suspected CAD, the continued role of SPECT as an important modality adopted for CAD (leading to less retesting), and reaffirming medical management trends and use of SPECT as an effective gatekeeper. These trends may help define how clinicians can improve patient care and adopt the appropriate testing and management strategies for stable CAD.

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