Angiography-Derived Fractional Flow Reserve Clinical Coverage Criteria

Overview

Fractional flow reserve (FFR) is an index of the physiological significance of a coronary artery stenosis. It is derived by using a coronary artery pressure guidewire to measure the distal coronary artery pressure.

Angiography-derived FFR refers to a group of emerging, wire-free technologies that enable functional assessment of coronary artery stenosis directly from standard coronary angiography. These methods use computational fluid dynamics, mathematical modeling, and/or artificial intelligence (AI) applied to angiographic images to estimate the physiologic significance of coronary lesions, without the use of intracoronary pressure wires or pharmacologic induction of hyperemia.

Policy

This Policy applies to the following Fallon Health products:

☒ Fallon Medicare Plus
☒ MassHealth ACO
☒ NaviCare HMO SNP
☒ PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
☒ Community Care

Fallon Health Clinical Coverage Criteria

Angiography-derived fractional flow reserve (FFR) is considered experimental and investigational for the physiologic assessment of coronary artery stenosis.

Medicare Variation

Medicare statutes and regulations do not have coverage criteria for angiography-derived fractional flow reserve. Medicare does not have an NCD for angiography-derived fractional flow reserve. National Government Services, Inc., the Part A/B Medicare Administrative Contractor with jurisdiction in the Plan's service area does not have an LCD for angiography-derived fractional flow reserve (Medicare Coverage Database search 6/22/2026). When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

MassHealth Variation

MassHealth does not have Guidelines for Medical Necessity Determination for angiography-derived fractional flow reserve, therefore, Fallon Health Clinical Coverage Criteria are applicable (MassHealth website search 06/22/2026).

Exclusions

- N/A

Summary of Evidence

Background

Coronary artery disease (CAD), primarily caused by atherosclerosis-induced narrowing or occlusion of the coronary arteries, is one of the most prevalent cardiovascular diseases globally. In fact, CAD is the leading cause of death worldwide, accounting for approximately 16% of global mortality (Mensah et al., 2019). Accurate assessment of CAD, particularly in cases of intermediate coronary artery stenosis, is

crucial for evaluating myocardial ischemia and determining the appropriate next steps in treatment. Coronary angiography is the established standard for identifying CAD. However, angiographic images often fall short in determining the functional significance of a stenosis. This limitation can result in unnecessary revascularizations or, conversely, the deferral of necessary interventions (Lawton et al., 2022).

FFR is an index of the physiological significance of a coronary stenosis and is defined as the ratio of maximal blood flow in a stenotic artery to normal maximal flow. It can be measured during coronary angiography by calculating the ratio of distal coronary pressure measured with a coronary pressure guide wire to aortic pressure measured simultaneously with the guiding catheter. FFR in a normal coronary artery equals 1.0. An FFR value of 0.80 or less identifies ischemia-causing coronary stenoses with an accuracy of more than 90%.

Pressure-derived fractional flow reserve (FFR), also referred to as invasive FFR, is obtained using a pressure-sensitive coronary guidewire and is widely regarded as the gold standard for assessing the functional significance of coronary artery stenoses. It provides a lesion-specific measure of ischemia and is strongly recommended by clinical guidelines as a key tool for guiding revascularization decisions, particularly in intermediate coronary lesions (Lawton et al., 2022, Neumann et al., 2018). FFR is highly sensitive and specific in detecting myocardial ischemia, and studies consistently demonstrate that FFR-guided percutaneous coronary intervention (PCI) reduces the number of implanted stents and significantly improves clinical outcomes compared to angiography alone (Pijls et al., 1996, Fearon WF, 2014).

Invasive FFR obtained using a pressure-sensitive guidewire is considered the reference standard for physiologic lesion assessment and has been shown in multiple randomized trials to improve clinical outcomes. Although invasive FFR is the gold standard, practical, economic, and procedural barriers significantly limit its real-world adoption, driving interest in angiography-derived alternatives.

Angiography-derived physiologic assessment technologies were developed to estimate FFR from invasive coronary angiography without the use of pressure wires or pharmacologic hyperemia. These included commercially available software platforms that compute FFR surrogates based on three-dimensional coronary reconstruction and flow modeling.

Angiography-derived physiologic technologies differ fundamentally from invasive FFR in that they provide a model-based estimate of coronary physiology derived from angiographic imaging rather than a direct measurement of intracoronary pressure. All systems utilize computational modeling, incorporating angiographic image acquisition and contrast flow dynamics, to provide lesion-specific estimates of coronary flow limitation.

It should be noted that these angiography-derived physiologic assessment technologies and their corresponding indices are not interchangeable, as they differ in underlying computational models, image acquisition requirements, and flow estimation methodologies. Accordingly, clinical evidence generated for a given platform should not be extrapolated to other systems.

Angiography-derived FFR technologies include, but are not limited to:
- FFRangio™ System (CathWorks, Ltd, Amherst, Massachusetts, USA)
- QFR (Quantitative Flow Ratio) calculated using QAngio XA 3D / QFR 3.0 (Medis Imaging Systems, Netherlands)
- 3D-QCA (quantitative coronary angiography) based vFFR (vessel fractional flow reserve),calculated using CAAS™ Workstation (Pie Medical Imaging, Netherlands)
- AccuFFRangio Plus (ArteryFlow Technology Co., Ltd., Hangzhou, China)
- QFR and μQFR calculated using AngioPlus QFR System (Pulse Medical Imaging Technology, Shanghai, China)

Regulatory

FFRangio™ System (CathWorks, Ltd, Amherst, Massachusetts) initially received FDA-510(k) clearance on December 19, 2018 (K18249) under Product Code QEK (Angiographic Coronary Vascular

Physiologic Simulation Software). A subsequent clearance was granted on December 9, 2019 (K192442). On April 20, 2026, Medtronic, plc announced it had completed the acquisition of CathWorks.

Indications for Use:
CathWorks FFRangio™ is a software device for the clinical quantitative and qualitative analysis of previously acquired angiography DICOM data for patients with coronary artery disease. It provides FFRangio™, a mathematically derived quantity, computed from simulated blood flow information obtained from a 3D computer model, generated from coronary angiography images. FFRangio™ analysis is intended to support the functional evaluation of coronary artery disease. The results of this analysis are provided as a supportive aid for qualified clinicians in the evaluation and assessment of coronary arteries physiology. The results of CathWorks FFRangio™ are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional evaluation.

QAngio XA 3D (Medis Medical Imaging Systems, Netherlands) received FDA-510(k) clearance on May 30, 2019 (K182611) under Product Code QHA (X-Ray Angiographic Imaging Based Coronary Vascular Simulation Software Device). Subsequently, on April 4, 2025, Medis Medical Imaging Systems received FDA clearance for its **QFR 3.0 system** (K243769), which shares the same indications for use as its predicate device, QAngio XA 3D. QFR 3.0 is a software-based coronary physiology solution that can be used either as a standalone workflow or integrated within the QAngio XA 3D platform, where it functions as the functional (QFR) analysis layer alongside 3D quantitative coronary angiography (QCA).

Indications for Use:
QAngio XA 3D is indicated for use in clinical settings where validated and reproducible quantified results are needed to support the assessment of coronary vessels in X-ray angiographic images, for use on individual patients with coronary artery disease.

When the quantified results provided by QAngio XA 3D are used in a clinical setting on X-ray images of an individual patient. The results are only intended for use by the responsible clinicians.

Indications for Use:
QFR 3.0 is indicated for use in clinical settings where validated and reproducible quantified results are needed to support the assessment of coronary vessels in X-ray angiographic images, for use on individual patients with coronary artery disease.

When the quantified results provided by QFR are used in a clinical setting on X-ray images of an individual patient, the results are only intended for use by the responsible clinicians.

CAAS Workstation 8.2 (Pie Medical Imaging, Netherlands) initially received FDA-510(k) clearance on March 25, 2014 (K133993) under Product Code IZI (System, X-Ray, Angiographic), and subsequently on March 11, 2016 (K151780), May 3, 2918 (K180019). On April 9, 2024 (K232147), the CAAS Workstation received clearance under Product Code QHA (X-Ray Angiographic Imaging Based Coronary Vascular Simulation Software Device).

Indications for Use:
CAAS Workstation features segmentation of cardiovascular structures, 3D reconstruction of vessel segments and catheter path based on multiple angiographic images, measurement and reporting tools to facilitate the following use:

- Calculate the dimensions of cardiovascular structures;
- Quantify stenosis in coronary vessels;
- Determine C-arm position for optimal imaging of cardiovascular structures;
- Quantify pressure drop in coronary vessels;
- Enhance stent visualization and measure stent dimensions;

CAAS Workstation is intended to be used by or under supervision of a cardiologist or radiologist.

AccuFFRangio Plus (ArteryFlow Technology Co., Ltd., Hangzhou, China) received FDA-510(k) clearance on March 2, 2023 under Product Code QHA (X-Ray Angiographic Imaging Based Coronary Vascular Simulation Software Device).

Indications for Use:
AccuFFRangio Plus is indicated for use in clinical settings where validated and repreproducible quantified results are needed to support the assessment of coronary vessels in X-ray angiographic images, for use on individual patients with coronary artery disease.

When the quantified results provided by AccuFFRangio Plus are used in a clinical setting on X-ray images of an individual patient, the results are only intended for use by the responsible clinicians.

