MILLIMAN REPORT

Patterns in cost and utilization of cardiac diagnostic procedures and cardiovascular events

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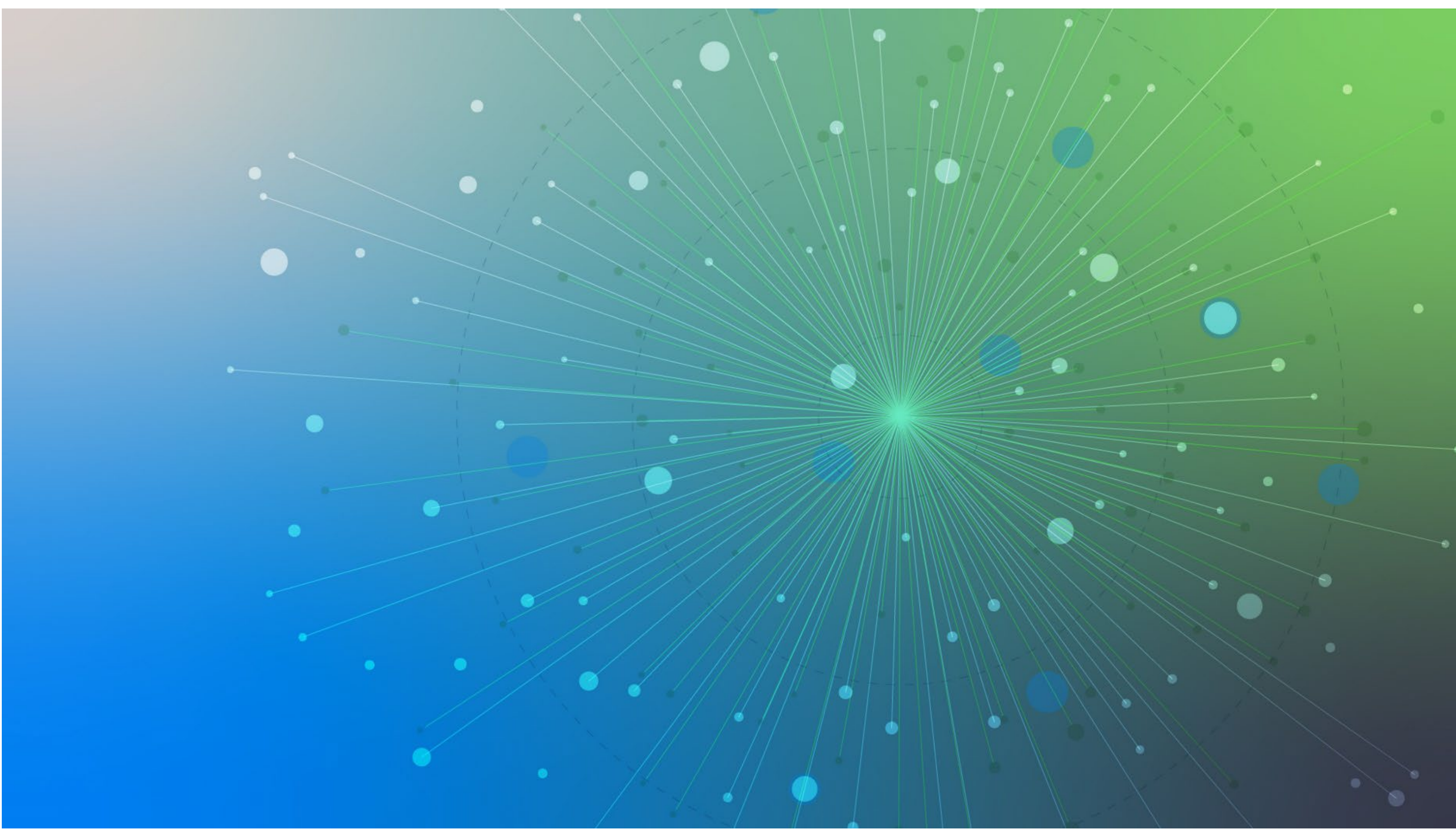

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Executive Summary

In the United States, approximately 80 million adults (1 in 3) have cardiovascular disease (CVD), which are disorders of the heart and blood vessels, such as coronary heart disease (CHD), cerebrovascular disease (stroke), heart failure, or high blood pressure.[1] CVD is one of the predominant causes of death globally, representing 1 in 3 global deaths in 2019.[2] In the U.S., CVD was the leading cause of death in 2019, with CHD causing 23.1% of total deaths and stroke causing 5.3% of total deaths. In 2020, during the COVID-19 pandemic, CVD remained the leading cause of death, at 25.3% of total deaths, compared to the proportion of total deaths caused by cancer (17.8%), COVID-19 (10.3%), diabetes (3.0%) and kidney failure (1.6%).[3]

The economic burden of CVD in the U.S. was estimated at approximately $216 billion in healthcare costs and $147 billion in lost productivity.[4] Real-world measures of the cost and utilization of CVD diagnostic tests and subsequent revascularization interventions have been less fully studied.

This report aims to summarize the observed cost and utilization patterns of CVD diagnostic tests, interventional revascularization procedures, and CVD events (and associated risk factors), based on analysis of the Milliman MedInsight nationwide Emerging Experience research database. This dataset represents healthcare claims for over 70 million unique patients across all 50 states in the U.S. with dates of service spanning January 2017 to December 2021.

Key Findings

- Of approximately 1.9 million CVD diagnostic tests incurred by continuously enrolled (see enrollment definition in the next bullet) patients in our dataset, invasive coronary angiograms comprised 15% of the total tests, and the remainder were non-invasive tests, including treadmill tests (41%), nuclear stress tests (32%), stress echocardiograms (10%), and coronary computerized tomography angiograms (CCTA) (2%).
- In male patients aged 65 years and older who were continuously enrolled for 90 days following the CVD diagnostic test, 18.9% of coronary angiograms led to outpatient percutaneous coronary intervention (PCI), almost 8.8% led to inpatient PCI, and 6.6% led to coronary artery bypass graft (CABG) within 0-90 days of the diagnostic test. Some patients underwent more than one intervention during this 90-day period. Women underwent approximately 30-50% less revascularization procedures than men of the same age, after the diagnostic tests described above.
- Coronary angiograms were the highest cost in all age groups and in all insurance groups, about 2.5 to 3-fold higher than nuclear stress tests. Costs for these two types of diagnostic procedures have risen every year for the last five years from January 2017 to December 2021. The 5-year mean allowed cost of a coronary angiogram ranges from $1,800 to $2,700 for Medicare beneficiaries and $3,100 to $4,300 for commercially insured patients.
- The 5-year mean cost of revascularization interventions was approximately $24,000 for outpatient PCI, $44,000 for inpatient PCI and $69,000 for CABG in 50-64 year old commercially insured patients, or $10,000 to $14,000 for outpatient PCI, $21,000 to $28,000 for inpatient PCI, and $33,000 to $49,000 for CABG in 65-74 year old Medicare Advantage and Medicare FFS beneficiaries. These are actual observed costs during this 2017 to 2021 time period. As described in the discussion section, when comparing to older studies that reported 2014 dollars, we adjusted for inflation using the medical component of the Consumer Price Index (Bureau of Labor Statistics).

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[1] Shaw LJ, Goyal A, Mehta C, *et al.* 10-Year Resource Utilization and Costs for Cardiovascular Care. Journal of the American College of Cardiology. Vol 71 (10). 2018. Accessed from https://doi.org/10.1016/j.jacc.2017.12.064 on October 14, 2022.

[2] World Health Organization. Fact Sheets. Cardiovascular diseases (CVDs). 11 June 2021. Accessed from https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) on October 1, 2022.

[3] Ahmad FB, Anderson RN. The Leading Causes of Death in the US for 2020. JAMA. 2021;325(18):1829–1830. doi:10.1001/jama.2021.5469. Accessed from https://www.doi.org/10.1001/jama.2021.5469 on October 1, 2022.

[4] CDC. Health and Economic Costs of Chronic Diseases. National Center for Chronic Disease Prevention and Health Promotion. Page last reviewed: September 8, 2022. Accessed from https://www.cdc.gov/chronicdisease/about/costs/index.htm on October 1, 2022.

- The 5-year mean costs of acute CV events were highest for acute hemorrhagic cerebrovascular disease (hemorrhagic stroke), followed by cerebral infarction (non-hemorrhagic stroke), acute heart failure and acute myocardial infarction.
- In the 6 months after an acute CV event, the highest follow-up costs were incurred for rehabilitation, followed by prescription drugs.
- The frequency of CV events increased with one or more cardiac risk factors.

The analyses in this report are based on real-world observational data from the Milliman MedInsight nationwide Emerging Experience research database. In preparation of our analysis, we relied upon the accuracy of data or information provided to us. We have not audited this information, although we have reviewed it for reasonableness. If the underlying data or information is inaccurate or incomplete, the results of our review may likewise be inaccurate or incomplete. Models used in the preparation of our analysis were applied consistently with their intended use. Where we relied on models developed by others, we have made a reasonable effort to understand the intended purpose, general operation, dependencies, and sensitivities of those models.

This report was commissioned by Prevencio, Inc., which is a developer of predictive and diagnostic biomarker tests, involving multiple proteins that are algorithmically combined and incorporated into a risk scoring system. The findings in this report reflect the independent exploratory research of the authors; Milliman does not intend to endorse any product or organization. If this report is reproduced, we require that it be reproduced in its entirety, as sections taken out of context can be misleading.

Data Source and Methodology

This study used the Milliman MedInsight Emerging Experience research database of nationwide de-identified healthcare claims data for over 70 million unique individuals with dates of service spanning 2017 to 2021. Approximately 75 healthcare organizations contribute monthly data to this research database, which is currently refreshed quarterly. The database provides a comprehensive view of services received by patients provided by any healthcare professional in any location or setting billed to insurance, including approximately 1.7 million medical professionals and 340,000 healthcare facilities.

As a reference comparison to the U.S. population, the United States Census Bureau and the American Community Survey estimated there were 300 million individuals with healthcare insurance in the United States in 2019.[5] The National Plan & Provider Enumeration System (NPPES)[6] estimated that 4.4 million unique individual providers and 1.7 million unique facilities exist in the United States in 2019.

STUDY DESIGN

Analysis of CVD diagnostic tests and subsequent revascularization interventions

The study population for the analysis of CVD diagnostic tests and subsequent revascularization interventions included adults aged 50-64, 65-74, 75+ years, who were enrolled in a commercial health insurance plan, Medicaid managed care plan, or Medicare Advantage plan, or received health benefits under Medicare fee-for-service (FFS). The most recent CVD test was identified as the index test (day 0) for each patient, then a look-forward for revascularization interventions between day 0 and day 90 after the index test was performed. Any individuals who were not continuously enrolled throughout the 90 days from the index test were removed from the study, to prevent loss or change of insurance coverage impacting the detection of interventions in this analysis. We did not use any exclusion logic. A supplemental analysis measures the number and proportion of patients who received more than

[5] Keisler-Starkey K and Bunch LN. Health Insurance Coverage in the United States: 2019. U.S. Census Bureau Current Population Reports, P60-271, 2020. https://www.census.gov/library/publications/2020/demo/p60-271.html Accessed October 2021.

[6] National Plan & Provider Enumeration System (NPPES). https://nppes.cms.hhs.gov Accessed October 2021.

one intervention and more than one CVD diagnostic test before an intervention (see the Supplemental Analysis section of this report).

CVD diagnostic tests were identified by Current Procedural Terminology (CPT) codes produced by the American Medical Association. Non-invasive tests included treadmill exercise stress tests, stress echocardiography, stress tests with nuclear myocardial perfusion imaging, and coronary computerized tomography angiograms. Invasive tests included coronary angiograms (also referred to as diagnostic cardiac catheterizations).

- Treadmill exercise stress tests*: 93015, 93018
- Stress echocardiograms: 93350, 93351, 93352
- Stress tests with nuclear imaging: 78429, 78430, 78431, 78432, 78433, 78434, 78452, 78459, 78491, 78492
- Coronary computerized tomography angiograms (CCTA): 75574
- Coronary angiograms: 93454, 93455, 93456, 93457, 93458, 93459, 93460, 93461, 93563, 93564

* 93016, 93017 are the professional component for conducting or evaluating treadmill tests and were excluded to avoid double-counting the encounter.

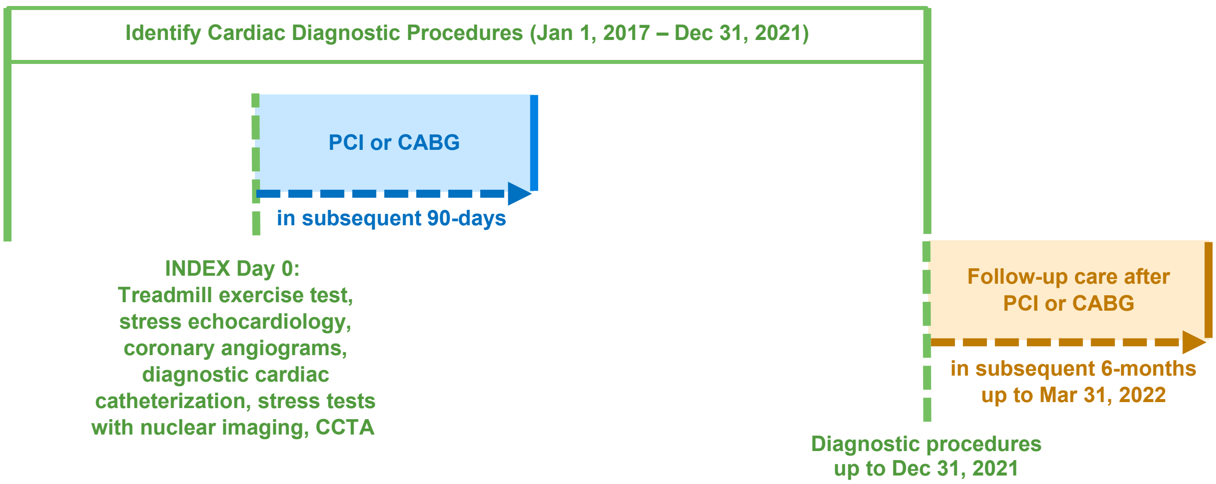
The utilization and allowed cost of each type of CVD diagnostic tests were measured. The allowed cost refers to the maximum amount a plan will pay for a covered health care service. This study reports the rate and costs of subsequent revascularization interventions within 90 days of the index test, and the patterns of cost and follow-up care for 6-months post intervention.