Evidence Summary

QFR and/or μQFR calculated using AngioPlus QFR System (Pulse Medical Imaging Technology, Shanghai, China)

FAVOR III China (Xu et al., 2021) was a large, multicenter randomized trial that evaluated whether quantitative flow ratio (QFR)-guided percutaneous coronary intervention (PCI) could improve clinical outcomes compared with conventional angiography-guided PCI in patients with coronary artery disease who had at least one intermediate coronary stenosis (50–90% diameter stenosis). The study enrolled 3,825 patients in the intention-to-treat population, randomized to either a QFR-guided strategy (n=1,913) or an angiography-guided strategy (n=1,912). Mean age was 62.7 years, 1,295 (33.9%) had diabetes, 986 (25.8%) presented with stable angina, and 2,221 (58.1%) presented with troponin-negative unstable angina. In the QFR-guided group, online QFR was measured in all target vessels with 2 angiographic imaging runs with minimum 25° separation in projection angle by the investigator team at each site. The QFR data was then transmitted to the AngioPlus system (Pulse Medical) for real-time QFR calculation. PCI was then performed only if the QFR was ≤ 0.80 or for lesions with a diameter stenosis >90%. If all lesions had a QFR >0.80 and diameter stenosis ≤ 90%, PCI was deferred, and the patient was treated with medical therapy alone.

At 1 year, the primary endpoint—a composite of all-cause death, myocardial infarction, or ischemia-driven revascularization—occurred significantly less frequently in the QFR-guided group than in the angiography-guided group (5.8% vs. 8.8%, respectively), demonstrating that a physiology-guided approach based on angiography-derived FFR improved clinical outcomes. The benefit was largely driven by a reduction in myocardial infarction and ischemia-driven revascularization. In addition to improving clinical outcomes, the QFR-guided strategy reduced the number of stents implanted and avoided the need for pressure-wire measurements and hyperemic agents, supporting its potential cost-effectiveness and procedural efficiency compared with standard angiography-guided PCI. The trial is registered with ClinicalTrials.gov NCT03656848.

In the prespecified 2-year follow-up of the FAVOR III China trial reported by Song et al., 2022, 3,825 patients were analyzed in the intention-to-treat population, with follow-up completed in 98.3% of participants and a median follow-up duration of 728 days. Major adverse cardiac events (MACE), defined as the composite of all-cause death, myocardial infarction (MI), or ischemia-driven revascularization, occurred in 161 of 1,913 patients (8.5%) assigned to QFR-guided PCI compared with 237 of 1,912 patients (12.5%) assigned to angiography-guided PCI (HR 0.66; 95% CI 0.54–0.81; P < 0.0001), representing a 34% relative reduction in risk with the QFR-guided strategy.

The reduction in MACE was primarily driven by significantly lower rates of myocardial infarction (4.0% vs 6.8%; HR 0.58; 95% CI 0.44–0.77; P = 0.0002) and ischemia-driven revascularization (4.2% vs 5.8%; HR 0.71; 95% CI 0.53–0.95; P = 0.02) in the QFR-guided group, while mortality rates were similar between treatment strategies.

QFR assessment altered the preplanned revascularization strategy more frequently than angiography alone, and the benefits of QFR guidance were evident regardless of whether the planned PCI strategy changed after randomization. However, the greatest reduction in MACE occurred among patients whose treatment plan was modified following QFR assessment (HR 0.34; 95% CI 0.21–0.55 versus HR 0.70; 95% CI 0.56–0.88 when no change occurred; P for interaction = 0.009). This benefit was largely attributable to the deferral of vessels that had initially been intended for PCI but were subsequently found not to be physiologically significant by QFR. Overall, the lower MACE rates in the QFR-guided group resulted from fewer adverse events arising from both treated and deferred vessels. Favor III China

compared a QFR-guided strategy with standard angiography-guided PCI rather than invasive FFR. Therefore, its findings primarily support the benefit of physiology-guided revascularization over angiographic guidance, rather than providing direct validation of QFR as a substitute for invasive FFR.

A key consideration when interpreting FAVOR III China is that the study exclusively evaluated the AngioPlus QFR system (Pulse Medical Imaging Technology, Shanghai, China) for angiography-derived fractional flow reserve assessment. Therefore, the clinical outcomes and prognostic benefits demonstrated in the trial cannot be assumed to apply to other angiography-based FFR technologies, which may use different image acquisition requirements, computational algorithms, fluid dynamic models, and validation methodologies.

FLAVOUR II (Hu et al., 2025), an open-label, multicentre, randomised, noninferiority trial, which was conducted in 22 centers in China, enrolled patients aged 18 years or older with suspected ischemic heart disease and with at least 50% stenosis in epicardial coronary arteries measuring at least 2.5 mm by visual estimation on coronary angiography. Patients were randomly assigned (1:1) to undergo PCI guided by either AngioFFR or intravascular ultrasound (IVUS), including revascularization decisions and optimization of the stent implantations based on prespecified PCI criteria and optimal PCI goals. In the AngioFFR, revascularization was indicated for vessels with angiography-derived FFR ≤0.80. *AngioFFR was assessed using either the QFR (Pulse Medical Technology, Shanghai, China) or the Murray law–based QFR (μQFR) (Pulse Medical Technology, Shanghai, China).* In the IVUS group, revascularization was performed for lesions with a minimal lumen area ≤3.0 mm2 or a minimal lumen area >3.0 mm2 and ≤4.0 mm2 accompanied by a plaque burden >70%. Use of both modalities simultaneously was not permitted. Clinical outcomes were analyzed on a per-vessel basis. The primary outcome was a composite of death, target vessel myocardial infarction, or target vessel revascularization at 12 month in the intention-to-treat population, and the non-inferiority margin was 2.5 percentage points. This trial is registered with ClinicalTrials.gov. NCT04397211. Long-term follow-up is ongoing.

Between May 29, 2020, and Sept 20, 2023, 1872 patients were enrolled. After 33 patients withdrew, 923 patients were randomly assigned to the angiography-derived FFR group and 916 to the intravascular ultrasound group. Revascularization was performed in 688 (69.5%) of 990 target vessels in the AngioFFR group and 797 (81.0%) of 984 target vessels in the intravascular ultrasound group. Median age of the study population was 66.0 years (IQR 58·0–72.0), and 1248 (67.9%) patients were male and 591 .(32.1%) were female. At a median follow-up of 12 months, the primary outcome event occurred in 56 (6.0%) patients in the angiography-derived FFR group and 54 (6.0%) patients in the IVUS group demonstrating that angiography-derived FFR guidance was noninferior to IVUS guidance for clinical outcomes at 1 year (6.3% vs 6.0%, absolute difference 0.2 percentage points [upper boundary of one-sided 97.5% CI 2-4], noninferiority = 0.022; hazard ratio 1.04 [95% CI 0-71 to 1-51]). Mortality did not differ between the two groups (1.8% in the AngioFFR group vs 1.3% in the IVUS group, p=0.45). The incidence of recurrent angina was low in both groups: 26 (2.8%) of 923 patients in the AngioFFR group and 35 (3.8%) of 916 patients in the intravascular ultrasound group. The angiography-derived FFR group received fewer stents per patient than the IVUS group (mean number 1.06 [SD 0.90] vs 1.22 [0.92], p < 0.0001).

The angiography-derived FFR-guided comprehensive PCI strategy, encompassing revascularization decision making and stent optimization, was non-inferior to IVUS guidance, however, pressure-wire FFR remains the invasive physiologic reference standard for assessing lesion-specific ischemia. Therefore, FLAVOUR II does not establish clinical equivalence or noninferiority of angiography-derived FFR relative to invasive FFR. Long-term follow-up is ongoing, and durability of the findings beyond one year remains uncertain. Target vessels were limited to major epicardial coronary arteries, including the left anterior descending artery, left circumflex artery, and right coronary artery, therefore, the findings may not be generalizable to all patients undergoing coronary angiography.

In a post hoc analysis of the FLAVOUR II trial, Yang et al. evaluated whether the comparative effectiveness of AngioFFR-guided versus intravascular ultrasound (IVUS)-guided PCI differed according to angiographic lesion complexity. The investigators developed a composite lesion risk score based on five angiographic characteristics: percent diameter stenosis, lesion length, true bifurcation anatomy, ostial

location, and heavy calcification. Patients were then stratified into low-risk and high-risk lesion subgroups to assess the impact of lesion complexity on treatment outcomes.

Among 1,726 patients with coronary stenosis ≥50% who were randomized to either AngioFFR-guided or IVUS-guided management, the primary outcome was target vessel failure (TVF), defined as the composite of cardiac death, target vessel myocardial infarction, and target vessel revascularization. Overall, TVF rates were similar between the AngioFFR and IVUS groups at 12 months (2.4% vs. 1.9%, respectively; P=0.50). However, increasing lesion risk scores were associated with progressively higher rates of TVF, with this relationship being more pronounced among patients managed with AngioFFR than with IVUS.

The key subgroup finding was that lesion complexity modified the relative performance of the two guidance strategies. In patients with high-risk lesions (composite lesion risk score >0.32), AngioFFR-guided treatment was associated with a significantly higher rate of TVF compared with IVUS-guided treatment (5.1% vs. 1.9%; P=0.010). In contrast, among patients with low-risk lesions (score ≤0.32), TVF rates were similar between AngioFFR and IVUS guidance (1.5% vs. 1.9%; P=0.531). Additionally, AngioFFR guidance resulted in substantially fewer PCI procedures in the low-risk subgroup (60.1% vs. 76.5%; P<0.001) without compromising clinical outcomes, whereas PCI rates were similarly high in both treatment arms among high-risk lesions.

Overall, this analysis suggests that angiographic lesion complexity may help identify patients most likely to benefit from a specific PCI guidance strategy. AngioFFR appears to safely reduce PCI utilization in low-risk lesions, while IVUS guidance may provide superior protection against target vessel failure in patients with more complex, high-risk coronary lesions.

Prospective diagnostic accuracy studies

In the DIAMOND study (Bennar et al., 2025), *μQFR analysis performed using the AngioPlus System (Pulse Medical Imaging Technology, Shanghai, China)* was compared with invasive pressure wire-derived fractional flow reserve (FFR) in patients with moderate-to-severe calcified coronary lesions (ACC/AHA lesion class B2 or C). FFR ≤ 0.80 was used as the reference standard for hemodynamically significant stenosis. μQFR analysis was performed by personnel blinded to the FFR results.

Murray law-based QFR (μQFR) is an angiography-derived FFR indices that provides an estimation of FFR. Based on Murray's law, which describes the relationship between vessel diameter and blood flow, μQFR uses computational fluid dynamics and angiographic image data to estimate coronary pressure gradients and lesion-specific functional significance without the need for a pressure wire or pharmacologically induced hyperemia. Unlike conventional QFR, which typically requires two angiographic views, μQFR can be calculated from a single angiographic image. Prior studies have demonstrated strong correlation between μQFR and conventional QFR (Tu et al., 2021, Cortés et al., 2022); however, evidence comparing μQFR directly with invasive pressure-wire FFR, particularly in calcified lesions, has been limited.

Between June 27, 2020, and August 22, 2024, a total of 125 patients met the inclusion and exclusion criteria and were enrolled in the study. Paired assessments of μQFR and FFR were available for 107 patients and 120 lesions. The mean age of the patients was 67.8 ± 9.9 years; 22.4% were women, 26.2% had diabetes mellitus, and 24% had a previous myocardial infarction. μQFR demonstrated a sensitivity of 75.0% (95%CI: 65.6%–84.6%), and a specificity of 77.8% (95%CI: 63.5%–92.0%) with FFR as the reference standard. The overall diagnostic accuracy of 75.8% (95%CI: 68.1%–83.6%). The area under the receiver operating characteristic curve (AUC) was 0.813 (95%CI: 0.714–0.911) for identifying hemodynamically significant stenoses defined as FFR ≤0.80. Positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were 88.7%, 57.1%, 3.38, and 0.32, respectively.

The findings of the DIAMOND study fall below the diagnostic performance reported for μQFR in broader lesion populations. For example, Tu et al., 2021 observed a diagnostic accuracy of 93% (95% CI: 90.3%–95.8%), a sensitivity of 87.5% (95% CI: 80.2%–92.8%), and a specificity of 96.2% (95% CI: 92.6%–98.3%) when analyzing all comer lesions. These discrepancies suggest that lesion characteristics,

particularly the presence and severity of calcifications, may significantly influence µQFR's diagnostic accuracy. Additionally, most lesions analyzed were located in the left anterior descending artery (73%) and classified as type B2 (86.7%). This may impact the generalizability of the findings, as the results may be more relevant to these specific lesion types rather than a broader spectrum of coronary lesions.

In the DIAMOND study, µQFR-FFR discordance was observed in 24.2% of vessels, consistent with Zuo et al. 2024, who reported discordance in 20% of vessels with intermediate-to-severe calcification, compared to only 11.7% of vessels with mild or no calcification before multivariable adjustment. This suggests that calcified plaques may play a substantial role in the observed discordance between µQFR and FFR. The investigators hypothesize that calcification could compromise the accuracy of vessel diameter measurements and flow assumptions, potentially leading to over- or underestimation of stenosis severity compared to FFR.

As a diagnostic accuracy study, it provides evidence of correlation with the physiologic reference standard but does not establish that µQFR-guided management improves clinical outcomes. Clinical decisions for the study population were based on FFR measurements, making it impossible to directly evaluate clinical outcomes using a µQFR-based diagnostic strategy. To address these gaps, randomized trials comparing FFR- and ad hoc µQFR-based diagnostic approaches for calcified coronary lesions are needed to establish their respective clinical efficacy and outcomes. The findings are specific to µQFR analysis performed using the AngioPlus System (Pulse Medical Imaging Technology, Shanghai, China) and should not be generalized to other angiography-derived FFR platforms without additional validation.

The FAVOR II China study (Xu et al., 2017) is a prospective, observational trial designed to evaluate the diagnostic accuracy of online QFR in identifying hemodynamically significant coronary artery disease (CAD) by using pressure wire–based FFR as the reference standard. QFR and QCA analyses were performed online before FFR measurement in a blinded fashion. Adults with suspected or known CAD, who were admitted for coronary angiography between June 13, 2017, and July 20, 2017, who had at least 1 lesion with a diameter stenosis of 30% to 90% and a reference diameter ≥ 2 mm according to visual estimation, were consecutively enrolled. QCA was performed by using angiogram vendor–integrated QCA software or by a QCA workstation. Two angiographic image runs acquired at different angles ≥ 25° were transferred by local network to the *QFR system (AngioPlus, Pulse Medical Imaging Technology, Shanghai Co., Ltd., Shanghai, China)* that used the same algorithms for QFR computation as described in Tu et al., 2016.

The primary endpoint was the diagnostic accuracy of online QFR (≤ 0.8 or > 0.8) to identify hemodynamically significant coronary stenosis with FFR (≤ 0.8 or > 0.8) as the reference standard. Major secondary endpoints were the sensitivity and specificity for online QFR and QCA in identifying hemodynamically significant coronary stenosis with FFR as the reference standard. The mean age of the patients was 61.3 ± 10.4 years, 81 (26.3%) were women, 86 (27.9%) had diabetes, and 48 (15.6%) had a previous myocardial infarction. A total of 185 (55.7%) interrogated vessels were left anterior descending arteries, 24.7% had bifurcation lesions, 14.2% had tortuous vessels, and 18.4% had moderate or severe calcified lesions. Among 332 interrogated vessels, QFR and QCA were successfully assessed in 329 vessels (99.1%), whereas FFR measurement was obtained in 330 vessels (99.4%). The interrogated vessels had an FFR of 0.82 ± 0.12. FFR ≤ 0.80 was noted in 113 vessels (34.2%). QFR and FFR were both assessed in 328 vessels from 304 patients, constituting the as diagnostic set for assessment of the primary and secondary study endpoints.

Good correlation between FFR and QFR was observed for both online (r = 0.86; p < 0.001) and offline (r = 0.88; p < 0.001) assessments. There was good agreement between QFR and FFR for both online (mean difference: - 0.01 ± 0.06; p= 0.006) and offline (mean difference: 0.002 ± 0.06; p = 0.61) assessments. The absolute numerical difference between QFR and FFR was >0.10 in 28 (8.5%) vessels and >0.05 in 103 (31.4%) vessels. In 10.3%, 5.5%,and 6.7% of the interrogated left anterior descending artery, left circumflex artery, and right coronary artery, the numerical difference exceed 0.10. Tandem lesions were present in 152 (46.3%) vessels. The difference between QFR and FFR was not statistically different between the subgroups with and without tandem lesions (-0.016 ± 0.068 vs. -0.004 ± 0.058; p = 0.10).

The primary endpoint, per-vessel diagnostic accuracy of QFR, was 92.7% (95% CI: 89.3% to 95.3%), which was significantly higher than the protocol-specified target value ($p < 0.001$). The accuracy was similar in different vessels. Clinical discordance occurred in 24 (7.3%) vessels: FFR > 0.80 but QFR ≥ 0.80 in 18 vessels, whereas FFR ≤ 0.80 but QFR >0.80 in 6 vessels. Patient-level analysis showed similar diagnostic accuracy of QFR: 92.4% (95%CI: 88.9% to 95.1%). By comparison, online QCA showed a lower diagnostic accuracy (59.6%; difference, 34.9%; $p < 0.001$).

The major secondary endpoints, sensitivity and specificity in the diagnosis of hemodynamically significant stenosis, were significantly higher with QFR than with QCA (sensitivity: 94.6% vs. 62.5%; difference: 32.0% [$p < 0.001$]; specificity: 91.7% vs. 58.1%; difference: 36.1% [$p < 0.001$]). PPV, NPV, + LR, and - LR were 85.5%, 97.1%, 11.4, and 0.06 for online QFR, respectively, and 43.8%, 74.9%, 1.49, and 0.65 for online QCA, respectively.

In this study, QFR demonstrated high feasibility and accuracy in identifying hemodynamically significant coronary stenosis when performed by clinical staff during standard invasive coronary angiography. Patient- and vessel-level diagnostic ac curacy of QFR were 92.4% (95% CI: 88.9% to 95.1%) and 92.7% (95% CI: 89.3% to 95.3%), respectively, which were both significantly higher than the prespecified target value ($p < 0.001$). Compared with anatomical assessment of coronary obstruction using QCA, QFR substantially improved the diagnostic performance of coronary angiography in identifying the stenosis that actually caused myocardial ischemia. Thus, the study met both the prespecified primary performance goal and the major secondary performance goal.

This study is the first that applied QFR computation online during the diagnostic angiography procedure. This study reported high feasibility of online QFR computation, and QFR can be readily available during the diagnostic angiography procedure. The high diagnostic accuracy found in this study warrants further investigation into the clinical benefit of a QFR-assisted management strategy for patients with stable CAD and intermediate stenosis.

Not all the vessels were interrogated for the enrolled patients. The vessels with diameter stenosis < 30% or > 90% were not assessed because performing physiological assessments in such lesions was left unnecessary. Side branches of bifurcation lesions with Medina type 1,1,1 or 1,0,1 were not assessed. Generalizability of QFR to the side branches of coronary bifurcation lesions requires further investigation. Although the accuracy of QFR was high in the present study, there were still numerical differences between QFR and FFR. Nevertheless, for the subgroup with FFR between 0.75 and 0.85, in which a small numerical difference between QFR and FFR can lead to clinical discordance, QFR had high diagnostic accuracy (86.0% [95% CI: 77.9% to 91.9%]).

QFR (Quantitative Flow Ratio) Calculated Using QAngio XA 3D / QFR 3.0 (Medis Imaging Systems, Netherlands)

FAVOR III Europe (Andersen et al., 2025) was a multicenter, randomized, open-label, noninferiority trial to compare clinical outcomes of quantitative flow ratio (QFR)-guided and fractional flow reserve (FFR)-guided revascularization in patients with intermediate coronary stenosis (40-90% diameter stenosis by visual estimation) at 12 months. The trial is registered with ClinicalTrials.gov NCT03729739 and long-term follow-up is ongoing.