Revascularization interventions were identified by CPT codes, ICD-10-PCS procedure codes grouped using the Clinical Classifications Software Refined (CCSR) from the Agency of Healthcare Research and Quality (AHRQ), and Medicare Severity Diagnosis Related Groups (MS-DRG) codes v39.1:

- Percutaneous coronary interventions (PCI):
  - CPT 92920, 92921, 92924, 92925, 92928, 92929, 92933, 92934, 92937, 92938, 92941, 92943, 92944, 92973, 92975, 92978, 92979, C9600, C9601, C9602, C9603, C9604, C9605, C9606, C9607, C9608;
  - ICD-10-PCS in AHRQ CCSR procedure category CAR004 for PCI.
- Coronary artery bypass graft (CABG):
  - MS DRG 231-236;
  - CPT 33140, 33141, 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33530, 33533, 33534, 33535, 33536, 35600, S2205, S2206, S2207, S2208, S2209, 33542, 33545, 33548.

In addition to the immediate costs of PCI or CABG, the analysis also measured utilization and cost of follow-up care during the 6 months following the revascularization intervention, including prescription medications, cardiovascular outpatient clinic visits, specialty office visits, primary care visits, inpatient rehabilitation, inpatient admissions, and ancillary services (including oxygen, durable medical equipment, and ambulance services).

FIGURE 1A: STUDY DESIGN TO IDENTIFY CVD DIAGNOSTIC TESTS AND SUBSEQUENT REVASCULARIZATION INTERVENTIONS



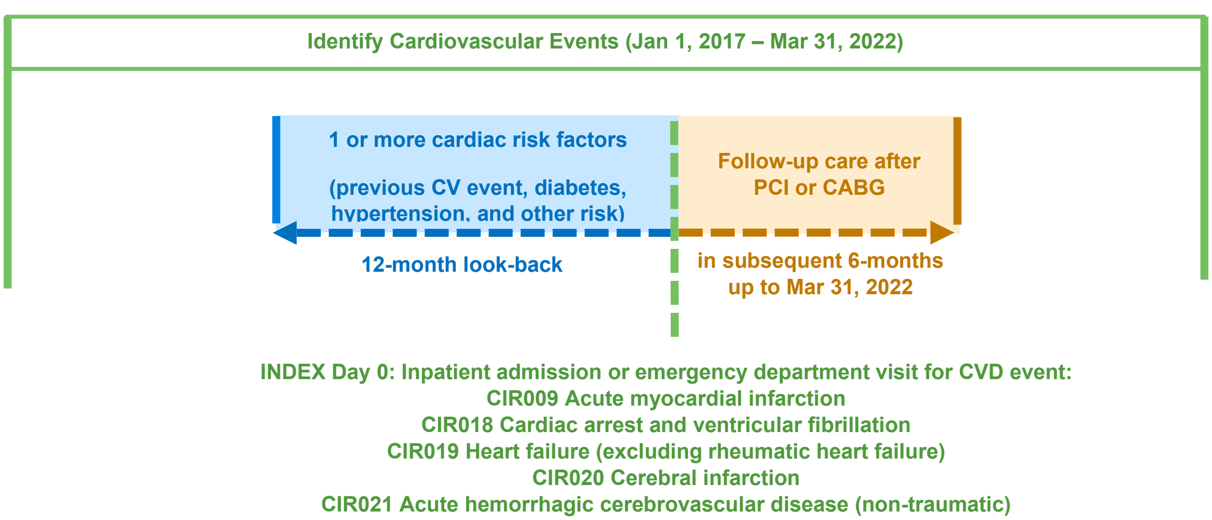
Analysis of CV events and risk factors

The study population for the analysis of CV events and risk factors focused on adults aged 20-39, 40-64, and 65+ years, who were enrolled in a commercial health insurance plan, Medicaid managed care plan, or Medicare Advantage plan, or received health benefits under Medicare FFS. Acute CV events were defined as a hospital inpatient admission and/or emergency department visit for one of the following conditions defined by AHRQ CCSR diagnostic categories:

- Acute myocardial infarction: CIR009
- Cardiac arrest and ventricular fibrillation: CIR018
- Heart failure (excluding rheumatic heart failure): CIR019
- Cerebral infarction: CIR020
- Acute hemorrhagic cerebrovascular disease (non-traumatic): CIR021

Transient ischemic attacks or transient cerebral ischemia (NSV012) was explored, but not reported as a CV event.

FIGURE 1B: SCHEMATIC OF STUDY DESIGN TO ANALYZE ACUTE CV EVENTS AND RISK FACTORS



The acute CV event was considered the index event (day 0), and the analysis looked for the following CVD risk factors in the 12-months prior to the CVD event:

- Prior CV events: ICD-10 codes I252, Z950, Z951, Z955, Z95811, Z95812
- Diabetes: AHRQ CCSR categories END002, END003, END004, END005, END006
- Hypertension: AHRQ CCSR categories CIR007, CIR008, CIR036
- CVD family history: ICD-10 codes Z8241, Z8249
- Obesity: AHRQ CCSR category END009
- Smoking: AHRQ CCSR category MBD024 and ICD-10 codes Z5731, Z716, Z720, Z7722, Z812
- High cholesterol: AHRQ CCSR category END010
- Physically inactive: ICD-10 codes Z723, Z7409
- Stress: AHRQ CCSR categories MBD005, MBD007, and ICD-10 codes Z563, Z6371, Z6379, Z733, Z8651
- Non rheumatic unspecified heart valve disorders: IC-10 codes Z952, Z953, Z954.

Key Findings

ANALYSIS OF CVD DIAGNOSTIC TESTS AND SUBSEQUENT INTERVENTIONS

CVD Diagnostic Tests

The gender distribution and mean age of patients receiving diagnostic tests, during the period from January 1, 2017 to December 31, 2021, are shown in Figure 2A.

FIGURE 2A: GENDER DISTRIBUTION AND MEAN AGE BY PAYER GROUP OF PATIENTS RECEIVING CVD DIAGNOSTIC TESTS *

	Commercial	Dual Eligible	Medicaid	Medicare Advantage	Medicare FFS	Overall
Female	21.54%	48.82%	35.72%	33.33%	33.39%	26.44%
Male	78.14%	51.04%	64.14%	66.60%	66.61%	73.34%
Unknown	0.32%	0.14%	0.14%	0.07%	0.00%	0.22%
Mean Age (years)	58.56	68.87	55.93	74.24	74.3	
Total unique patients receiving a CVD diagnostic test	5,250,770	138,211	284,701	1,012,586	1,459,848	8,146,116

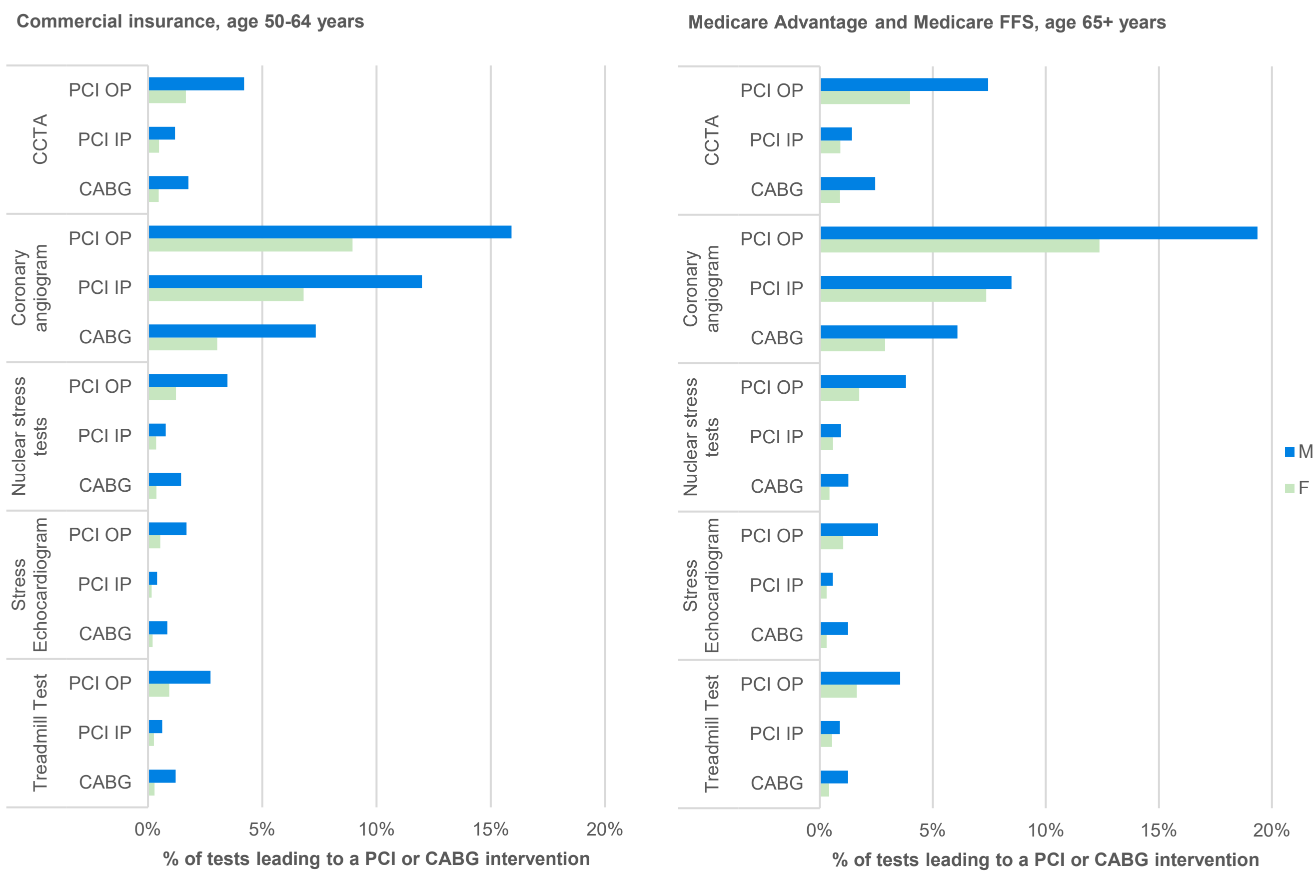
Payer Group	Age (years)	Number of unique patients				
		CCTA	Coronary angiogram	Nuclear stress test	Stress echocardiogram	Treadmill test
Commercial	50-64	111,990	592,584	1,309,645	540,994	1,880,354
	65-74	12,754	93,924	212,503	64,525	263,911
	75+	3,465	26,159	56,495	14,757	66,710
Dual Eligible	50-64	636	6,146	12,916	2,975	13,434
	65-74	1,003	10,486	24,045	4,467	24,588
	75+	534	5,888	14,709	1,760	14,624
Medicaid	50-64	5,424	39,710	81,720	27,544	99,570
	65-74	323	2,551	6,672	1,986	7,105
	75+	281	1,648	4,563	898	4,706
Medicare Advantage	50-64	1,457	14,917	32,331	5,702	34,603
	65-74	7,597	80,834	181,528	40,099	202,103
	75+	4,744	72,002	154,772	20,168	159,729
Medicare FFS	50-64	1,894	20,726	44,172	9,293	47,488
	65-74	12,739	109,613	258,645	66,568	288,044
	75+	9,126	99,147	226,414	31,399	234,580

* Sourced from the Milliman MedInsight Emerging Experience research database

Figure 2B shows the percentage of diagnostic tests that led to revascularization procedures in two example groups – patients age 40-64 years with Commercial insurance and patients age 65 years and over covered by Medicare Advantage or Medicare FFS. The percentage of diagnostic tests leading to revascularization procedures was higher in male than female patients, in all categories of diagnostic tests and interventional procedures.

Clinical information on the severity of coronary stenosis and types of symptoms are not available in claims data, and therefore could not be considered in the analysis.

FIGURE 2B: MEAN PERCENTAGE OF DIAGNOSTIC TESTS LEADING TO REVASCULARIZATION INTERVENTIONS, 2017 TO 2021 *



Abbreviations: OP refers to outpatient. IP refers to inpatient.

* Sourced from the Milliman MedInsight Emerging Experience research database

The lower rate in female patients may relate to underdiagnosis and/or undertreatment. The American College of Cardiology published a review of quality and equitable health care gaps for women, which noted a less intensive pattern of appropriate guideline-indicated care for women, and lower use of symptom-guided use of procedures, evidence-based therapies, and lifestyle recommendations for women.[7] Another study surveying 200 primary care physicians and 100 cardiologists found that heart disease in women was not a top tier concern, and the majority had not fully implemented the cardiac risk assessment for women, as recommended by the American Heart Association

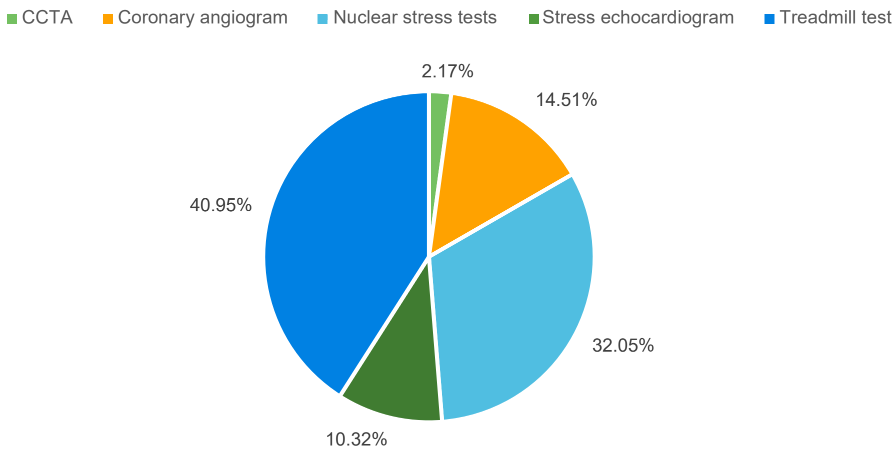
[7] Shaw LJ, Pepine CJ, Xie J *et al.* Quality and Equitable Health Care Gaps for Women: Attributions to Sex Differences in Cardiovascular Medicine. Journal of the American College of Cardiology. Vol. 70, No. 3, 2017. Accessed from http://dx.doi.org/10.1016/j.jacc.2017.05.051 on October 19, 2022.

guidelines.[8] The consequences of these discrepancies are worse outcomes and higher mortality after major cardiovascular events in women than in men.[9]

A more detailed table of the mean rates of revascularization interventions following diagnostic tests for each age band, gender, and payer group is provided in Appendix A.