The study was conducted in 34 centers across 11 European countries. It enrolled 2,000 adult patients with an indication for invasive coronary angiography due to stable angina, acute non–ST-segment elevation myocardial infarction (NSTEMI), or staged evaluation following NSTEMI or STEMI >24 hours prior, with at least one intermediate nonculprit lesion. Patients were randomized 1:1 to either revascularization with a QFR-guided strategy (1,008 patients) or an FFR-guided strategy (992 patients). The primary endpoint was the rate of major adverse cardiovascular events (MACE); a composite of all-cause death, myocardial infarction, and unplanned revascularization assessed at 12 months. The median age was 67.3 years (IQR 59.9-74.7); 1538 (76.9%) patients were male and 462 (23.1%) were female.

At 12 months, the primary endpoint occurred in 67 (6.7%) patients in the QFR group and in 41 (4.2%) patients in the FFR group (hazard ratio, 1.63; 95% confidence interval [CI], 1.11-2.41). The event proportion difference was 2.5% (90% two-sided CI, 0.9-4.2). Given that the upper limit of the CI exceeded

the prespecified noninferiority margin (3.4%), the results of this study do not support using QFR if FFR is available. Moreover, the total number of stents implanted was higher in the QFR-guided strategy (n=823) when compared to the FFR-guided strategy (n=650). Interestingly, compared to FFR, QFR showed more functionally significant lesions in the left circumflex system (37.1% vs. 15.4).

Unlike FAVOR III China (Xu et al., 2021) which assessed QFR to angiography alone, FAVOR III Europe was unable to show noninferiority of QFR to FFR in revascularization of intermediate coronary stenoses. Additional research is needed to assess the feasibility of QFR to improve clinical outcomes in intermediate coronary stenoses.

Prospective diagnostic accuracy studies

The FAVOR II Europe-Japan Study (Westra et al., 2018), was a prospective, observational study designed to validate the in-procedure feasibility and compare the diagnostic performance of QFR computation with 2-dimensional quantitative coronary angiography (2D-QCA) in a multicenter setting, using FFR as a reference standard. The primary comparison was sensitivity and specificity of QFR compared with 2D-QCA to detect hemodynamically significant coronary lesions with FFR as a gold standard. For FFR and QFR, significant obstructions were defined as FFR and QFR ≤0.80 whereas >50% diameter stenosis (% DS) was used for 2D-QCA. FAVOR II E-J was conducted at 11 sites in Europe and Japan. *QFR was computed with the CE-marked software; QAngio XA 3D/QFR solution (Medis medical imaging system bv., Leiden, The Netherlands)*. The ClinicalTrials.gov identifier is NCT02959814.

Three hundred twenty-nine patients were included from February 22, 2017 to October 17, 2017. In procedure QFR was computed in 345 (96%) vessels with successful FFR measurements. After exclusion based on predefined FFR core-lab criteria, 272 patients and 317 vessels were included in the final analysis. Mean FFR was 0.83 ± 0.09 and mean % DS (2D-QCA) was 45 ± 10%. An FFR ≤ 0.80 was found in 104 (33%) vessels.

Sensitivity and specificity of QFR were significantly higher than of 2D-QCA 50% DS with FFR as a reference (sensitivity, 86.5% [95% confidence interval {CI}, 78.4–92.4] versus 44.2% [95% CI, 34.5–54.3]; P<0.001 and specificity, 88.9% [95% CI, 81.6–91.1] versus 76.5% [95% CI, 70.3–82.9]; P=0.002). Overall diagnostic accuracy was significantly higher for QFR compared with 2D-QCA 50% DS using FFR ≤ 0.80 as a reference (86.8% versus 65.9%; P<0.001). Area under receiver curve (AUC) was larger for QFR compared with 2D-QCA with FFR as a reference (AUC, 0.92 [95% CI, 0.89–0.95] versus 0.64 [95% CI, 0.57–0.70]; P<0.001). QFR was also superior on a per-patient level (sensitivity, 83.5% [95% CI, 74.9–90.1] versus 40.8% [95% CI, 31.2–50.9]; P<0.001); specificity, 83.4% [95% CI, 77.0–88.7] versus 74% [95% CI, 66.7–80.4]; P=0.03; and AUC, 0.91 [95% CI, 0.87–0.94] versus 0.60 [95% CI, 0.53 0.67]; P<0.001.

QFR showed per-vessel correlation (r=0.83; P<0.001) and agreement (mean difference, 0.01 0.06) with FFR (Figure 4). QFR showed per-patient correlation (r=0.80; P<0.001) and agreement (mean difference, 0.01 0.07).

Paired assessment of time to QFR and FFR was available for 295 lesions (93%). Time to completed QFR was significantly shorter than time to completed FFR (median time to QFR, 5.0 minutes [interquartile range, 3.5–6.1] versus median time to FFR 7.0 minutes [interquartile range, 5.0–10.0]; P<0.001).

FAVOR II E-J confirmed the primary hypothesis with superior specificity and sensitivity of QFR compared with standard anatomical assessment by 2D-QCA with FFR as a reference standard, and (2) QFR was feasible in a multicenter setting and was faster than FFR when analyzed during coronary angiography. The reported accuracy of QFR may be somewhat optimistic because some technically difficult lesions were excluded. QFR performed well in straightforward stable-coronary lesions, but complex bifurcation lesions, post-MI patients, and situations involving microvascular dysfunction were excluded.

FFRangio (CathWorks Ltd, Amherst, Massachusetts)

ALL-RISE (Fearon et al., 2026) is a prospective, randomized multicenter study designed to test whether FFRangio-guided treatment is non-inferior to conventional pressure wire-guided treatment in adult patients with one or more study lesion(s) (diameter stenosis 50-90%) being evaluated for percutaneous

coronary intervention (PCI) (ClinicalTrials.gov: NCT05893498). FFRangio (CathWorks Ltd, Amherst, Massachusetts) uses a proprietary flow resistance analysis algorithm to conduct multivessel analysis. FFRangio requires 3 angiographic views separated by at least 30 degrees to provide a quantitative analysis of the functional significance of coronary lesions. The primary end point in ALL-RISE was a composite of death, myocardial infarction, or unplanned, clinically indicated coronary revascularization at 1 year. The noninferiority margin was 3.5 percentage points.

A total of 1,930 patients, enrolled at 60 sites globally, were randomly assigned to physiological assessment with FFRangio (FFRangio group; 965 patients) or a pressure-wire-based approach (pressure-wire group; 965 patients). They subsequently either underwent immediate PCI if the FFRangio ≤ 0.80 or deferred PCI if the FFRAngio > 0.80. Similarly, immediate PCI was performed if the FFR ≤ 0.80 or NHPR ≤ 0.89 and deferred PCI if the FFR >0.80 or NHPR > 0.89. The mean age was 68 years, of whom 75.5% were men. Diabetics accounted for approximately 60% of the patients (11-13% were insulin-requiring). Just under 80% had hypertension or dyslipidemia, and 17% had a previous MI. Of note, 39% had previous PCI. Less than 10% were admitted with an NSTE acute coronary syndrome. Only 13% had an EF ≤ 50%. The left anterior descending artery accounted for ~50%, left circumflex artery ~20%, and right coronary artery ~30%. Intravascular imaging was employed in ~50% of the procedures in each arm.

At 1 year, a primary end-point event had occurred in 64 patients (Kaplan-Meier estimate, 6.9%) in the FFRangio group and 65 patients (Kaplan-Meier estimate, 7.1%) in the pressure-wire group (hazard ratio, 0.98; 95% confidence interval, 0.70 to 1.39; difference, -0.2 percentage points; upper boundary of the one-sided 97.5% confidence interval, 2.1 percentage points; P<0.001 for noninferiority). All subjects with follow-up in the 12-month visit window (days 335-395) were included in the analysis. Unplanned clinically driven revascularization occurred in 4.1 and 4.6% respectively. No differences were observed in bleeding, acute kidney injury or procedure-related adverse events. The FFRangio approach, compared with the pressure-wire approach, was faster (39 vs. 42 minutes), required lower fluoroscopy exposure (9.0 min vs. 12 min) and use of contrast material (100 mL vs. 105.0 mL), and avoided additional procedural steps.

Noted limitations of the trial include its open-label design and relatively short follow-up. The primary analysis was performed at 1 year. Although ALL-RISE demonstrated that FFRangio-guided PCI was noninferior to pressure-wire-guided physiology in a randomized clinical trial, the enrolled population was selected according to trial eligibility criteria and may not fully represent patients encountered in routine clinical practice. The trial included patients with coronary anatomy suitable for both pressure wire-based and FFRAngio based physiology measurements. Patients who had undergone coronary artery bypass grafting were excluded and the majority of patients CCS with no biomarker elevation. As such, its role in assessing patients with complex coronary anatomy, prior CABG and acute myocardial infarction remains unknown. Consequently, the results should be viewed as applicable primarily to the stable, intermediate-lesion population studied rather than all patients undergoing physiologic lesion assessment.

Registry study

Witberg et al. (2026) reported the results of the Japan FFRangio Registry (NCT05648396), a prospective multicenter registry evaluating FFRangio-guided management in consecutive patients undergoing coronary angiography at six Japanese centers and one Israeli center between January 2021 and December 2023. The study enrolled patients in whom physiology assessment of at least one lesion was performed using FFRangio at the operator's discretion. Patients were excluded if treatment decisions were discordant with the FFRangio result, if wire-based FFR was measured concomitantly, or if intravascular imaging was used for lesion assessment. Of 2,427 patients undergoing FFRangio assessment, 182 patients with treatment decisions discordant with FFRangio findings were excluded, resulting in a final cohort of 2,245 patients (1,489 CCS and 756 ACS) with 3,236 lesions.