The relative frequency of each type of diagnostic test is shown in Figure 2C.

FIGURE 2C: DISTRIBUTION OF CVD DIAGNOSTIC TEST UTILIZATION, ALL PAYER TYPES, ALL GENDERS, ALL AGE BANDS *



* Sourced from the Milliman MedInsight Emerging Experience research database

While treadmill tests are the most common diagnostic test observed, non-invasive nuclear stress tests (which involve radioactive tracers) are the second most frequently conducted diagnostic test. Traditional invasive coronary angiograms, during which a flexible catheter tube is threaded from the blood vessels in the groin or arm to the heart or coronary arteries, represent 14.5% of the total diagnostic tests observed in our dataset. This traditional angiogram approach can also be used for treatment of a coronary artery blockage or constriction for patients with known coronary artery disease. Coronary CT angiograms are the least frequently utilized CVD test at present, however their use is expected to grow rapidly. This has consequences, given the need for intravenous contrast use, exposure to radiation, and need for specialized interpretation. Contemporary scanners and protocols deliver less radiation than a nuclear stress test, and the risks of cancer associated with CCTA are small, yet not zero.[10] However, a CCTA increases the probability of a subsequent nuclear stress test, and the cumulative effect of radiation is associated with increased cancer risk.[11]

Figure 2D shows the costs per diagnostic test from 2017 to 2021 for patients enrolled in Commercial, Medicare Advantage, Medicare FFS, Medicaid, or Dual Eligible insurance. In all insurance groups, the cost per coronary angiogram and cost per nuclear stress test have risen every year for the last five years. The cost of CCTA, stress echocardiogram and treadmill tests have remained relatively stable from 2017 to 2021.

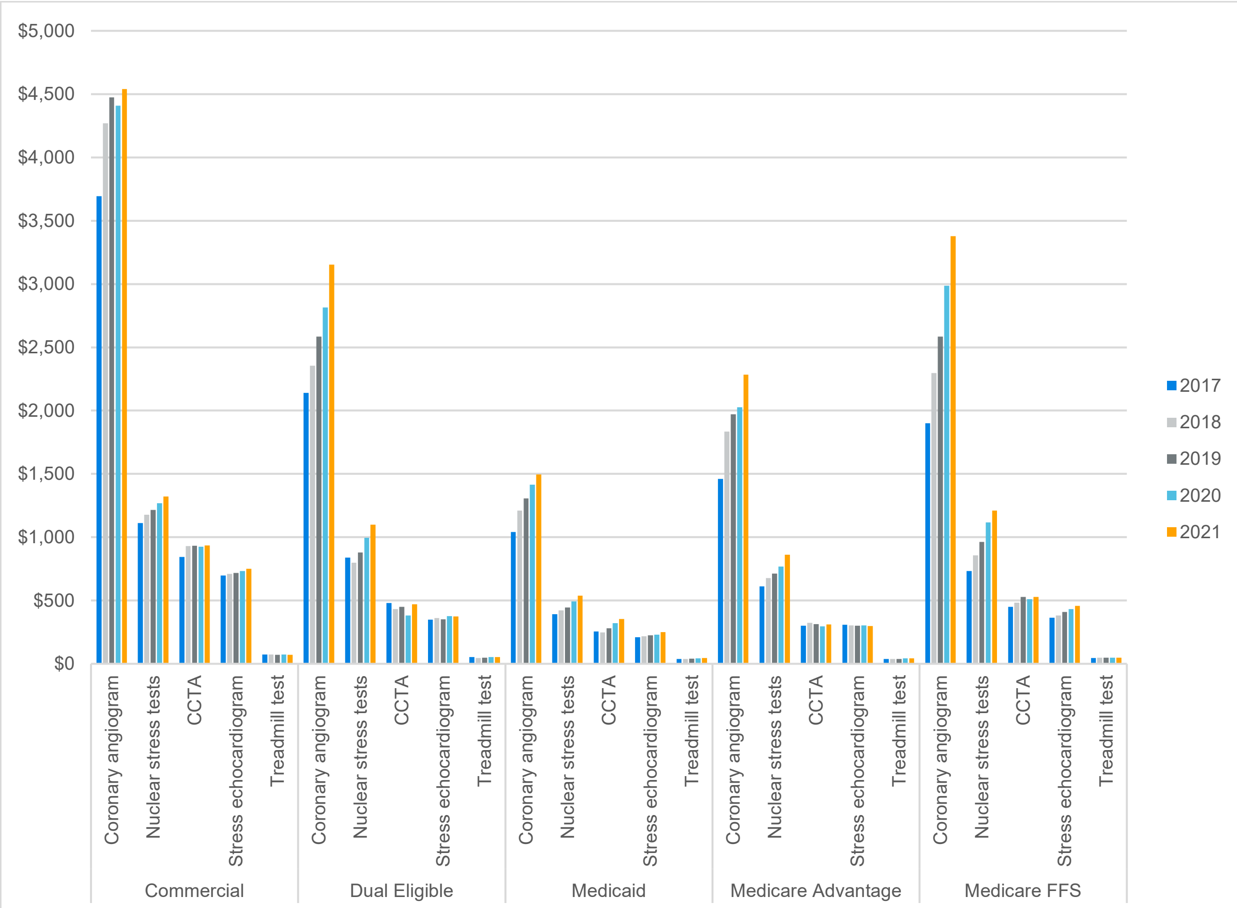
[8] Andersen H, Bairey-Merz NC, Burns A, *et al.* Abstract 14226: Physicians Speak up About Heart Health Awareness and Action: A Women's Heart Alliance Research Report. Circulation. November 2015. Accessed from https://doi.org/10.1161/circ.132.suppl_3.14226 on October 19, 2022.

[9] Stehlo J, Duffy SJ, Burgess S *et al.* Sex Disparities in Myocardial Infarction: Biology or Bias? Heart, Lung and Circulation. Volume 30 (1): 18-26. January 2021. Accessed from https://doi.org/10.1016/j.hlc.2020.06.025 on October 19, 2022.

[10] Perisinakis K, Seimenis I, Tzedakis A, Papadakis AE, Damilakis J. Individualized assessment of radiation dose in patients undergoing coronary computed tomographic angiography with 256-slice scanning. Circulation. 2010 Dec 7;122(23):2394-402. doi:10.1161/CIRCULATIONAHA.109.935346. Epub 2010 Nov 22. PMID: 21098451. Accessed from https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.109.935346 on December 14, 2022.

[11] Cordiner D, Al-Ani M, Jia X, Marchick M, Allen B, Winchester DE. Estimates of radiation exposure and subsequent risk of malignancy due to cardiac imaging in the emergency department for evaluation of chest pain: a cohort study. Coron Artery Dis. 2019 Dec;30(8):626-628. doi: 10.1097/MCA.0000000000000806. PMID: 31577617; PMCID: PMC6832827. Accessed from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6832827/pdf/nihms-1538638.pdf on December 14, 2022.

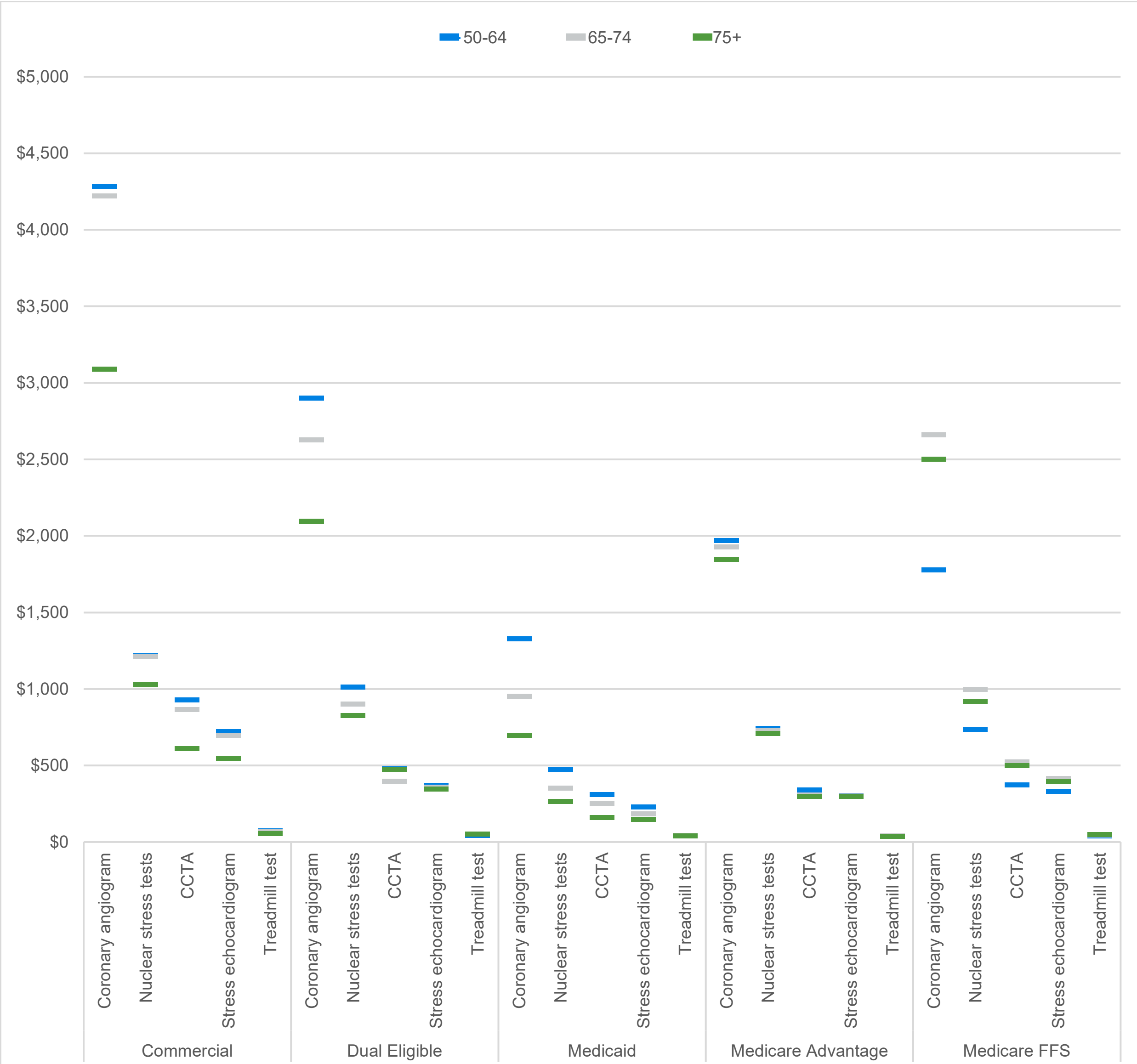
FIGURE 2D: TREND IN ALLOWED COST OF PER CVD DIAGNOSTIC TEST, INCLUDING ALL AGES AND ALL GENDERS *



* Sourced from the Milliman MedInsight Emerging Experience research database

Comparisons of the mean allowed (contracted) cost for each type of diagnostic test are shown for each age group and insurance type in Figure 2E.

FIGURE 2E: MEAN ALLOWED COST PER DIAGNOSTIC TEST IN PATIENTS FOR EACH AGE BAND AND INSURANCE TYPE, ALL GENDERS *



Note: Markers overlay each other if approximately the same value. Figure 2D tabulates these values.

* Sourced from the Milliman MedInsight Emerging Experience research database

Both Medicare FFS and Medicare Advantage include both patients who are age 65 years and older, and younger patients who are disabled with severe chronic illness, such as end stage renal disease (ESRD).[12]

The cost of non-invasive tests is generally below $1,000 in all insurance groups and age bands, with the exception of nuclear stress tests in the commercially insured group. Invasive coronary angiograms range in cost from $1,800 to $2,700 for Medicare beneficiaries and $3,100 up to $4,300 for commercial members.

[12] AHIP. https://www.ahip.org/resources/medicare-advantage-what-is-changing-for-beneficiaries-with-end-stage-renal-disease-esrd-in-2021 March 2020. Accessed December 1, 2022.

Revascularization interventions

The mean per procedure allowed costs of acute revascularization intervention procedures are shown in Figure 3A.