Patients with CCS were older and had higher rates of hypertension, prior myocardial infarction, and prior PCI, whereas patients with ACS had higher rates of smoking, diabetes, and multivessel disease. Mean FFRangio values were higher in CCS than ACS patients (0.85 vs. 0.77, P<0.001). After a median follow-up of 730 days, the primary endpoint of major adverse cardiac events occurred more frequently in ACS than CCS patients (9.8% vs. 5.6%; adjusted HR 1.80, 95% CI 1.31–2.46; P<0.001), driven primarily by

higher rates of repeat revascularization. Rates of death and myocardial infarction did not differ significantly between groups.

When stratified by treatment strategy, outcomes following FFRangio-guided deferral (FFRangio >0.80) were similarly low in ACS and CCS patients (5.4% vs. 4.7%; adjusted HR 1.08; P=0.67). In contrast, among patients undergoing revascularization, ACS presentation was associated with higher event rates than CCS (11.7% vs. 7.3%). The authors concluded that FFRangio-guided deferral was associated with favorable and comparable 2-year outcomes in both ACS and CCS populations and that overall outcomes were consistent with those previously reported for wire-based FFR-guided management.

Importantly, the Japan FFRangio Registry represents one of the largest prospective real-world evaluations of angiography-derived FFR and provides evidence that FFRangio-guided clinical decision-making can be safely implemented across diverse presentations, including both ACS and CCS. These findings help address an important evidence gap by demonstrating favorable outcomes outside the highly selected populations typically enrolled in randomized trials.

AccuFFRangio (ArteryFlow Technology Co., Ltd., Hangzhou, China)

The ACCURATE study (Jiang et al., 2025) was a prospective, multicenter, observational study designed to evaluate the feasibility and diagnostic performance of AccuFFRangio (ArteryFlow Technology Co., Ltd., Hangzhou, China) in identifying physiologically significant CAD by using invasive FFR as the reference standard. The trial is registered with ClinicalTrials.gov NCT04814550. The primary end point was the diagnostic accuracy of on-site AccuFFRangio in detecting hemodynamic significance using wire-based FFR as the reference standard with a clinical threshold of 0.80. Secondary end points were sensitivity and specificity of AccuFFRangio compared with invasive FFR. Consecutive patients (≥18 years) with stable or unstable angina pectoris, or myocardial infarction occurring ≥ 6 days before screening, who were admitted for angiography were eligible for inclusion. Inclusion criteria required that each patient had at least 1 lesion with a percentage diameter stenosis (%DS) of 30% to 90% by visual estimation and that invasive FFR measurement was planned. Two angiographic projections ≥25° apart with the entire vessel visualized, with minimum foreshortening, avoiding vessel overlap, were required for AccuFFRangio analysis. Angiographic images were promptly transferred by local network to the on-site AccuFFRangio system, following which the AccuFFRangio computations were performed. All AccuFFRangio values were obtained at the same vessel site of FFR measurement for better comparison. FFR was performed according to clinical guidelines after the AccuFFRangio analysis completion and the operator was blinded to the AccuFFRangio results. Certus pressure wires (St. Jude Medical, St. Paul, MN) were used in all patients. Hyperemia was induced by intravenous administration of adenosine-5′-triphosphate via median cubital vein at 140 μg/kg per min. A total of 304 patients with 304 vessels were included in the final analysis. The mean age of the patients was 65 ± 11 years; 202 (66%) were men, and 14 (5%) had a previous myocardial infarction. The predominant patient presentation was stable angina pectoris (77%), and 66% of lesions were located in the left anterior descending artery. Among 304 interrogated vessels, AccuFFRangio and QCA were successfully assessed in all vessels.

The primary end point, the diagnostic accuracy of AccuFFRangio was 95.07% (95% CI, 91.99%–97.21%), exceeded the prespecified performance goal (P<0.001). Using FFR as the reference standard, AccuFFRangio led to 15 (4.9%) clinical discordant results: 4 false negatives and 11 false positives. The secondary end points, sensitivity and specificity for detecting significant stenosis of AccuFFRangio, were 95.83% (95% CI, 89.67%–98.85%) and 94.71% (95% CI, 90.73%–97.33%), accompanied with the positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of 89.32% (95% CI, 82.45%–93.71%), 98.01% (95% CI, 94.96%–99.23%), 18.12 (95% CI, 10.18–32.26), and 0.04 (95% CI, 0.02–0.11), respectively. When compared with QCA, AccuFFRangio showed significantly better diagnostic performance (accuracy: 95.07% versus 49.67%, P<0.001; sensitivity: 95.83% versus 91.67%, P<0.001; specificity: 94.71% versus 30.29%; P<0.001). The area under the receiver-operator characteristic curve was significantly larger for AccuFFRangio than for QCA (0.972 versus 0.775; P<0.001). The total operating time of AccuFFRangio was 4.20±1.53 minutes. For the gray zone with FFR between 0.75 and 0.85, where a small error can lead to significant clinical difference, AccuFFRangio had high diagnostic accuracy (87.62% [95% CI, 79.76%–93.24%]). In a subgroup where 0.75≤FFR ≤0.80, AccuFFRangio also showed good diagnostic power compared with subgroups with

FFR<0.75 or FFR> 0.80 (90.48% versus 95.8%, *P*=0.140). AccuFFRangio accurately detected ischemia-causing lesions, no matter where they were located. The accuracy for lesions in the left anterior descending artery, left circumflex artery, and right coronary artery was comparable (95% versus 93.94% versus 97.10%, P=0.502), all significantly exceeding 90%. The diagnostic performance was consistently maintained across lesion locations, with accuracies of 92.56% in proximal segments, 96.67% in medial segments, and 96.97% in distal segments. Similarly, lesion size had no influence on the diagnostic ability of AccuFFRangio, with high accuracy across the strata of lesion length (100% for lesions <15 mm; 94.51% for lesion between 15 and 30 mm; 95.08% for lesion ≥ 30 mm; P=0.097), and vessel diameter (diameter < 2.5 mm versus 2.5 ≤ diameter < 3.5 mm versus diameter ≥ 3.5 mm, 97.06% versus 93.71% versus 95.70%, P=0.544).

The ACCURATE study was the first adequately powered trial to assess the feasibility and value of a novel angiography-based technique, AccuFFRangio, for the calculation of FFR without the need for a pressure wire. The main findings of the present study were as follows: (1) AccuFFRangio achieved very high diagnostic accuracy (95.1%), sensitivity (95.8%) and specificity (94.7%), all of which exceeded the prespecified performance goals; (2) AccuFFRangio substantially improved the diagnostic performance of coronary angiography in identifying ischemia-causing stenosis; and (3) the diagnostic accuracy of AccuFFRangio remained high across vessels with varying lesion types, stenosis severities, and within the FFR “gray zone,” indicating the potential value of this approach in clinical practice. The generalizability of AccuFFRangio in real-world settings requires further investigation. Interpreting of the results should consider the prevalence of nonischemic stenoses in this cohort, which might have influenced the specificity of AccuFFRangio. Future randomized trials regarding AccuFFRangio-guided therapeutic strategies and clinical outcomes are warranted to validate the clinical value of this new approach.

3D Quantitative Coronary Angiography (3D QCA) Based Vessel Fractional Flow Reserve (Vffr) Calculated by the CAAS Workstation 8.2 (Pie Medical Imaging)

The FAST II study (Masdjedi et al., 2022) was a prospective, international, multicenter trial designed to evaluate the diagnostic accuracy of a novel three-dimensional quantitative coronary angiography (3D-QCA)-based software tool (CAAS Workstation 8.2, Pie Medial Imaging, Netherlands) to calculate vessel FFR (vFFR), an angiography-based method for assessing coronary lesion significance, using invasive pressure wire-based fractional flow reserve (FFR ≤0.80) as the reference standard. The study is registered on ClinicalTrials.gov under the identifier NCT03791320. FAST II enrolled patients with intermediate coronary lesions (30–70% diameter stenosis by visual assessment) from centers across Europe, the United States, and Japan. Angiographic images, hemodynamic data, and pressure-wave tracings were anonymized and analyzed by an independent, blinded core laboratory. vFFR was calculated offline using three two-dimensional angiographic images, exported to the CAAS Workstation, including two orthogonal projections for three-dimensional vessel reconstruction and one view to determine pressure-wire position. The primary endpoint was the accuracy of core laboratory–derived vFFR in identifying physiologically significant coronary stenoses, while the key secondary endpoint assessed the accuracy of site-determined vFFR.

Between October 2018 and September 2020, 391 patients were enrolled. After excluding 57 patients due to angiographic criteria or missing FFR values, 334 patients (one vessel per patient) were included in the final analysis. Mean age was 66 ± 12 years and 73% of patients were male. The majority of patients had hypertension (72%), 27% were diabetic and 88% presented with stable or unstable angina. Target vessels included the left anterior descending artery (66%), right coronary artery (25%), and left circumflex artery (9%). The mean diameter stenosis was 42%, lesion length was 20 mm, and 72% of lesions were focal. Invasive FFR was ≤0.80 in 36% of vessels. Mean invasive FFR, core laboratory vFFR, and site-determined vFFR were 0.83, 0.83, and 0.82, respectively.

Core laboratory vFFR demonstrated excellent diagnostic performance for identifying lesions with invasive FFR ≤0.80, with an area under the receiver operating characteristic curve (AUC) of 0.93. Using a vFFR cutoff of ≤0.80, sensitivity was 81%, specificity 95%, positive predictive value (PPV) 90%, negative predictive value (NPV) 90%, and overall diagnostic accuracy 90%. Core laboratory vFFR also showed a strong correlation with invasive FFR (R=0.74, p<0.001) and minimal measurement bias. Site-determined

vFFR produced similar results, with an AUC of 0.91, sensitivity of 71%, specificity of 89%, PPV of 79%, NPV of 85%, and diagnostic accuracy of 83%. Correlation between site-reported vFFR and invasive FFR was also strong (R=0.76, p<0.001), and agreement between core laboratory and site-generated vFFR was high (R=0.87, p<0.001).