FIGURE 3A: MEAN ALLOWED COST OF REVASCULARIZATION INTERVENTIONS, ALL GENDERS *

	2017	2018	2019	2020	2021	5-yr mean
Commercial						
PCI OP						
50-64	$23,553	$24,274	$24,165	$25,207	$22,450	$23,930
65-74	$22,017	$22,888	$22,964	$23,299	$22,323	$22,698
75+	$15,194	$17,533	$17,995	$18,925	$16,109	$17,151
PCI IP						
50-64	$41,048	$42,827	$44,750	$45,783	$45,829	$44,047
65-74	$39,555	$42,918	$44,171	$45,923	$43,976	$43,309
75+	$32,437	$33,798	$38,615	$35,595	$32,967	$34,683
CABG IP						
50-64	$65,563	$66,773	$69,502	$73,627	$68,165	$68,726
65-74	$61,838	$63,081	$66,710	$70,311	$62,296	$64,847
75+	$56,077	$59,980	$54,933	$63,523	$51,704	$57,243
Medicare Advantage						
PCI OP						
50-64	$9,716	$10,672	$10,077	$10,451	$10,383	$10,260
65-74	$9,399	$10,080	$9,966	$10,085	$9,855	$9,877
75+	$9,254	$9,619	$9,981	$9,860	$9,504	$9,644
PCI IP						
50-64	$18,244	$24,387	$22,810	$23,057	$20,214	$21,742
65-74	$20,328	$19,860	$22,029	$21,352	$21,143	$20,943
75+	$20,754	$21,627	$21,967	$21,554	$19,796	$21,140
CABG IP						
50-64	$29,429	$32,983	$39,758	$43,017	$40,432	$37,124
65-74	$34,432	$32,485	$32,917	$34,763	$30,062	$32,932
75+	$33,143	$33,922	$38,036	$36,493	$33,392	$34,997
Medicare FFS						
PCI OP						
50-64	$10,624	$12,297	$10,936	$11,842	$10,476	$11,235
65-74	$11,345	$13,222	$14,161	$15,497	$13,957	$13,636
75+	$11,374	$12,331	$12,418	$13,469	$12,465	$12,411
PCI IP						
50-64	$22,431	$22,593	$27,105	$27,182	$26,325	$25,127
65-74	$23,736	$26,544	$28,941	$31,983	$30,477	$28,336
75+	$25,115	$29,696	$30,022	$31,949	$30,439	$29,444
CABG IP						
50-64	$40,403	$45,059	$37,373	$51,543	$38,895	$42,654
65-74	$39,058	$46,092	$49,307	$59,881	$50,732	$49,014
75+	$51,638	$53,571	$54,228	$59,041	$55,237	$54,743
Dual Eligible						
PCI OP						
50-64	$9,195	$9,960	$10,409	$11,854	$9,326	$10,149
65-74	$9,870	$11,866	$10,803	$11,335	$11,190	$11,013
75+	$10,801	$10,847	$10,663	$10,358	$9,554	$10,445
PCI IP						
50-64	$23,063	$21,367	$24,989	$25,022	$24,236	$23,735
65-74	$25,707	$24,865	$24,412	$26,009	$22,798	$24,758
75+	$23,865	$24,558	$23,631	$29,383	$20,933	$24,474
CABG IP						
50-64	$31,289	$30,527	$37,095	$41,562	$42,180	$36,531
65-74	$39,579	$36,565	$47,412	$46,434	$41,941	$42,386
75+	$58,238	$40,085	$49,191	$58,668	$56,583	$52,553
Medicaid						
PCI OP						
50-64	$7,105	$6,855	$6,725	$6,712	$6,905	$6,860
65-74	$2,174	$3,131	$2,686	$5,870	$4,184	$3,609
75+	$4,019	$3,911	$3,917	$4,691	$6,213	$4,550
PCI IP						
50-64	$19,541	$17,896	$18,851	$19,599	$18,272	$18,832
65-74	$13,078	$16,627	$13,991	$11,668	$15,053	$14,083
75+	$12,562	$15,525	$18,834	$11,386	$12,992	$14,260
CABG IP						
50-64	$38,051	$32,480	$36,665	$35,389	$30,705	$34,658
65-74	$23,435	$31,122	$28,797	$38,773	$37,945	$32,015
75+	$20,803	$21,116	Insufficient data	$14,976	$41,012	$42,857

Note: Relatively few patients met the continuous enrollment criteria in the Medicaid and Dual Eligible insurance groups, resulting in wider variation in the mean from year to year.

* Sourced from the Milliman MedInsight Emerging Experience research database

Patients undergoing inpatient procedures tend to have more complex care needs, have more comorbidities, and greater use of emergency and hospital services, resulting in higher costs.

The mean months of continuous enrollment post-intervention in the study cohort was 22.4 months.

Total costs depend both on unit costs and utilization patterns. Figure 3B shows the unit costs for follow-up services in the six months after intervention. Unit costs for commercial insurance were higher than other payer groups, and particularly high for cardiovascular facility outpatient clinic visits.

FIGURE 3B: MEAN ALLOWED COST PER UTIL FOR POST-INTERVENTION FOLLOW-UP, ALL GENDERS, ALL AGES *

	Commercial	Medicare FFS	Medicare Advantage	Dual Eligible	Medicaid
Mean months of continuous enrollment post-intervention	**22.4**	**24.6**	**23.8**	**20.1**	**21.3**
CABG					
Cardiovascular (Facility Outpatient)	$486	$185	$129	$118	$95
Rehabilitation	$269	$271	$239	$218	$158
Specialist Office Visit	$122	$106	$98	$92	$71
Primary Care Physician Visit	$116	$99	$97	$93	$67
Cardiovascular (Professional)	$79	$58	$51	$46	$33
All Rx	$108	$69	$95	$79	$58
Plavix/Clopidogrel	$12	$21	$25	$7	$10
PCI IP					
Cardiovascular (Facility Outpatient)	$546	$198	$159	$157	$96
Rehabilitation	$332	$274	$214	$221	$167
Specialist Office Visit	$126	$102	$99	$87	$68
Primary Care Physician Visit	$118	$95	$97	$88	$65
Cardiovascular (Professional)	$82	$51	$47	$39	$29
All Rx	$131	$82	$112	$78	$63
Plavix/Clopidogrel	$12	$20	$20	$6	$8
PCI OP					
Cardiovascular (Facility Outpatient)	$502	$205	$141	$134	$86
Rehabilitation	$167	$168	$125	$129	$105
Specialist Office Visit	$119	$105	$99	$90	$63
Primary Care Physician Visit	$112	$98	$97	$88	$55
Cardiovascular (Professional)	$82	$57	$47	$47	$28
All Rx	$138	$94	$118	$88	$68
Plavix/Clopidogrel	$12	$24	$22	$6	$8

* Sourced from the Milliman MedInsight Emerging Experience research database

Figures 3C, 3D and 3E are frequency distribution charts showing the patterns in the utilization of post-intervention follow-up services per 1000 members who received a CABG or PCI.

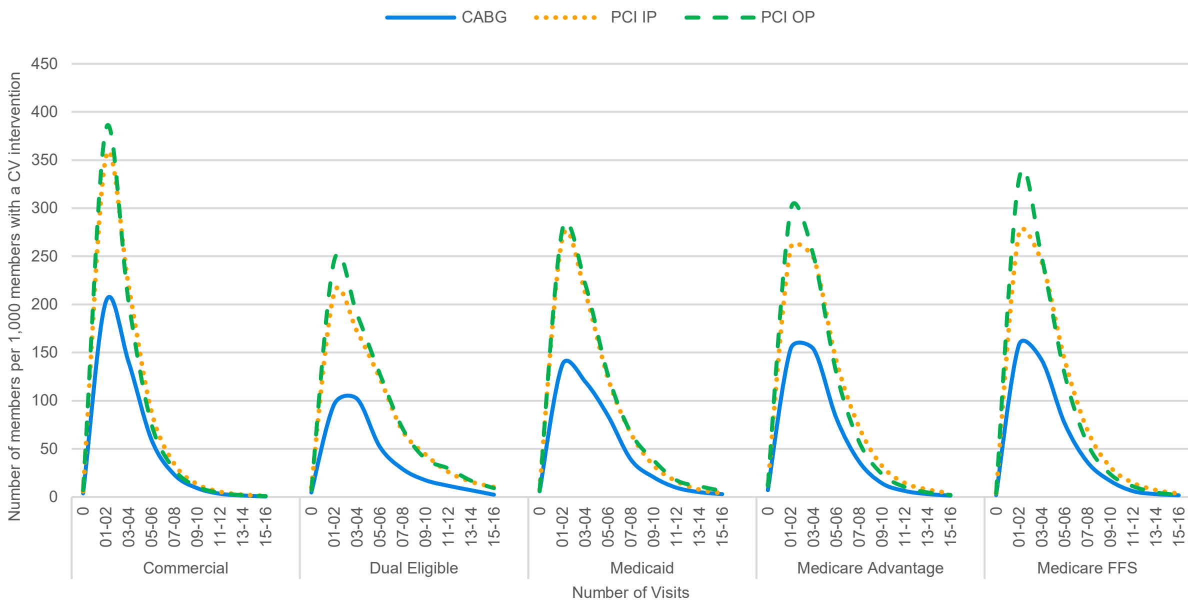
The most frequent pattern of follow-up after PCI included 1 to 2 follow-up visits to cardiovascular facility outpatient clinics for all payer groups, and a greater number primary care visits, most dual eligible, Medicaid and Medicare patients receiving 2 to 4 primary care visits after PCI. The widening of the distribution curve in the dual eligible group indicates patients receiving 5 to 8 primary care visits post-PCI. This pattern is expected in patients with more comorbidities, more severe conditions, or more complex needs.

After CABG, commercially insured patients exhibited the greatest number of visits to cardiovascular facility outpatient clinics compared to other insurance groups, followed by Medicare FFS. In contrast, the commercial group had only 1-2 primary care visits post-CABG. Medicaid patients had the highest utilization of primary care visits for post-CABG follow-up services, as indicated by the area under the curve.

Our interest in exploring patterns of follow-up utilization was to understand types of post-procedural services sought by patients in each coverage group. Practicing cardiologists, cardiac nurses, internists and health outcomes researchers, recommended including six months of subsequent care after intervention.

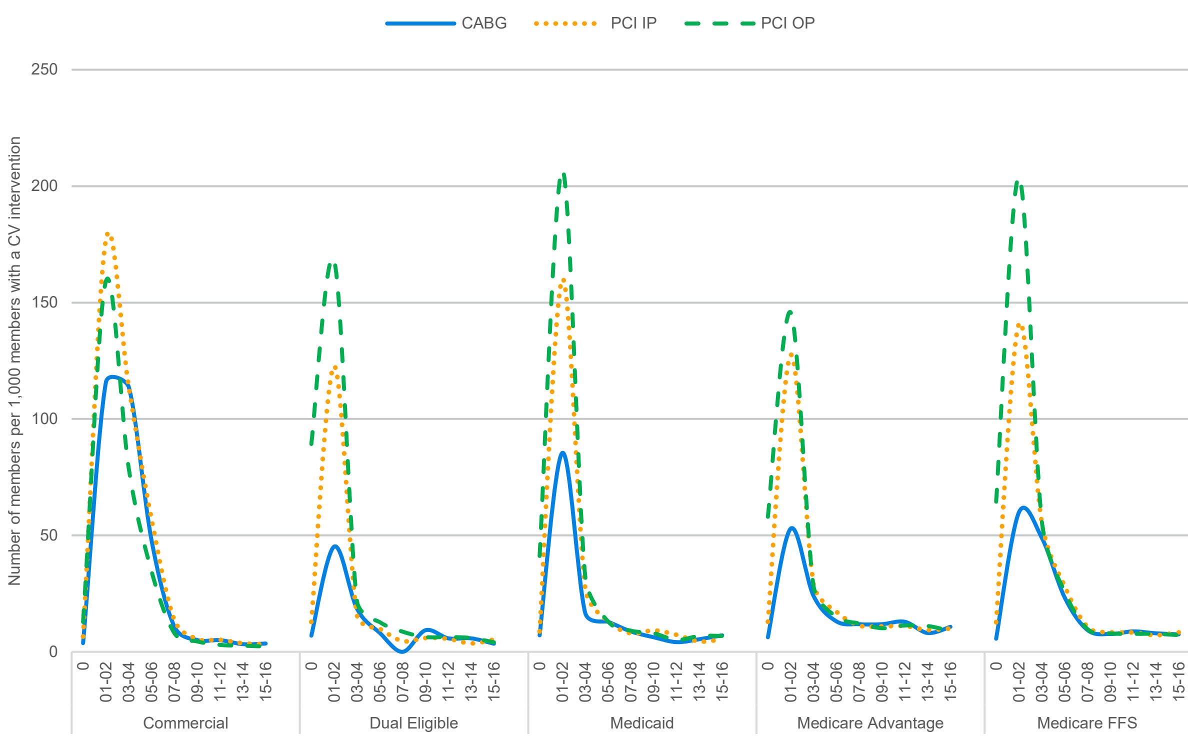
We did not restrict the post-acute services to only claims with cardiovascular principal diagnoses, because we wanted to be inclusive of all care received. More than one chronic or acute cardiovascular condition may co-exist, and patients may be receiving care for related comorbidities (such as diabetes, smoking cessation, weight management, kidney disease, and stress management), as well as other conditions (such as musculoskeletal, behavioral health, and cancer). Figure 3F shows that cardiovascular facility outpatient clinic visits are a main driver of post-intervention follow-up costs per patient.

FIGURE 3C: PATTERNS OF UTILIZATION OF FOLLOW-UP VISITS TO PRIMARY CARE PROVIDERS IN THE SIX MONTHS POST-INTERVENTION, ALL AGES, ALL GENDERS, ALL YEARS *



* Sourced from the Milliman MedInsight Emerging Experience research database

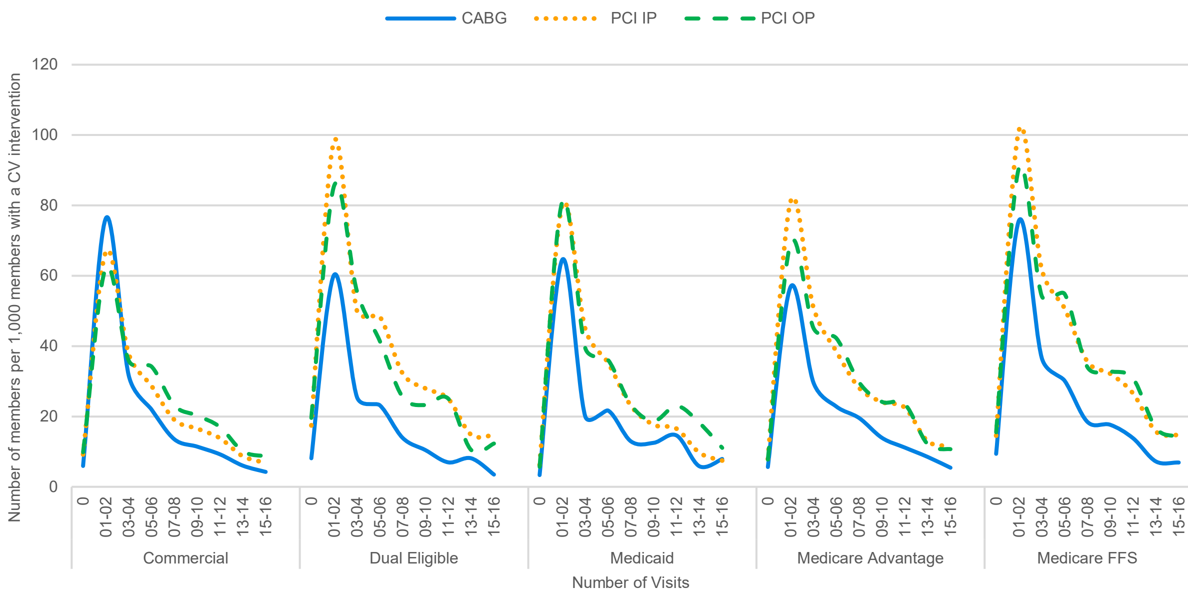
FIGURE 3D: PATTERNS OF UTILIZATION OF FOLLOW-UP VISITS TO CARDIOVASCULAR FACILITY OUTPATIENT CLINICS IN THE SIX MONTHS POST-INTERVENTION, ALL AGES, ALL GENDERS, ALL YEARS *



* Sourced from the Milliman MedInsight Emerging Experience research database

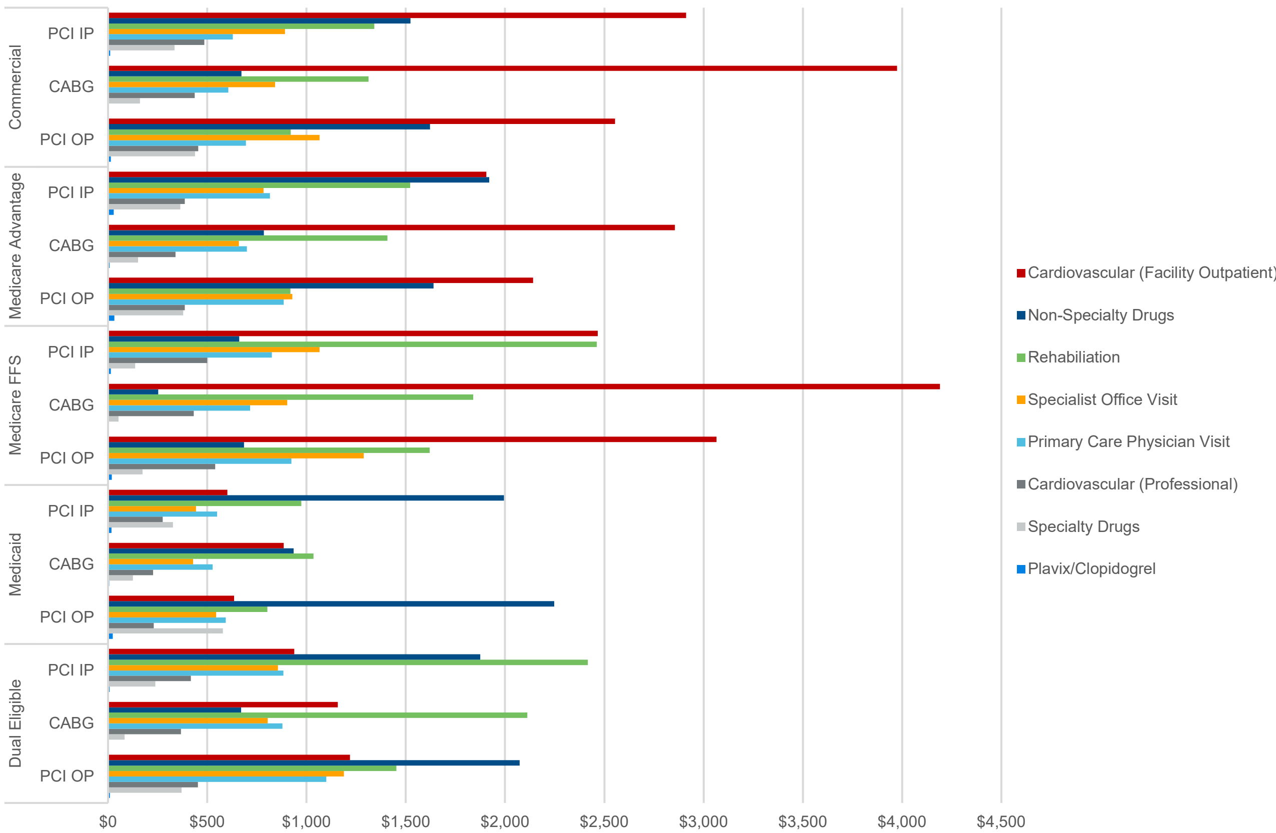
As shown in Figures 3B and 3D, cardiovascular facility outpatient visits are a significant cost driver when considering post-intervention follow-up services in the 6 months following CABG, PCI IP or PCI OP. Rehabilitation services exhibit the second highest unit cost of the follow-up services measured. However, as shown in Figure 3E, the volume of utilization is relatively low, compared to the cardiovascular and primary care visits above.

FIGURE 3E: PATTERNS OF REHABILITATION SERVICES UTILIZATION IN THE SIX MONTHS POST-INTERVENTION, ALL AGES, ALL GENDERS, ALL YEARS *



* Sourced from the Milliman MedInsight Emerging Experience research database

FIGURE 3F: TOTAL ALLOWED COST OF FOLLOW-UP SERVICES PER PATIENT IN THE SIX MONTHS POST-INTERVENTION, ALL AGES, ALL GENDERS, ALL YEARS *

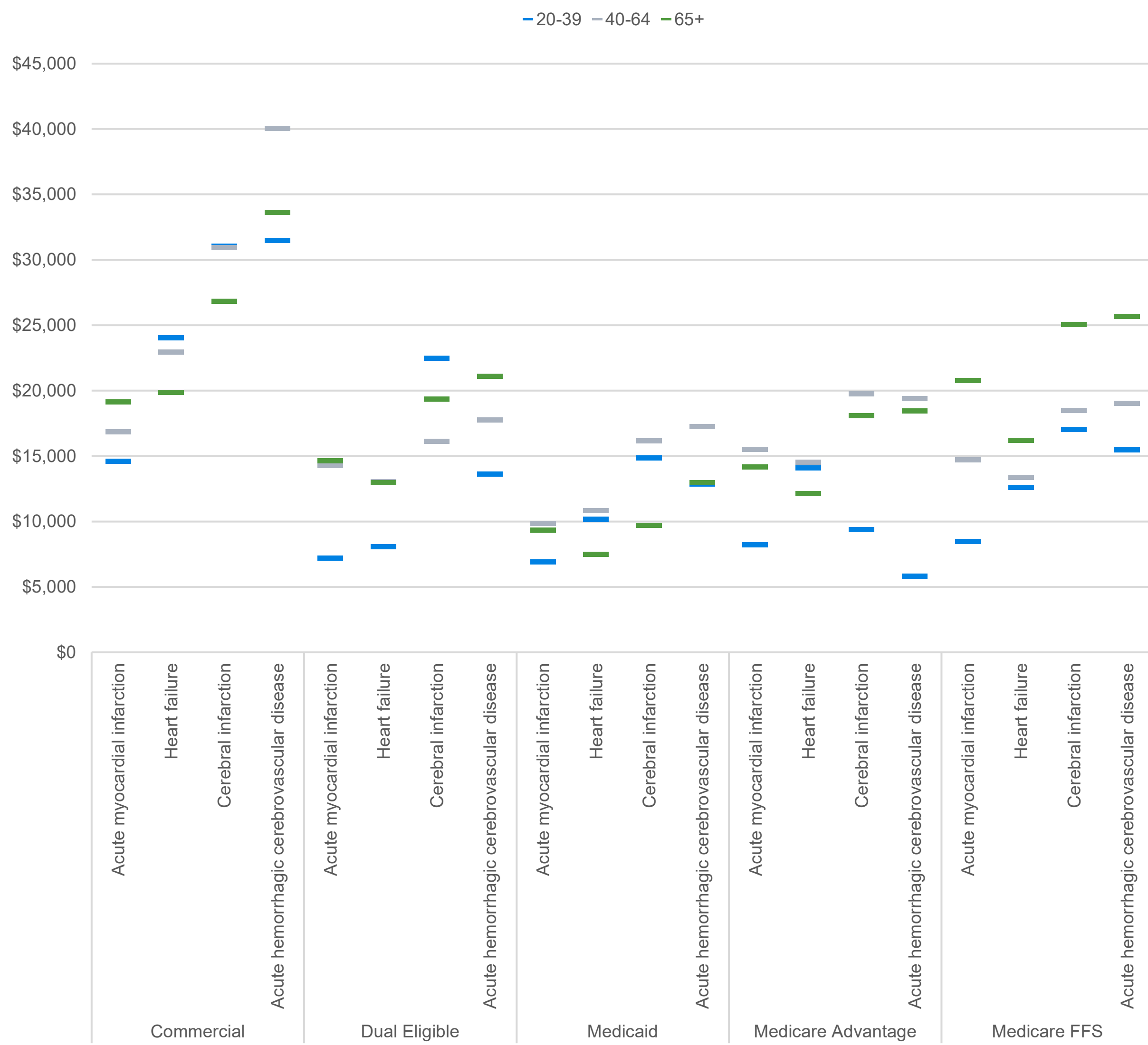


* Sourced from the Milliman MedInsight Emerging Experience research database

COST ANALYSIS OF ACUTE CV EVENTS AND RISK FACTORS

Only categories with at least 1,000 occurrences in our research database are displayed in the charts below.

FIGURE 4A: MEAN ALLOWED COST PER ACUTE CARDIOVASCULAR EVENT *



* Sourced from the Milliman MedInsight Emerging Experience research database

Each of the above cardiovascular events were defined by an inpatient admission or an emergency department visit, in association with the diagnostic category.

Transient ischemic attacks or transient cerebral ischemia can be considered an event ("early stroke") or a risk factor. For clarity of definition and clarity of cost and utilization charts, this condition was not prioritized for reporting.

The average allowed costs of a transient cerebral ischemia event ranged by age band, from $7,300 to $8,700 for commercially insured patients, $5,100 to $8,300 for Medicare FFS patients, and $3,800 to $5,500 for Medicare Advantage, each group reflecting several thousand occurrences. There were fewer transient cerebral ischemia events in the Medicaid and Dual Eligible groups, which ranged in costs from $3,100 to $4,400, or $2,600 to 6,800, respectively.

Figure 4B shows the association between the number of cardiac risk factors with each CV event and the number of management visits received per 1,000 patients for screening or management of cardiac risk factors. CV events were more frequent in patients with at least 1 cardiac risk factor, as shown in Figure 4B.

FIGURE 4B: VISITS PER 1,000 FOR SCREENING OR MANAGEMENT OF CARDIAC RISK FACTORS IN THE 12 MONTHS PRECEDING THE CV EVENT (INPATIENT AND OUTPATIENT) *

	Number of cardiac risk factors				
	0	**1**	**2**	**3**	**3+**
Commercial					
Acute hemorrhagic cerebrovascular disease	132.0	290.5	293.3	221.3	177.5
Acute myocardial infarction	67.9	156.5	253.0	279.6	331.6
Cardiac arrest and ventricular fibrillation	180.2	175.2	220.0	218.4	243.3
Cerebral infarction	84.3	189.8	283.2	286.6	267.3
Heart failure	38.6	119.6	237.2	316.7	577.7
Medicare Advantage					
Acute hemorrhagic cerebrovascular disease	63.1	168.8	315.9	348.5	360.3
Acute myocardial infarction	59.4	96.9	214.9	336.6	535.7
Cardiac arrest and ventricular fibrillation	56.1	98.8	207.0	284.0	467.5
Cerebral infarction	71.1	119.2	285.4	360.5	397.0
Heart failure	52.8	76.5	204.6	367.8	791.5
Medicare FFS					
Acute hemorrhagic cerebrovascular disease	44.2	153.0	309.0	349.4	342.3
Acute myocardial infarction	42.1	87.9	226.4	339.0	496.2
Cardiac arrest and ventricular fibrillation	37.2	92.5	223.2	308.9	464.3
Cerebral infarction	49.4	118.7	282.6	339.1	348.3
Heart failure	30.1	71.7	207.7	363.8	709.7
Dual Eligible					
Acute hemorrhagic cerebrovascular disease	68.4	158.6	251.1	351.4	392.6
Acute myocardial infarction	46.8	84.1	185.8	306.6	603.6
Cardiac arrest and ventricular fibrillation	69.4	129.8	229.7	392.7	571.4
Cerebral infarction	45.8	108.0	222.6	326.0	440.7
Heart failure	18.9	81.9	195.0	350.1	904.7
Medicaid					
Acute hemorrhagic cerebrovascular disease	125.1	267.0	325.0	263.5	256.2
Acute myocardial infarction	37.0	111.8	205.0	273.1	595.5
Cardiac arrest and ventricular fibrillation	158.9	196.1	243.8	242.7	327.4
Cerebral infarction	64.2	142.2	246.7	309.6	445.3
Heart failure	28.0	119.5	268.8	394.7	946.9

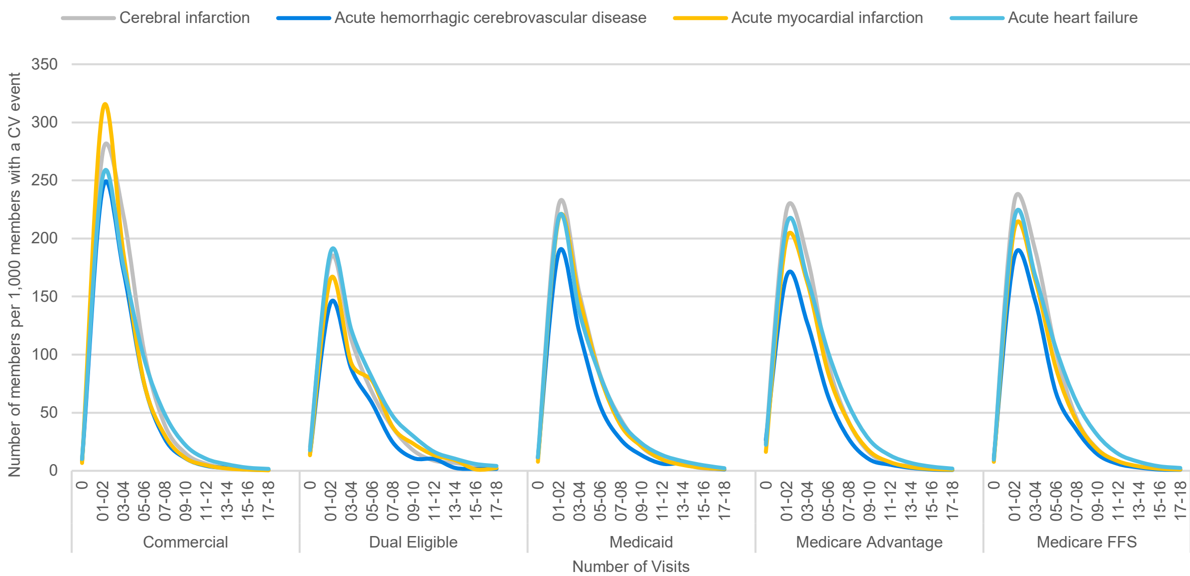
* Sourced from the Milliman MedInsight Emerging Experience research database

Patients who did not have any identified cardiac risk factors are not necessarily healthy, given that they also had a CV event. Lack of detection of CV risk factors may indicate lack of screening for risk factors, under-diagnosis, lesser access to healthcare, and less active management of modifiable cardiac risk factors.[13]

[13] Barghi, A., Torres, H., Kressin, N.R. *et al.* Coverage and Access for Americans with Cardiovascular Disease or Risk Factors After the ACA: a Quasi-experimental Study. J GEN INTERN MED 34, 1797–1805 (2019). Accessed from https://doi.org/10.1007/s11606-019-05108-1 on October 19, 2022.