Overall, the FAST II study demonstrated that vFFR can accurately identify physiologically significant coronary artery disease without the need for a pressure wire or pharmacologic hyperemia, showing excellent agreement with invasive FFR. However, several limitations were noted. vFFR was calculated offline, so its real-time applicability during procedures remains uncertain. In addition, accuracy depends heavily on high-quality angiographic images with adequate contrast and appropriately separated viewing angles. Although previous studies found that many routine angiograms are unsuitable for angiography-based FFR analysis, FAST II showed that dedicated site training increased the proportion of analyzable angiograms to 88%. Finally, computation times for vFFR were not systematically recorded. Further evaluation of procedural efficiency and clinical implementation is anticipated in the ongoing FAST III randomized trial.

FAST III (Daemen et al., 2026) was an investigator-initiated, open-label, randomized, controlled noninferiority trial conducted at 37 sites in seven European countries that enrolled 2,211 patients with either acute (19%) or chronic (81%) coronary syndromes and intermediate coronary lesions (30–80% diameter stenosis). Patients were randomized to revascularization guided by 3D quantitative coronary angiography (3D QCA) based vessel fractional flow reserve (vFFR) calculated by the CAAS workstation 8.2 (Pie Medical Imaging). The trial is registered at ClinicalTrials.gov NCT04931771 and was sponsored by ECRI.

At one year the primary endpoint event, a composite of all-cause death, any MI or any revascularization, occurred in 80 patients in the vFFR group and in 79 patients in the FFR group (risk difference, −0.02 percentage points; 95% confidence interval, −2.25 to 2.21; P=0.004 for noninferiority). Looking at the key secondary endpoint of study-vessel failure that had been examined by vFFR or FFR, a composite of cardiac death, MI or any revascularization, the incidence was similar (4% of the vFFR group and 4.6% of the FFR group).

vFFR identified a higher percentage of functionally significant lesions and this led to more revascularization procedures in the vFFR group than in the FFR group (45% vs. 36%) (the investigators note this as an area of future study). Despite this more aggressive revascularization strategy, clinical outcomes remained comparable between the groups. In addition, procedural duration was shorter with vFFR than with FFR (55.8 versus 60.9 minutes), and intraprocedural complications were less frequent (3.7% versus 6.0%). Adverse event rates overall were similar between the two strategies. Physiologic assessment was successfully completed in 97% of patients assigned to vFFR and 99% of those assigned to FFR. Rates of the key secondary endpoint of study-vessel failure, defined as cardiac death, myocardial infarction, or repeat revascularization involving a vessel previously assessed by vFFR or FFR, occurred in 4.0% of the vFFR group and 4.6% of the FFR group.

FAST III demonstrated that vFFR-guided revascularization was noninferior to pressure wire–based FFR-guided revascularization at 1 year. While this supports vFFR as a viable alternative physiologic assessment strategy additional studies are needed to establish long-term durability and clinical outcomes beyond the first year. The broader applicability of FAST III remains uncertain because the study population was predominantly composed of patients with stable coronary disease. Additionally, vFFR identified more lesions as physiologically significant and resulted in more revascularization procedures than FFR (45% vs. 36%). Whether this finding reflects improved lesion detection or a tendency toward more intervention remains uncertain and warrants further study.

Lastly, FAST III evaluated a specific angiography-derived physiologic platform (vFFR) and its results cannot automatically be generalized to other angiography-based indices which use different computational methods.

Systematic review of the diagnostic accuracy, clinical efficacy and practical implementation of QAngio XA 3D/QFR and CAAS vFFR imaging software for assessing the functional significance of coronary obstructions in people with intermediate coronary stenosis

Duarte et al., 2021 conducted a systematic review of the diagnostic accuracy, clinical efficacy and practical implementation of QAngio XA 3D/QFR and CAAS vFFR imaging software for assessing the functional significance of coronary obstructions in people with intermediate coronary stenosis (i.e. stenoses where preceding tests have been insufficient to make a revascularization decision). A total of 41 studies were included in the systematic review, of which 39 (5,440 patients) evaluated QAngio XA 3D/QFR and three (500 patients) assessed CAAS vFFR. Only one study directly compared QAngio XA 3D/QFR with CAAS vFFR. A total of 17 included studies were reported only as conference abstracts. Most studies included a mix of patients with stable and unstable coronary syndromes. Stenosis severity varied widely across studies; mean/median fractional flow reserve ranged from 0.75 to 0.88, and mean percentage diameter stenosis from 37% to 66%. Only seven studies were conducted prospectively, and 11 studies (all of QAngio XA 3D/QFR) were rated as being at low risk of bias.

Diagnostic Accuracy
The average difference between quantitative flow ratio (measured using QAngio XA 3D/QFR) and fractional flow reserve was 0.01. In 50% of patients, quantitative flow ratio and fractional flow reserve differed by no more than 0.04; in 95% of patients, values differed by no more than 0.14. The quantitative flow ratio was highly correlated with the fractional flow reserve (r = 0.8). The QAngio XA 3D/QFR quantitative flow ratio had good diagnostic accuracy to predict fractional flow reserve (≤ 0.80 cut-off point); contrast-flow quantitative flow ratio had a sensitivity of 85% (95% confidence interval 78% to 90%) and a specificity of 91% (95% confidence interval 85% to 95%); fixed-flow quantitative flow ratio mode had a sensitivity of 82% (95% confidence interval 68% to 91%) and a specificity of 89% (95% confidence interval 77% to 95%). Where reported, quantitative flow ratio had significantly higher diagnostic accuracy than standard invasive coronary angiography. Data on how diagnostic accuracy may vary by key patient characteristics were too limited to draw any firm conclusions.

Using data extracted from figures, simulating a grey-zone strategy, where only patients with a QAngio XA 3D/QFR quantitative flow ratio between 0.78 and 0.84 receive confirmatory fractional flow reserve, improved diagnostic accuracy compared with quantitative flow ratio alone to a sensitivity of 93.1% (95% confidence interval 90.1% to 94.9%) and a specificity of 92.1% (95% confidence interval 88.3% to 94.5%). A total of 20.1% patients fell in the grey zone and would receive confirmatory fractional flow reserve. However, only 30.4% of patients with quantitative flow ratio results in the grey zone had results that were discordant with their fractional flow reserve.

Only three retrospective studies of CAAS vFFR were available, limiting the scope for reliable meta-analysis. Only one conference abstract directly compared the diagnostic accuracy of QAngio XA 3D/QFR and CAAS vFFR with fractional flow reserve. The abstract reported that QAngio XA 3D/QFR quantitative flow ratio had a higher overall diagnostic accuracy, with areas under the curve of 0.719 (95% confidence interval 0.621 to 0.804) for vessel fractional flow reserve and 0.886 (95% confidence interval 0.807 to 0.940) for contrast-flow quantitative flow ratio.

Clinical Effectiveness
No evidence was found on the effectiveness of QAngio XA 3D/QFR on major cardiovascular events and death. Three studies that reported clinical outcomes found that QAngio XA 3D/QFR may predict long-term major cardiovascular adverse events.

A simulation study based on the results of the meta-analysis found that using quantitative flow ratio in place of fractional flow reserve may slightly increase the number of revascularizations (from 40.2% to 42.0%), with a possible small increase in the number of coronary events (an extra one major adverse cardiac event per 1000 patients). Using a grey-zone approach of performing a confirmatory fractional flow reserve where the quantitative flow ratio is close to 0.8 might further increase revascularizations rates (to 43.2%) but with no impact on incidence of major adverse cardiac events.

Cost-effectiveness
No full cost-effectiveness studies of QAngio XA 3D/QFR or CAAS vFFR were identified by the systematic review.

Discussion
This review includes a comprehensive systematic review of all the published literature on quantitative

flow ratio as assessed by QAngio XA 3D/QFR and CAAS vFFR and has been conducted following recognized guidelines to ensure high quality. The review identified a substantial literature on the diagnostic accuracy of QAngio XA 3D/QFR, so the findings of the analysis of diagnostic accuracy are likely to be conclusive.

Although there is substantial evidence demonstrating the good diagnostic accuracy of quantitative flow ratio assessment using QAngio XA 3D/QFR overall, it remains largely unclear which patient or lesion characteristics might significantly affect the diagnostic accuracy of QAngio XA 3D/QFR.

The clinical value of QAngio XA 3D/QFR to support decision-making on revascularization remains uncertain, particularly regarding what impact it might have on preventing or causing future coronary events, and whether the 0.8 cut-off point or the proposed grey zone are clinically appropriate. However, it appears unlikely that its clinical value or use will differ substantially from widespread use of fractional flow reserve.

Conclusion
Quantitative flow ratio measured using QAngio XA 3D/QFR has good agreement and diagnostic accuracy compared with fractional flow reserve and is more accurate than standard invasive coronary angiography for the evaluation of functionally significant stenoses. The good association between quantitative flow ratio and fractional flow reserve, and the high diagnostic accuracy of quantitative flow ratio, suggest that, pending further evidence on clinical benefits, quantitative flow ratio assessment could represent a reasonable alternative to invasive fractional flow reserve, particularly where fractional flow reserve is not available.

Evidence on the CAAS vFFR technology was limited to three studies. This prevented any full meta-analyses of diagnostic accuracy for CAAS vFFR, or any assessment of its clinical effectiveness. The cost-effectiveness results for CAAS vFFR should be interpreted with caution because of the limited diagnostic information available.

Recommendations for research
The substantial existing evidence for diagnostic accuracy of QAngio XA 3D/QFR suggests that further studies of diagnostic accuracy are not required. Large, multicentre prospective studies are required to assess the diagnostic accuracy and clinical feasibility of CAAS vFFR. Ideally these should compare CAAS vFFR with invasive coronary angiography assessment and, if possible, with quantitative flow ratio.

Large ongoing randomised trials will hopefully inform decision-makers of the clinical value of quantitative flow ratio compared with angiography and fractional flow reserve-guided revascularization.

Systematic Review to evaluate the diagnostic accuracy of angiography-derived QFR methods compared with invasive FFR for identifying functionally significant coronary stenosis

Huang et al., 2026 conducted a systematic review and meta-analysis of studies assessing the diagnostic performance of angiography-derived quantitative flow ratio (QFR) systems. Quantitative flow ratio (QFR) is an angiography-derived method that uses computational modeling—often incorporating machine learning—to reconstruct three-dimensional coronary vessel geometry from standard angiographic images and estimate fractional flow reserve (FFR) using contrast flow (TIMI frame count). Compared with invasive FFR, QFR eliminates the need for pressure wires, pharmacologically induced hyperemia, and associated procedural costs, while offering faster assessment. However, early evidence has been largely derived from single-center studies with relatively small sample sizes. Therefore, this study aimed to systematically evaluate the diagnostic performance of QFR for detecting functionally significant coronary stenosis, using invasive FFR as the reference standard.

Quantitative flow ratio (QFR) can be derived using four distinct flow models: (1) fixed-flow QFR (fQFR), which applies an empirically defined hyperemic flow velocity (HFV) based on prior FFR studies; (2) adenosine-flow QFR (aQFR), which uses measured HFV obtained during adenosine-induced maximal hyperemia; (3) contrast-flow QFR (cQFR), which estimates HFV from contrast flow observed during routine coronary angiography without pharmacologic hyperemia; and (4) Murray law–based QFR (μQFR), which enables automated vessel contour detection and rapid FFR estimation, often from a single angiographic projection. The objective of this systematic review and meta-analysis was to compare the

diagnostic performance of fQFR, aQFR, cQFR, and μQFR against invasive FFR for evaluating the functional significance of coronary stenoses.

Fifty-seven studies comprising 13,215 patients and 16,125 vessels were included in the final analysis: 11 studies on fQFR (2403 patients, 2958 vessels), 33 studies on cQFR (6,009 patients, 7,830 vessels), 2 studies on aQFR (90 patients, 99 vessels), 9 studies on μQFR (3,108 patients, 3378 vessels), and 8 studies on non-specified QFR (1605 patients, 1860 vessels). Notably, some studies included more than one QFR mode.

This meta-analysis confirmed that QFR demonstrates strong diagnostic performance, with a pooled AUC of 0.94 (95% CI: 0.91–0.96). Additionally, the high pooled sensitivity [0.826 (95% CI: 0.798–0.851)] and specificity [0.919 (95% CI: 0.902–0.933)] further validate the reliability of this novel tool in assessing coronary stenosis. The strong pooled LR+ [10.198 (95% CI 8.469–12.281)] and low pooled LR− [0.189 (95% CI 0.163–0.219)] provide compelling diagnostic evidence of the usefulness of QFR in the clinical setting. Moreover, the high pooled DOR suggests that a positive QFR lesion is 54 times more likely to correspond to a functionally significant lesion (measured FFR ≤ 0.80) compared to a non-functionally significant lesion.

Despite its demonstrated diagnostic accuracy, QFR has inherent limitations, particularly when considered within the broader framework of comprehensive invasive coronary physiology. Unlike wire-based techniques—such as coronary flow reserve (CFR) or acetylcholine provocation testing—QFR is fundamentally a computational estimate derived from angiographic anatomy and contrast flow dynamics. As such, it cannot evaluate microvascular dysfunction or coronary vasospasm, both of which are important contributors to ischemic heart disease and require dedicated invasive assessment.

In addition, QFR presents practical workflow limitations. With pressure wire–based techniques, the same device used for physiological assessment can be seamlessly transitioned to guide percutaneous coronary intervention (PCI), enabling procedural continuity. In contrast, QFR is typically performed as an offline or semi-online analysis and lacks this “one-wire” integration into the interventional workflow.

QFR accuracy is also highly dependent on angiographic image quality. Suboptimal lesion visualization, inadequate contrast opacification, vessel overlap, or insufficient projection angles can adversely affect computational reliability. Furthermore, its performance in complex anatomical settings—including ostial or bifurcation lesions, severe vessel tortuosity, and diffuse disease—as well as in certain clinical conditions such as arrhythmias or microvascular dysfunction, remains an area of ongoing investigation.

Further studies are needed to better define these technical and clinical limitations. In particular, direct comparisons with other angiography-derived fractional flow reserve modalities may help clarify the optimal role of QFR in routine clinical practice.

Evidence-Based Guidelines

2021 ACC/ AHA/SCAI guideline for coronary artery revascularization: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines (Lawton et al., 2022)

4.3 Recommendations for the Use of Coronary Physiology to Guide Revascularization with PCI

1. In patients with angina or anginal equivalent, undocumented ischemia, and angiographically intermediate stenoses, the use of fractional flow reserve or instantaneous wave-free ration (IFR) is recommended to guide the decision to proceed with PCI (Class of Recommendation 1, Level of Evidence A).
2. In stable patients with angiographically intermediate stenoses and FFR > 0.80 or IFR > 0.89, PCI should not be performed (Class of Recommendation No Benefit, Level of Evidence B-R).

FFR and iFR are 2 of the most commonly used physiological methods of assessing lesion significance. FFR is defined as the ratio of maximal blood flow in a region distal to a lesion compared with the normal maximal blood flow of an artery. iFR, an index of lesion severity, is the instantaneous wave-free ratio (in diastole) of coronary pressure distal to the coronary lesion (Pd) to the aortic pressure (Pa). The potential advantage of iFR, which is a resting physiological index, is that it obviates the use of adenosine because

it does not require a state of maxi mal hyperemia. These 2 measures—FFR and iFR—have been studied in randomized trials with clinical endpoints of death, myocardial infarction (MI), or repeat revascularization (Tonino et al., 2009, De Bruyne et al., 2012, De Bruyne et al., 2014, Davies et al., 2017, Xaplanteris et al., 2018).

The FAME 2 (Fractional Flow-Reserve-Guided PCI versus Medical Therapy in Stable Coronary Disease) trial2 tested a strategy of PCI for all lesions with abnormal FFR compared with optimal medical therapy alone. Recruitment into the trial was stopped early because of a significant benefit of PCI over medical therapy in patients with an abnormal FFR with respect to death, MI, or urgent revascularization, with the benefit derived largely from a reduction in ischemia-driven revascularization.

2018 ESC/ EACTS Guidelines on Myocardial Revascularization (Neumann et al., 2019)

3.2 Invasive diagnostic tools

3.2.1 Pressure-derived fractional flow reserve

3.2.1.1 Use of fractional flow reserve in patients with intermediate-grade coronary stenosis including left main stenosis

Coronary pressure-derived FFR is the current standard of care for the functional assessment of lesion severity in patients with intermediate-grade stenosis (typically around 40 – 90% stenosis) without evidence of ischemia in non-invasive testing, or in those with multivessel disease.

Studies have shown that PCI can be safely deferred in patients with FFR > 0.75, as demonstrated in the DEFER trial, where outcomes were similar between patients who underwent PCI and those in whom intervention was deferred (Pijls et al., 2007). However, more recent evidence supports a higher threshold, with FFR > 0.80 now widely accepted for deferring PCI. Large contemporary studies such as DEFINE-FLAIR and iFR-SWEDEHEART have used the 0.80 cut-off and demonstrated favorable clinical outcomes, establishing 0.80 as the standard threshold for identifying hemodynamically significant coronary lesions (Davies et al., 2017, Gotberg et al., 2017).

Hemodynamic relevance, as defined by FFR ≤ 0.80, correlates poorly with diameter stenosis by visual assessment. In the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) trial, only 35% of the 50–70% stenoses were hemodynamically relevant and, of the 71–90% stenoses, 20% were not. Only an estimated diameter stenosis >90% predicted hemodynamic relevance with high accuracy (96% correct classification). In the FAME trial (Tonino et al., 2009), FFR was measured using a coronary pressure wire under hyperemic conditions, which is the standard invasive method and gold standard for physiological lesion assessment. A number of studies have shown that utilization of an FFR-based assessment strategy at the time of angiography results in reclassification of the revascularization strategy (PCI, bypass surgery, or medical therapy) in a high proportion of patients with intermediate-grade lesions (>40% of patients are reclassified).

Recommendations on functional testing and intravascular imaging for lesion assessment

1. When evidence of ischemia is not available, FFR or instantaneous wave-free ratio (iwFR) are recommended to assess the hemodynamic relevance of intermediate-grade stenosis (Class of Evidence I, Level of Evidence A).
2. FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI (Class of Evidence IIa, Level of Evidence B).

2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines (Gulati et al., 2021)

Recommendations for Patients With Obstructive CAD Who Present With Stable Chest Pain

1. For patients with obstructive CAD who have stable chest pain despite guideline-directed medical therapy (GDMT) and moderate-severe ischemia, invasive coronary angiography (ICA) is recommended for guiding therapeutic decision-making (Class of Recommendation I, Level of Evidence A).

2. For patients with obstructive CAD who have stable chest pain despite optimal GDMT, those referred for ICA without prior stress testing benefit from FFR or instantaneous wave free ratio (Class of Recommendation I, Level of Evidence A).

3. For symptomatic patients with obstructive CAD who have stable chest pain with CCTA-defined ≥ 50% stenosis in the left main coronary artery, obstructive CAD with FFR with CT ≤ 0.80, or severe stenosis (≥ 70%) in all 3 main vessels, ICA is effective for guiding therapeutic decision-making (Class of Recommendation I, Level of Evidence B-R).