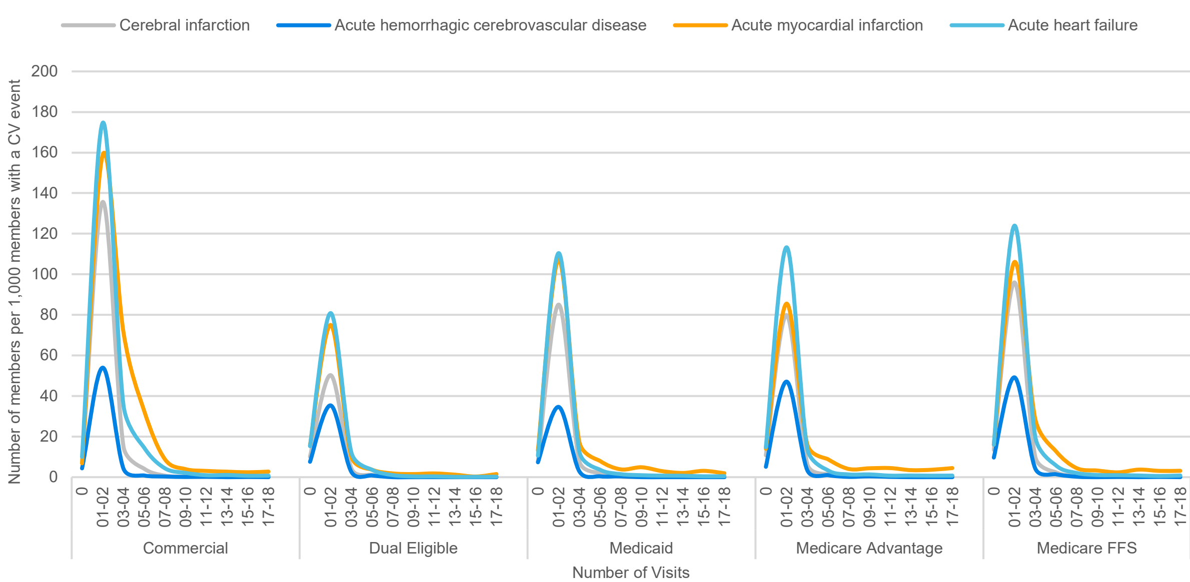
In the 6 months after a CV event, the majority of follow-up visits were to primary care providers, as shown in Figure 4C, suggesting both post-discharge management and longer-term management of underlying risk factors. Patients who had a myocardial infarction received 1 to 6 cardiovascular facility outpatient clinic visits to manage the consequences of that event. Most patients with other CV events visited the cardiovascular outpatient clinic once or twice in this time period, shown in Figure 4D, suggesting a greater emphasis on management by primary care.

FIGURE 4C: PATTERNS OF UTILIZATION OF FOLLOW-UP VISITS TO PRIMARY CARE PROVIDERS IN THE SIX MONTHS AFTER THE CV EVENT, ALL AGES, ALL GENDERS, ALL YEARS *



* Sourced from the Milliman MedInsight Emerging Experience research database

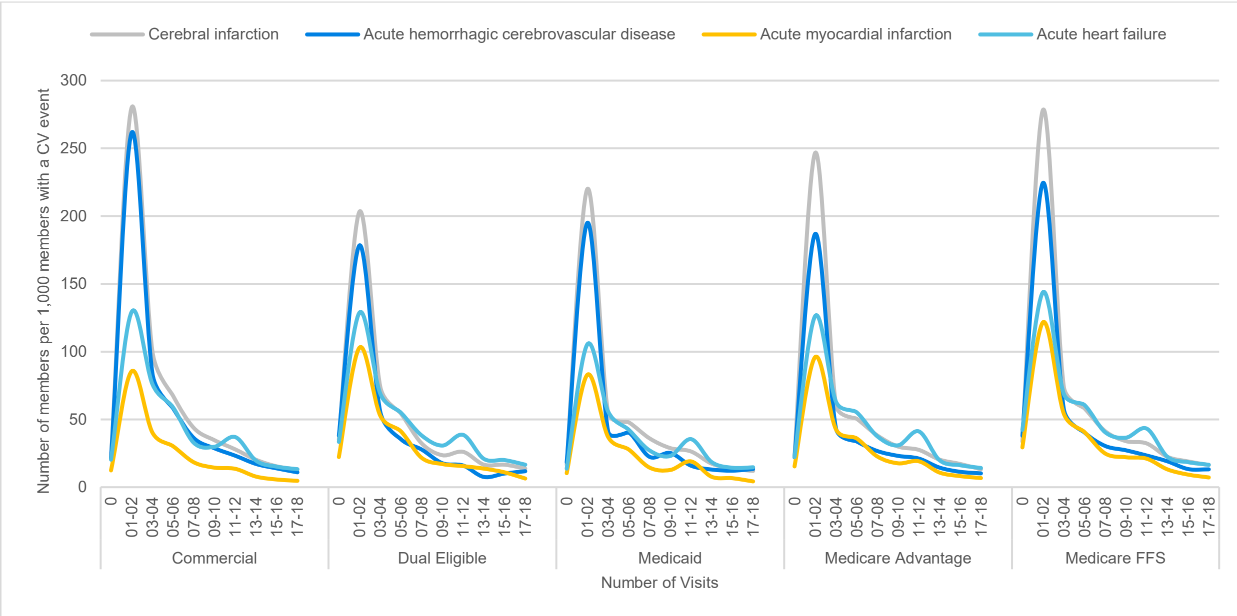
FIGURE 4D: PATTERNS OF UTILIZATION OF FOLLOW-UP VISITS TO CARDIOVASCULAR FACILITY OUTPATIENT CLINICS IN THE SIX MONTHS AFTER THE CV EVENT, ALL AGES, ALL GENDERS, ALL YEARS



* Sourced from the Milliman MedInsight Emerging Experience research database

Patients suffering ischemic stroke (cerebral infarction), hemorrhagic stroke (hemorrhagic cerebrovascular disease) utilized the greatest volume of rehabilitation services in the commercially insured population, as shown by the area under the frequency distribution curves in Figure 4E. In the Medicare and dual-eligible populations, patients with cerebral infarction or acute heart failure utilized the greatest number of rehabilitation services.

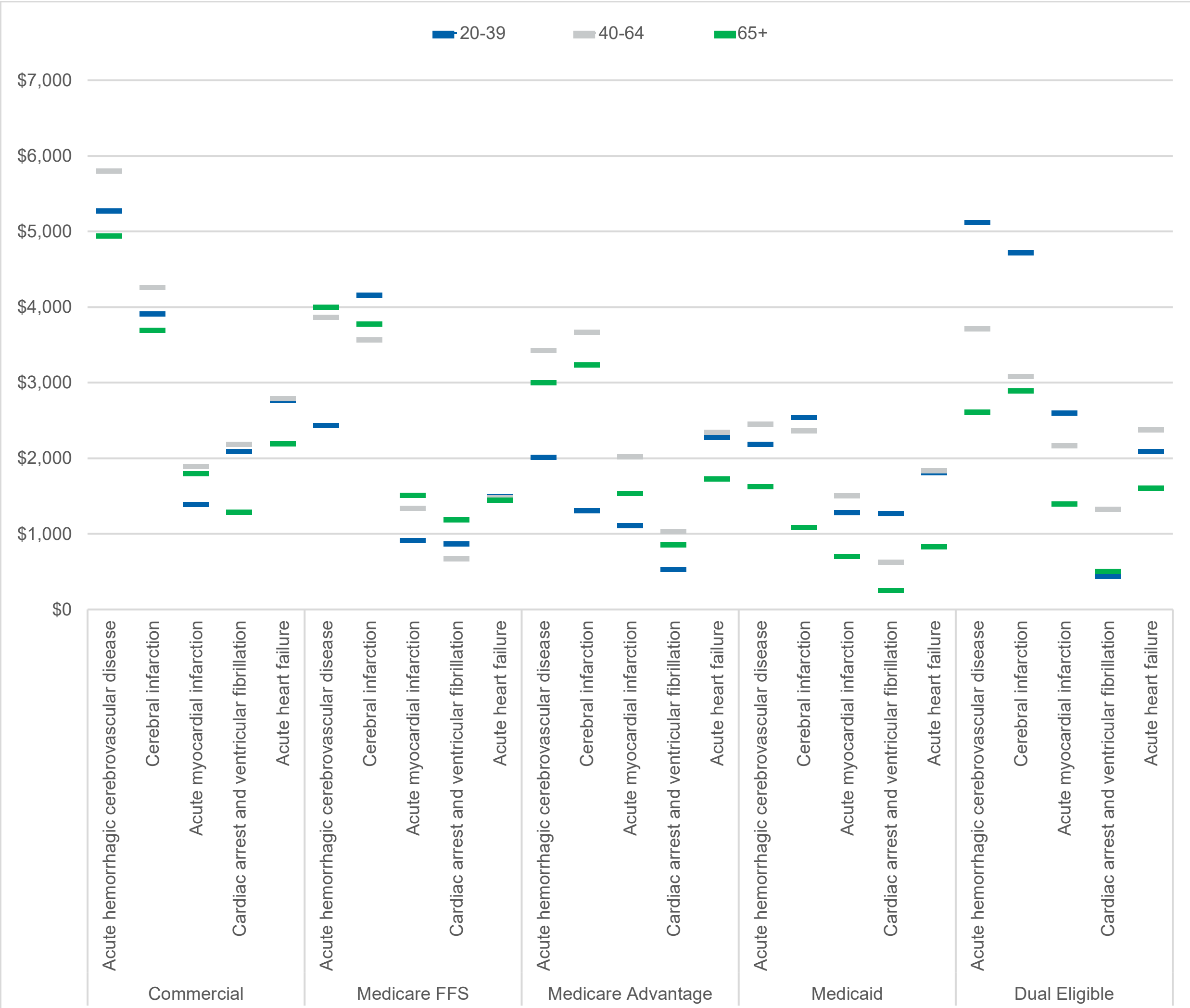
FIGURE 4E: PATTERNS OF UTILIZATION OF REHABILITATION SERVICES IN THE SIX MONTHS AFTER THE CV EVENT, ALL AGES, ALL GENDERS, ALL YEARS *



* Sourced from the Milliman MedInsight Emerging Experience research database

Finally, we measured the costs of follow-up care in the 6 months following the acute CV event by age band for each payer group. Total follow-up costs per member are shown in Figure 4C, and costs of types of follow-up services are portrayed in Figure 4D.

FIGURE 4C: MEAN TOTAL FOLLOW-UP COSTS PER PATIENT DURING THE 6 MONTHS AFTER EACH CV EVENT *



* Sourced from the Milliman MedInsight Emerging Experience research database

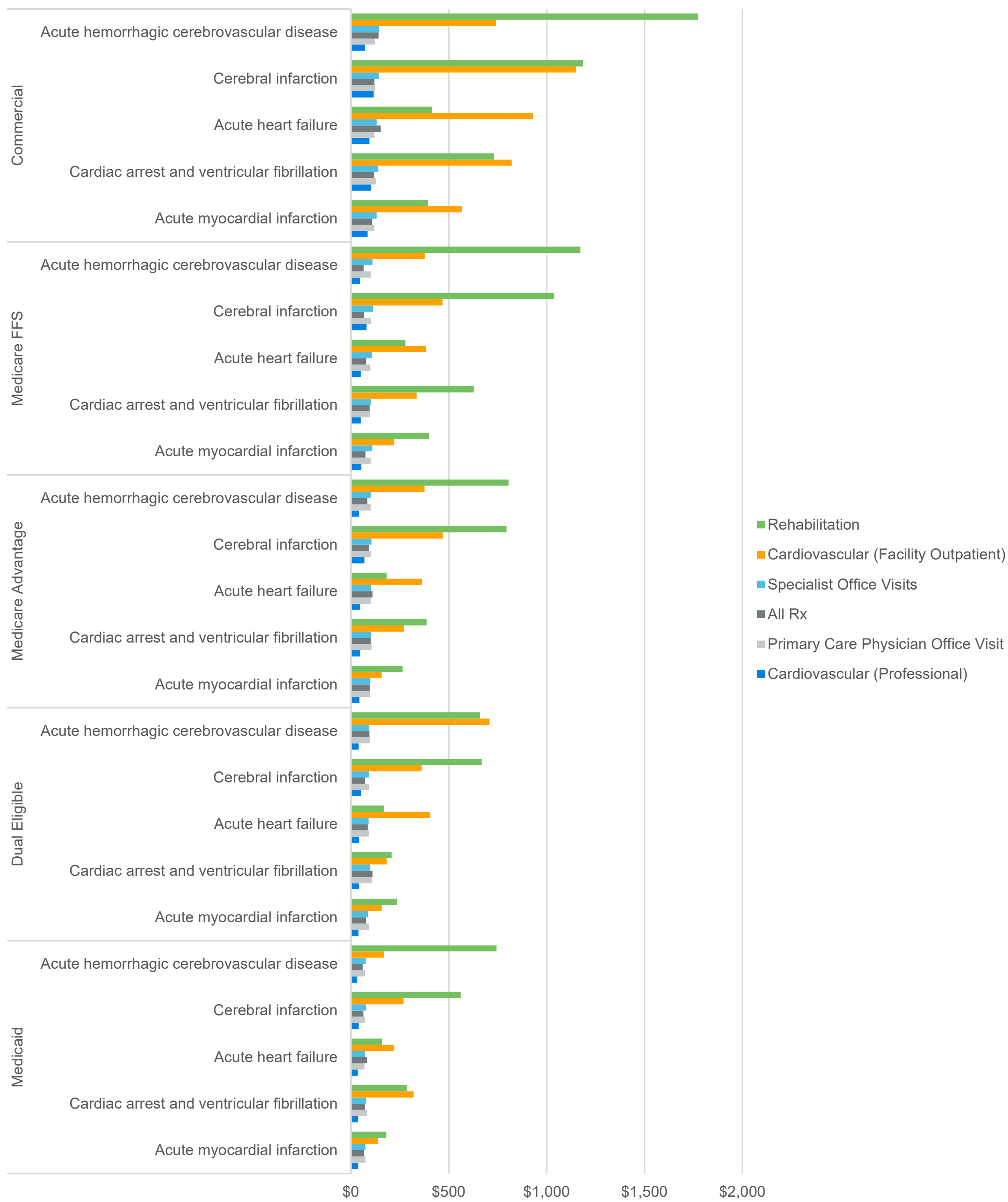
Older patients, on average, utilized more follow-up services than younger patients, recovering from the same type of CV event. However, costs for hemorrhagic or ischemic stroke were high for all age bands, driven mostly by high post-acute needs for inpatient and outpatient rehabilitation services for stroke survivors.

Patients who are dually eligible for Medicaid and Medicare coverage tend to have more complex needs and higher costs of care, and may include those with physical disabilities, multiple chronic conditions, mental illness, dementia and developmental disabilities. Low numbers of dual eligible patients in our datasets can cause wider variation and potential outlier costs, and it is known that this group accounts for a disproportionate share of health expenditures.[14]

The highest total follow-up costs per patient were incurred for rehabilitation, followed by cardiovascular facility outpatient clinic visits. Stroke (hemorrhagic or ischemic) incurred the highest rehabilitation costs in all payer groups, as shown in Figure 4D.

[14] Medicaid and CHIP Payment and Access Commission (MACPAC). Dually Eligible Beneficiaries. Accessed from https://www.macpac.gov/topics/dually-eligible-beneficiaries/ on October 19, 2022.

FIGURE 4D: MEAN ALLOWED TOTAL COST OF FOLLOW- UP SERVICES PER PATIENT DURING THE 6 MONTHS AFTER EACH CV EVENT *



* Sourced from the Milliman MedInsight Emerging Experience research database

Supplemental Analysis

To gain additional understanding of the patterns of CVD diagnostic tests and interventions, we also assessed the number of patients receiving multiple interventions or multiple diagnostic tests in the six months before an intervention, shown in Figure 5.

Approximately 90% of CABG and inpatient PCI patients received only 1 CVD intervention. Sixteen percent of outpatient PCI patients received 2 CVD interventions (of any type). There are a few instances of patients receiving 6 to 12 interventions (of any type), particularly in the outpatient PCI group.

The majority of outpatient PCI and CABG patients received more than one diagnostic test. The majority of inpatient PCI patients received only 1 diagnostic test before the intervention.

FIGURE 5: FREQUENCY OF INTERVENTIONS AND CVD DIAGNOSTIC TESTS IN THE STUDY COHORT *

			Patients receiving 1 or more interventions (any kind) from July 1, 2017 to Dec 31, 2021		Number of CV diagnostic tests (any type) in the 6 months prior to the intervention			
Type of intervention	**% of patients receiving that intervention**	**Total number of interventions (any kind) received for each patient**	**Number of patients**	**Percentage of total**	**1 CV test**	**2 CV tests**	**3 CV tests**	**4 CV tests**
CABG	**18%**		**70,097**	**100%**	**44.4%**	**18.6%**	**30.6%**	**5.3%**
		1	62,452	89%	44.0%	18.7%	31.4%	5.0%
		2	6,410	9%	49.8%	17.2%	24.3%	6.6%
		3	929	1%	39.9%	22.7%	22.2%	9.7%
		4	205	0%	27.3%	22.9%	25.4%	15.6%
		5	65	0%	33.8%	21.5%	20.0%	13.8%
		6	20	0%	30.0%	20.0%	30.0%	10.0%
		7	8	0%	50.0%	25.0%	0.0%	12.5%
		8	4	0%	0.0%	50.0%	25.0%	0.0%
		9	2	0%	0.0%	0.0%	50.0%	0.0%
		10	1	0%	100.0%	0.0%	0.0%	0.0%
		11	1	0%	0.0%	0.0%	100.0%	0.0%
PCI IP	**36%**		**136,026**	**100%**	**76.1%**	**12.5%**	**8.8%**	**1.9%**
		1	122,638	90%	79.4%	11.2%	7.9%	1.2%
		2	10,429	8%	47.8%	24.2%	17.3%	7.4%
		3	2,052	2%	38.4%	26.3%	18.4%	10.6%
		4	535	0%	36.1%	25.2%	19.3%	11.0%
		5	217	0%	35.5%	24.9%	18.4%	9.2%
		6	76	0%	30.3%	23.7%	17.1%	11.8%
		7	33	0%	36.4%	30.3%	21.2%	3.0%
		8	20	0%	35.0%	15.0%	25.0%	10.0%
		9	12	0%	25.0%	25.0%	25.0%	8.3%
		10	9	0%	22.2%	33.3%	11.1%	11.1%
		11	3	0%	33.3%	0.0%	0.0%	33.3%
		12	2	0%	50.0%	50.0%	0.0%	0.0%
PCI OP	**46%**		**172,974**	**100%**	**33.8%**	**19.4%**	**36.7%**	**7.9%**
		1	139,691	81%	34.5%	18.4%	39.0%	6.8%
		2	27,454	16%	30.4%	24.4%	27.2%	12.8%
		3	4,263	2%	31.5%	19.5%	28.4%	11.6%
		4	990	1%	32.5%	22.1%	24.1%	11.3%
		5	323	0%	31.9%	24.5%	24.1%	9.6%
		6	147	0%	33.3%	22.4%	23.8%	12.2%
		7	61	0%	29.5%	26.2%	18.0%	6.6%
		8	28	0%	28.6%	32.1%	21.4%	3.6%
		9	8	0%	25.0%	50.0%	12.5%	12.5%
		10	4	0%	25.0%	75.0%	0.0%	0.0%
		11	3	0%	66.7%	0.0%	0.0%	0.0%
		12	2	0%	100.0%	0.0%	0.0%	0.0%

* Sourced from the Milliman MedInsight Emerging Experience research database

Discussion

A study of patient data from the American College of Cardiology National Cardiovascular Data Registry, found that invasive coronary angiograms identified obstructive coronary artery disease (CAD) in approximately 60% of 1,989,779 patients with a history of cardiac disease (defined as prior myocardial infarction, previous PCI, CABG, cardiac transplant or valve surgery), but only in 38% of 397,954 patients without known coronary artery disease (median age 61 years).[15] Both categories have relatively low yields and this is consistent with the observations in our research dataset.

A cost-effectiveness derivation study modeled outcomes and costs, based on patient data from the prospective randomized PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) of 10,003 real-life US patients from 192 US sites presenting with stable chest pain and suspicion of obstructive coronary artery disease.[16] That model used cost estimates from the PROMISE trial, specifically CCTA $404, other non-invasive testing $174-$1,061, invasive coronary angiograms $3,656, PCI $12,779, and CABG $32,546 in 2014 dollars based on Medicare cost-to-charge ratios and the Medicare Physician Fee Schedule.[17, 18] Those findings are comparable to our Medicare Advantage, Medicaid and Dual observations when adjusted for inflation using medical price index factor of 1.21, obtained from the medical care component of the Consumer Price Index from the Bureau of Labor Statistics.[19] Our results for commercially insured patients were 32% higher than these Medicare dollars for outpatient PCI and 55% higher for inpatient CABG, after adjusting for inflation using the same factor.

The PROMISE trial focused on low risk, symptomatic patients, and studied the diagnostic accuracy of CCTA compared to functional tests (treadmill exercise tests, stress echocardiography, and nuclear stress tests). It found no difference between anatomic CCTA and functional testing for the primary endpoint of all-cause mortality, acute myocardial infarction, hospitalization for unstable angina, and major complications from a CV procedure.[20] CCTA was associated with greater radiation exposure, and more cardiac catheterizations at 90 days.[21] A 2012 Institute of Medicine report on breast cancer identified medical imaging as a preventable cause of breast cancer.[22]

The International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial also revealed no improvement in outcomes with routine cardiac catheterization followed by invasive revascularization interventions in patients with stable chest pain and moderate to severe ischemic heart disease. The primary end-point was a composite of cardiovascular death, non-fatal myocardial infarction, resuscitated cardiac arrest, or hospitalization for unstable angina or heart failure.[23]

The 75+ year age band for all payer groups in our study had a lower number of patients than other age bands, which is consistent with average life expectancy.[24] A lower rate of testing in this age range that may reflect increased

[15] Patel MR, Peterson ED, Dai D, *et al.* Low diagnostic yield of elective coronary angiography. N Engl J Med. 2010; 362(10):886-895. doi:10.1056/NEJMoa0907272n. Accessed from https://www.nejm.org/doi/full/10.1056/NEJMoa0907272 on October 12, 2022.

[16] Douglas, PS, Hoffmann U. Patel MR, *et al.* Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease. N Engl J Med 2015; 372:1291-1300. April 2015. DOI: 10.1056/NEJMoa1415516 Accessed from https://www.nejm.org/doi/full/10.1056/NEJMoa1415516 on October 12, 2022.

[17] Mark DB, Federspiel JJ *et al.* Economic Outcomes With Anatomical Versus Functional Diagnostic Testing for Coronary Artery Disease. Annals of Internal Medicine. July 2016. Retrieved from https://doi.org/10.7326/M15-2639 on October 15, 2022.

[18] Karády J, Mayrhofer T, Ivanov A, *et al.* Cost-effectiveness Analysis of Anatomic vs Functional Index Testing in Patients With Low-Risk Stable Chest Pain. JAMA Netw Open. 2020;3(12):e2028312. doi:10.1001/jamanetworkopen.2020.28312. Accessed from https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774097 on October 12, 2022.

[19] U.S. Bureau of Labor Statistics. Medical care in U.S. city average, all urban consumers, not seasonally adjusted. Annual averages for 2014 and 2021. Retrieved from https://data.bls.gov/timeseries/CUUR0000SAM?output_view=data on October 15, 2022.

[20] Oberweis BS and Taylor AJ. The PROMISE Trial: The CTA Perspective. July 2015. The American College of Cardiology. Accessed from https://www.acc.org/latest-in-cardiology/articles/2015/07/27/10/58/the-promise-trial-the-cta-perspective on October 19, 2022.

[21] Duffy E, Blumenthal RS, and Zadeh AA. CCTA as a Tool for Prevention in Patients with Stable Chest Pain. American College of Cardiology. September 2020. https://www.acc.org/latest-in-cardiology/articles/2020/09/10/12/16/ccta-as-a-tool-for-prevention-in-patients-with-stable-chest-pain on October 15, 2022.

[22] Smith-Bindman R. Environmental causes of breast cancer and radiation from medical imaging: findings from the Institute of Medicine report. Arch Intern Med. 2012 Jul 9;172(13):1023-7. doi:10.1001/archinternmed.2012.2329. Accessed from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3936791/ on December 12, 2022.

[23] International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA). ClinicalTrials,gov. Last update posted August 2022. Accessed on International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) - Full Text View - ClinicalTrials.gov October 19, 2022.

[24] CDC. Provisional Life Expectancy Estimates for 2021. National Vital Statistics Rapid Release Report No. 23. August 2022. Accessed from https://www.cdc.gov/nchs/data/vsrr/vsrr023.pdf on October 12, 2022.

patient frailty or greater severity of conditions and multiple comorbidities compared to younger patients.[25]

We chose not to risk-adjust the observational measures, because the patients in our study were already identified based on their utilization of cardiovascular disease diagnostic tests, revascularization procedures, or cardiac events, and would be expected to have similar levels of risk within our age, gender and payer groups. Risk adjustment models tend to be based on previous cost and utilization history, which might result in patients who have less access to healthcare appearing as low risk due to lower consumption of services. It is possible that the need for care is under-recognized for patients in this age group.

Researchers from Toronto in Canada found that non-invasive stress testing only led to improved outcomes in high-risk patients (prior myocardial infarction, unstable angina, or prior PCI or CABG) presenting to the emergency department (ED) with chest pain. Increased follow-up with primary care and cardiologists after ED discharge, higher invasive angiography and revascularization interventions was associated with lower myocardial infarction events and cardiovascular deaths at one year after the index ED visit for assessment of chest pain. This improvement in outcomes did not occur in patients receiving diagnostic tests, who were characterized as intermediate risk (more than one cardiovascular risk factor) and low risk (zero cardiovascular risk factors).[26]

In 2022, the American Heart Association (AHA) published a new scientific statement about strategies to reduce cardiovascular “low-value care”, defined as services that provide little or no benefit to patients, are potentially harmful, and costly, and discusses studies on overuse of coronary angiograms, stress echocardiography, and nuclear stress tests.[27] The American Board of Internal Medicine Foundation’s Choosing Wisely initiative outlines common clinical scenarios in which low value care occurs, based on appropriate use criteria and recommendations from expert professional bodies such as the American College of Cardiology and the American Heart Association.[28] These include coronary angiography in patients without cardiac symptoms unless high-risk markers are present, and stress cardiac imaging or advanced non-invasive imaging in the initial evaluation of patients without cardiac symptoms unless high-risk markers are present.[29]

An emerging strategy to improve diagnostic accuracy, as well as primary and secondary prevention of cardiovascular events, is the use of predictive clinical biomarkers, which might be helpful in assessing patients presenting with chest pain who are characterized as intermediate risk or low risk. Biomarker researchers at Massachusetts General Hospital and the University Heart & Vascular Center Hamburg, Germany, applied machine learning models to determine a predictive, algorithmically-weighted panel of multiple protein biomarkers.[30] These novel models may improve predictive accuracy compared to traditional risk scores, such as the Thrombolysis In Myocardial Infarction (TIMI) score[31] and the Framingham risk score[32]. The multiple protein, algorithmically-weighted biomarker approach

[25] Benetos A, Petrovic M and Strandberg T. Hypertension Management in Older and Frail Older Patients. Circulation Research. 2019;124:1045–1060. March 2019. https://doi.org/10.1161/CIRCRESAHA.118.313236 Accessed on October 12, 2022.