2024 ESC Guidelines for the Management of Chronic Coronary Syndromes (Vrints et al., 2024)

New 3D angiographically derived wireless coronary pressure parameters, such as quantitative flow ratio (QFR) or vessel fractional flow reserve (vFFR), are at different stages of clinical investigation (NCT03729739) and have important features that may help to increase the use of coronary pressure measurement during ICA significantly. These technologies have indeed the unique advantage of providing both distal coronary pressure measures and a coronary pressure map along the coronary vessel without requiring the use of any pressure wire. The lack of benefits shown in some recent FFR trials demonstrates that it is not sufficient to validate such new coronary pressure indexes against FFR alone to demonstrate their clinical value, and it is important to also show benefit in a direct comparative trial vs. angiography. In that context, the results of the FAVOR III China study (Song et al., 2022) are important, demonstrating an improved clinical outcome in the QFR-guided group compared with the angiography-guided group, driven by fewer MIs and ischemia-driven revascularizations.

Table 12. Recommendations for functional assessment of epicardial artery stenosis severity during invasive coronary angiography to guide revascularization

During ICA, selective assessment of functional severity of intermediate diameter stenoses is recommended to guide the decision to revascularize, using the following techniques:

- FFR/ Instantaneous wave-free ratio (iFR) (significant ≤0.8 or ≤0.89, respectively) (Class I, Level of Evidence A)
- QFR (significant ≤0.8) (Class I, Level of Evidence B)

“New 3D angiographically derived wireless coronary pressure parameters, such as quantitative flow ratio (QFR) or vessel fractional flow reserve (vFFR), are at different stages of clinical investigation and have important features that may help to increase the use of coronary pressure measurement during ICA significantly. These technologies have indeed the unique advantage of providing both distal coronary pressure measures and a coronary pressure map along the coronary vessel without requiring the use of any pressure wire. The lack of benefits shown in some recent FFR trials demonstrates that it is not sufficient to validate such new coronary pressure indexes against FFR alone to demonstrate their clinical value, and it is important to also show benefit in a direct comparative trial vs. angiography. In that context, the results of the FAVOR III China study (Song et al., 2022) are important, demonstrating an improved clinical outcome in the QFR-guided group compared with the angiography-guided group, driven by fewer MIs and ischemia-driven revascularizations (page 3447).”

Table 22. Recommendations for revascularization in patients with chronic coronary syndrome

Assessment of procedural risks and post-procedural outcomes

Intracoronary pressure measurement (FFR or iFR) or computation (QFR) :

- is recommended to guide lesion selection for intervention in patients with multivessel disease (Class I, Level of Evidence A);
- should be considered at the end of the procedure to identify patients at high risk of persistent angina and subsequent clinical events (Class IIa, Level of Evidence B);
- may be considered at the end of the procedure to identify lesions potentially amenable to treatment with additional PCI (Class IIb, Level of Evidence B).

Table 24. Recommendations for management of chronic coronary syndrome patients with chronic heart failure

Managing CCS in heart failure patients

- In HF patients with LVEF >35% and suspected CCS with very high (>85%) pre-test likelihood of obstructive CAD, ICA (with FFR, iFR, or QFR when needed) is recommended (Class I, Level of Evidence C).

Applied coronary physiology for planning and guidance of percutaneous coronary interventions. A clinical consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the European Society of Cardiology (Escaned et al., 2023)

FFR is the most widely used intracoronary tool to define flow-limiting epicardial stenoses, with randomised clinical trials and observational studies supporting deferral or performance of revascularization based on FFR values, predominately in patients with chronic coronary syndromes (CCS).

Computed tomography-derived FFR (CT FFR) is obtained by merging a three-dimensional (3D) reconstruction of vessels from computed tomography coronary angiography with computational fluid dynamics, thereby providing a reliable estimate of invasive FFR. Similarly, several FFR-equivalent measurements can also be derived from invasive coronary angiograms these are supported by prospective validation studies.

Quantitative flow ratio (QFR) is the only angiography-based physiological index that has been prospectively validated and has already been demonstrated to be associated with improved clinical outcomes when used to decide upon coronary revascularization, compared with conventional angiography (Xu et al., 2021). A distinct advantage of all functional coronary angiography modalities is that they provide longitudinal vessel analysis, allowing accurate length measurements and localization of flow-limiting disease to vessel anatomy.

Analysis of Evidence (Rational for Determination)

According to the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines (Gulati et al., 2021), invasive coronary angiography is the guideline-endorsed standard for guiding therapeutic decision-making and is recommended as a Class I recommendation with Level A evidence.

Because angiography-derived physiologic assessment technologies are distinct methodologies with different algorithms, validation studies, and evidence bases, their clinical performance and outcomes must be evaluated independently; consequently, evidence supporting one technology should not be extrapolated to another without direct comparative data. Differences in algorithm design, image-processing techniques, physiological modeling, image acquisition requirements, and operator workflow may result in meaningful variation in diagnostic accuracy, treatment recommendations, and clinical outcomes. Each platform requires independent assessment in both controlled trials and real-world practice to establish its clinical utility, effectiveness, and reproducibility.

Angiography-derived physiologic assessment technologies have been investigated extensively in diagnostic accuracy studies, many of which have demonstrated favorable agreement with wire-based fractional flow reserve (FFR). However, diagnostic accuracy alone is insufficient to establish clinical utility. As noted by Vrints et al., 2024, evidence of improved patient outcomes from prospective comparative trials is necessary to determine whether these technologies provide meaningful clinical benefit beyond existing standards of care. Additional evidence is needed to further define the role of angiography-derived physiologic assessment relative to wire-based FFR in the management of coronary artery disease, helping to determine when these technologies can safely serve as alternatives or adjuncts to established physiologic assessment methods and informing future guideline recommendations.

Coding

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

ASC Special Payment Policy for OPPS Complexity-Adjusted Comprehensive Ambulatory Payment Classifications (C–APCs)
In the CY 2023 OPPS/ASC final rule (86 FR 72078- 72080), CMS discussed and finalized the ASC special payment policy for OPPS complexity adjusted C–APCs. CMS operationalized a complexity adjustment into the payment rate for primary surgical procedure and packaged add-on code combinations that are eligible for complexity adjustments under the OPPS and also performed in the ASC setting through the assignment of new HCPCS C-codes. At this time, CMS is utilizing the billing of these new C-codes to provide a complexity adjustment to ASCs when performing these specific code pairs. These new C-codes have been added to the ASC covered procedures list. The list of ASC Complexity-Adjusted (CPX) codes is published annually in the OPPS and ASC Final Rule and available on the CMS website.

HCPCS codes C7557, C7562 and C7570 are OPPS complexity adjusted C–APCs. Accordingly, C7557, C7562, C7570 should only be billed by ASCs reimbursed under Medicare ASC payment methodology.

Code	Description
0523T	Intraprocedural coronary fractional flow reserve (FFR) with 3d functional mapping of color-coded FFR values for the coronary tree, derived from coronary angiogram data, for real-time review and interpretation of possible atherosclerotic stenosis(es) intervention (list separately in addition to code for primary procedure)
C7557	Catheter placement in coronary artery(s) for coronary angiography, including intraprocedural injection(s) for coronary angiography, imaging supervision and interpretation with left heart catheterization including intraprocedural injection(s) for left ventriculography, when performed and intraprocedural coronary fractional flow reserve (FFR) with 3D functional mapping of color-coded FFR values for the coronary tree, derived from coronary angiogram data, for real-time review and interpretation of possible atherosclerotic stenosis(es) intervention
C7562	Catheter placement in coronary artery(ies) for coronary angiography, including intraprocedural injection(s) for coronary angiography, imaging supervision and interpretation; with right and left heart catheterization including intraprocedural injection(s) for left ventriculography, when performed with intraprocedural coronary fractional flow reserve (FFR) with 3D functional mapping of color-coded FFR values for the coronary tree, derived from coronary angiogram data, for real-time review and interpretation of possible atherosclerotic stenosis(es) intervention
C7570	Catheter placement in coronary artery(s) for coronary angiography, including intraprocedural injection(s) for coronary angiography, imaging supervision and interpretation with intraprocedural coronary fractional flow reserve (FFR) with 3D functional mapping of color-coded FFR values for the coronary tree, derived from coronary angiogram data, for real-time review and interpretation of possible atherosclerotic stenosis(es) intervention (list separately in addition to code for primary procedure)

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Policy history

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Instructions for Use

Fallon Health complies with CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations for Medicare Advantage members. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

Fallon Health generally follows Medical Necessity Guidelines published by MassHealth when making medical necessity determinations for MassHealth members. In the absence of Medical Necessity Guidelines published by MassHealth, Fallon Health may create clinical coverage criteria in accordance with the definition of Medical Necessity in 130 CMR 450.204.

For plan members enrolled in NaviCare, Fallon Health first follows CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, or if the NaviCare member does not meet coverage criteria in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health then follows Medical Necessity Guidelines published by MassHealth when making necessity determinations for NaviCare members.

Each PACE plan member is assigned to an Interdisciplinary Team. PACE provides participants with all the care and services covered by Medicare and Medicaid, as authorized by the interdisciplinary team, as well as additional medically necessary care and services not covered by Medicare and Medicaid. With the exception of emergency care and out-of-area urgently needed care, all care and services provided to PACE plan members must be authorized by the interdisciplinary team.

Not all services mentioned in this policy are covered for all products or employer groups. Coverage is based upon the terms of a member's particular benefit plan which may contain its own specific provisions for coverage and exclusions regardless of medical necessity. Please consult the product's Evidence of Coverage for exclusions or other benefit limitations applicable to this service or supply. If there is any discrepancy between this policy and a member's benefit plan, the provisions of the benefit plan will govern. However, applicable state mandates take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, federal mandates will apply to all plans.