[26] Roifman I, Sivaswamy A, Chu A, Austin PC, Ko DT, Douglas PS, Wijeysundera HC. Clinical Effectiveness of Cardiac Noninvasive Diagnostic Testing in Outpatients Evaluated for Stable Coronary Artery Disease. J Am Heart Assoc. 2020 Jul 7;9(13):e015724. doi: 10.1161/JAHA.119.015724. Epub 2020 July 1. PMID: 32605412; PMCID: PMC7670545. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7670545/pdf/JAH3-9-e015724.pdf. Accessed October 8, 2022.

[27] American Heart Association. Kini V, Breathett K, Groeneveld PW, *et al.* AHA Scientific Statements: Strategies to Reduce Low-Value Cardiovascular Care: A Scientific Statement From the American Heart Association. Circulation: Cardiovascular Quality and Outcomes. Volume 15, Issue 3, March 2022. Accessed from https://www.ahajournals.org/doi/10.1161/HCQ.0000000000000105 on December 15, 2022.

[28] American Board of Internal Medicine Foundation. Choosing Wisely. Accessed from https://www.choosingwisely.org/ on December 12, 2022.

[29] Wolk MJ, Bailey SR, Doherty JU, *et al.* ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons, Journal of the American College of Cardiology, Volume 63, Issue 4, 2014. Accessed from https://www.sciencedirect.com/science/article/pii/S0735109713061470?via%3Dihub#sec11 on December 12, 2022.

[30] Neumann JT, Sorensen NA, Zeller T, *et al.* Application of a machine learning-driven,multibiomarker panel for prediction of incident cardiovascular events in patients with suspected myocardial infarction. Biomarkers in Medicine: 10.2217/bmm-2019-0584. Accessed from www.futuremedicine.com/doi/10.2217/bmm-2019-0584 on October 31, 2022.

[31] Sun BC, Laurie A, Fu R, *et al.* Comparison of the HEART and TIMI Risk Scores for Suspected Acute Coronary Syndrome in the Emergency Department. Crit Pathw Cardiol. 2016 Mar;15(1):1-5. doi: 10.1097/HPC.0000000000000066. PMID: 26881812. Accessed from https://journals.lww.com/critpathcardio/Fulltext/2016/03000/Comparison_of_the_HEART_and_TIMI_Risk_Scores_for.1.aspx on November 12, 2022.

[32] Ko DT, Sivaswamy A, Sud M, *et al.* Calibration and discrimination of the Framingham Risk Score and the Pooled Cohort Equations. Canadian Medical Association Journal, 2020. Volume 192, Issue 17, Pages E442-E449. Accessed from https://www.clinicalkey.com/#!/content/journal/1-s2.0-S082039462030211X on November 12, 2022.

might enable earlier detection of CVD, may enhance the sensitivity and specificity of other non-invasive CVD diagnostic tests, and might be useful for patients with contraindications to other non-invasive tests, such as CCTA in patients with renal impairment or renal failure.[33]

Limitations and Next Steps

PURPOSE AND LIMITATIONS

This study is intended to be used to understand and estimate the patterns of cost and utilization for CVD diagnostic tests and subsequent revascularization interventions, and it may not be appropriate for other purposes.

Healthcare claims data that are relied on for our conclusions are documented and collected primarily for administrative purposes and often lack clinical details such as lab values, clinician notes, and plans of care. Despite this limitation, claims data has the advantage of providing a comprehensive view of healthcare services incurred and billed to insurance from any healthcare professional or facility. The claims research database we used comprises over 10 billion lines of healthcare claims data from approximately 75 healthcare organizations spread across all 50 states and can be considered a randomized sample. We examined the geographical, age, and gender distribution of the research database, which was found to be similar to the American Community Survey (ACS) results for each census region.

This study does not include uninsured individuals, and it does not include undiagnosed individuals who are estimated to represent 60% of all U.S. adults with coronary heart disease[34] and 21.4% of all U.S. adults with diabetes.[35]

The analysis of CVD diagnostic tests excludes patients who did not have continuous insurance coverage during the 90-day look-forward period after the test. The analysis of acute CVD events excludes patients who lacked continuous insurance coverage during the 12 months preceding the event. The analysis of 6-month post-CVD event does not include patients who died during the acute event or in the subsequent six months, however both patients who died and patients who survived are included in the analysis of acute CVD events.

Cardiovascular deaths are only partially represented in claims databases, because death is only reported in the discharge status field on facility claims.

Costs and utilization can vary from person to person. Actual experience will vary from our estimates for many reasons, potentially including differences in population health status, reimbursement levels, delivery systems, random variation, or other factors. It is important that actual experience be monitored, and adjustments made, as appropriate.

POTENTIAL FUTURE RESEARCH

The observational findings from this nationwide research database can be weighted to the age and gender distribution of an organization’s specific population, and/or tailored to a particular geography.

Additional research is needed to learn about the impacts of screening on different populations, particularly racial and ethnic groups that have a high prevalence of CVD. Further research might also be able to explore the cost effectiveness of currently available and novel CVD diagnostic tests.

Conclusion

Cardiovascular disease is a global problem, impacting well-being, mortality, and healthcare expenditures. This report outlines the patterns of cost and utilization associated with CVD diagnostic tests, CVD interventions and CV events. It studied $4.96 billion of spend on diagnostic tests by commercially insured patients aged 50-64 years, and $1.67

[33] McCarthy CP, Neumann JT, Januzzi Jr JL, *et al.* Derivation and External Validation of a High-Sensitivity Cardiac Troponin–Based Proteomic Model to Predict the Presence of Obstructive Coronary Artery Disease. J Am Heart Assoc. 2020;9:e017221. DOI: 10.1161/JAHA.120.017221 Accessed from http://ahajournals.org on October 31, 2022.

[34] Bularga A., Hung J. *et al.* Coronary Artery and Cardiac Disease in Patients With Type 2 Myocardial Infarction: A Prospective Cohort Study. Circulation. 2022;145:1188–1200. March 2022. https://doi.org/10.1161/CIRCULATIONAHA.121.058542 Accessed on October 4, 2022.

[35] CDC Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. Accessed on October 15, 2022 from https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

billion of spend on diagnostic tests by Medicare patients aged 65 years and older, from 2017 to 2021. This was based on a research database of approximately 73 million lives, and reported unit costs by payer group, age and gender for greater generalizability. Ongoing advancements in diagnostic accuracy may reduce the need for and cost of multiple tests, particularly in patients with moderate to low risk. In addition to reducing redundancy, "low-value care", and associated expense of multiple tests, there is an opportunity to reduce the increased cancer risk associated with medical imaging.

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Appendix

APPENDIX A: MEAN PERCENTAGE OF DIAGNOSTIC TESTS LEADING TO REVASCULARIZATION INTERVENTIONS, 2017 TO 2021 *

		Commercial			Medicare Advantage			Medicare FFS			Medicaid			Dual Eligible		
	Age	50-64	65-74	75+	50-64	65-74	75+	50-64	65-74	75+	50-64	65-74	75+	50-64	65-74	75+
CCTA																
CABG																
	M	1.78%	2.66%	2.18%	2.94%	2.83%	1.77%	1.20%	2.97%	1.75%	0.99%	4.11%	0.00%	4.37%	4.59%	4.10%
	F	0.47%	0.78%	1.63%	1.78%	1.22%	0.62%	0.60%	0.83%	0.79%	0.65%	2.36%	2.92%	2.49%	1.13%	1.87%
PCI IP																
	M	1.18%	1.40%	1.61%	2.12%	1.34%	1.93%	1.46%	1.08%	1.75%	1.73%	4.16%	5.12%	3.96%	1.79%	2.85%
	F	0.49%	0.65%	1.91%	1.24%	0.78%	1.21%	0.95%	0.54%	1.43%	0.91%	0.00%	4.14%	0.00%	1.35%	1.61%
PCI OP																
	M	4.20%	6.20%	5.40%	5.24%	7.55%	6.53%	5.31%	7.42%	7.87%	2.33%	4.24%	5.76%	4.75%	5.22%	4.76%
	F	1.65%	3.29%	3.50%	2.17%	3.19%	4.52%	3.20%	3.91%	4.58%	1.19%	2.39%	5.01%	1.72%	3.07%	2.63%
Coronary angiogram																
CABG																
	M	7.34%	8.64%	5.81%	4.49%	7.29%	4.90%	4.13%	7.07%	4.70%	5.74%	5.69%	2.65%	3.30%	4.35%	3.14%
	F	3.04%	3.88%	2.29%	2.64%	3.55%	2.54%	2.42%	3.24%	2.24%	3.12%	3.26%	1.41%	2.07%	3.39%	1.54%
PCI IP																
	M	11.99%	9.64%	8.21%	8.50%	8.51%	9.23%	8.01%	8.10%	8.42%	11.87%	9.38%	9.07%	8.50%	9.18%	9.16%
	F	6.81%	6.84%	8.24%	7.09%	6.80%	8.67%	6.59%	6.37%	7.95%	8.14%	6.27%	6.36%	7.58%	7.22%	8.13%
PCI OP																
	M	15.91%	18.49%	16.56%	14.08%	18.10%	17.98%	14.52%	19.98%	20.67%	10.95%	13.31%	17.02%	12.21%	14.41%	14.49%
	F	8.95%	11.11%	10.28%	10.08%	11.57%	12.07%	9.97%	12.59%	12.98%	7.76%	9.87%	12.37%	7.36%	10.36%	11.90%
Nuclear stress tests																
CABG																
	M	1.45%	1.69%	1.18%	0.95%	1.52%	1.04%	1.00%	1.50%	0.96%	1.07%	0.84%	0.36%	0.66%	0.91%	0.57%
	F	0.37%	0.49%	0.35%	0.39%	0.53%	0.40%	0.41%	0.47%	0.36%	0.37%	0.39%	0.23%	0.24%	0.47%	0.25%
PCI IP																
	M	0.78%	0.83%	0.99%	1.03%	0.86%	1.05%	1.07%	0.86%	1.02%	1.02%	1.42%	0.94%	1.00%	1.01%	0.79%
	F	0.36%	0.41%	0.53%	0.64%	0.55%	0.63%	0.62%	0.53%	0.63%	0.66%	0.58%	0.38%	0.87%	0.73%	0.59%
PCI OP																
	M	3.47%	3.90%	3.11%	3.11%	3.92%	3.47%	3.29%	4.05%	3.70%	2.08%	1.39%	1.77%	2.49%	2.60%	2.19%
	F	1.23%	1.56%	1.29%	1.70%	1.79%	1.75%	1.67%	1.78%	1.67%	1.02%	1.04%	0.63%	1.30%	1.39%	1.42%
Stress Echocardiogram																
CABG																
	M	0.85%	1.19%	1.04%	0.86%	1.38%	1.22%	0.76%	1.23%	1.15%	0.57%	0.54%	2.24%	0.44%	0.63%	0.86%
	F	0.20%	0.27%	0.15%	0.16%	0.42%	0.24%	0.31%	0.27%	0.26%	0.18%	0.84%	0.00%	0.24%	0.19%	0.88%
PCI IP																
	M	0.39%	0.46%	0.41%	0.61%	0.52%	0.75%	0.54%	0.48%	0.69%	0.52%	0.55%	1.68%	0.67%	0.61%	0.72%
	F	0.15%	0.20%	0.23%	0.34%	0.29%	0.44%	0.24%	0.24%	0.36%	0.26%	0.45%	1.70%	0.44%	0.36%	0.78%
PCI OP																
	M	1.69%	2.29%	2.27%	1.26%	2.44%	2.83%	1.60%	2.56%	2.67%	1.14%	1.37%	1.41%	1.61%	1.26%	1.73%
	F	0.54%	0.93%	0.96%	0.74%	1.04%	1.10%	0.66%	1.00%	1.09%	0.55%	0.88%	1.41%	0.61%	0.86%	0.89%
Treadmill Test																
CABG																
	M	1.21%	1.55%	1.15%	0.95%	1.49%	1.06%	0.91%	1.44%	0.96%	0.92%	0.77%	0.40%	0.58%	0.86%	0.60%
	F	0.29%	0.42%	0.33%	0.37%	0.51%	0.37%	0.40%	0.44%	0.34%	0.31%	0.36%	0.21%	0.23%	0.46%	0.23%
PCI IP																
	M	0.63%	0.74%	0.86%	0.98%	0.79%	1.01%	1.00%	0.80%	0.98%	0.88%	1.00%	1.04%	0.92%	0.87%	0.76%
	F	0.27%	0.36%	0.47%	0.59%	0.51%	0.63%	0.60%	0.47%	0.61%	0.49%	0.38%	0.33%	0.76%	0.65%	0.52%
PCI OP																
	M	2.74%	3.39%	2.90%	2.81%	3.61%	3.32%	3.08%	3.69%	3.52%	1.79%	1.13%	1.77%	2.27%	2.39%	2.02%
	F	0.93%	1.32%	1.19%	1.61%	1.65%	1.68%	1.49%	1.60%	1.60%	0.82%	0.79%	0.54%	1.22%	1.28%	1.33%

* Sourced from the Milliman MedInsight Emerging Experience research database

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