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REVIEW

A Year in Coronary Artery Disease: A Focussed 2024 Update

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Abstract

2024 has been a remarkable year in the field of coronary artery disease. There have been key breakthroughs at every stage of a patient's journey, from investigation to medical treatment and intervention, and many new findings are already changing practice. In this review article, we appraise and summarise the most important new evidence published in 2024 from five of the highest impact factor cardiology journals. Topics discussed include acute myocardial infarction in the elderly, antiplatelet de-escalation after percutaneous coronary intervention, the role of beta-blockers after myocardial infarction and efficacy of the microaxial flow pump in cardiogenic shock, alongside many more. We refer to the new changes in the 2024 European Society of Cardiology Chronic Coronary Syndrome guidelines in parallel to provide the reader with a clinically relevant and up-to-date review of coronary artery disease.

Key words: coronary artery disease; ischaemic heart disease; cardiology; angiography; acute coronary syndrome; chronic coronary syndrome

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Introduction

Cardiovascular disease (CVD) is the leading cause of death globally. The 2024 American Heart Associated (AHA) heart disease and stroke statistics show that CVD causes almost 20 million deaths worldwide annually (Martin et al, 2024). This is an increase of over 20% over the past decade, despite therapeutic advances lowering the age-standardised death rate almost 15%. The increased prevalence is due to an ageing population which will only increase in future years. Coronary artery disease (CAD) is a major component of CVD and has a prevalence of 7.1% in the USA (Stierman et al, 2021). In Europe, the story is similar; the European Society of Cardiology (ESC) Atlas of CVD Statistics, published in 2024 shows 11% of all healthcare budget is spent on CVD, which remains the leading cause of death in the continent (Timmis et al, 2024).

2024 has seen developments across the spectrum of CAD understanding and management. The ESC published new guidelines for management of chronic coronary syndrome (CCS) and broadened the definition of CCS to include functional issues with the coronary arteries and/or microcirculation, moving away from the historical framework involving a fixed atherosclerotic stenosis (Vrints et al, 2024). Furthermore, landmark papers were published in 2024 that addressed gaps in evidence highlighted in the ESC 2023 acute coronary syndrome (ACS) guidelines (Byrne et al, 2023b) and the ESC 2024 CCS guidelines including:

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• The optimal management strategy for management of ACS in older patients;
• The role of beta-blockers after ACS with preserved left ventricular ejection fraction (LVEF);
• The optimal long-term antithrombotic regimen after percutaneous coronary intervention (PCI);
• Biomarkers of inflammation to guide CAD risk assessment;
• The extent and timing of revascularisation for patients with multiple-vessel CAD.

Given the ever-expanding wealth of available information, this review focusses on articles published in 2024 to provide a contemporary update. This article is structured to mirror a patient's journey, with sections on assessment and investigation, medical therapy, and intervention. Finally, there will be sections on two special groups of patients: cardiogenic shock and ischaemia with non-obstructed coronary arteries (INOCA). Each section begins with discussion of practice-changing evidence published in 2024 followed by comment on relevant guideline updates, specifically the 2024 ESC CCS guidelines. Fig. 1, the central illustration, shows the breadth of the field and lists areas that experienced significant developments this year.

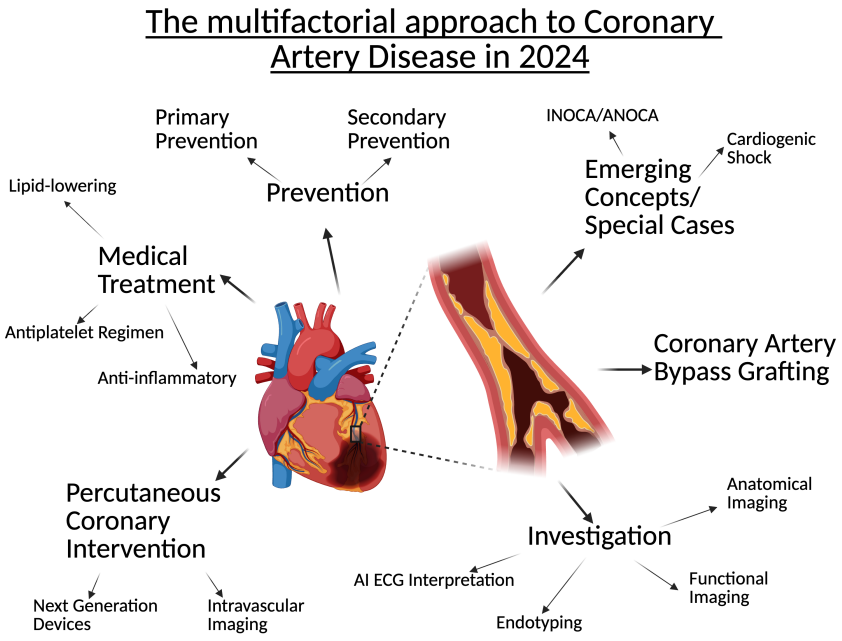

Fig. 1. Central illustration showing the multiple facets of coronary artery disease and areas that had key breakthroughs in 2024. INOCA, ischaemia with non-obstructed coronary arteries; ANOCA, angina with non-obstructed coronary arteries; AI, artificial intelligence; ECG, electrocardiogram. Fig. 1 was created using BioRender (https://BioRender.com/4fsi6ir). The authors have no financial or personal relationship with BioRender, and the use of this tool does not imply any endorsement.

Table 1. Summary of studies for investigation in coronary artery disease in 2024.

Authors	Acronym	Country	Population	Intervention	Comparator	Primary outcome	Result
McLaren et al, 2024	Review article			N/A			STEMI is limited and poor surrogate marker for coronary artery occlusion.
Chan et al, 2024	ORFAN	UK	Patients undergoing CTCA	Assessing perivascular fat attentuation	N/A (cohort study)	MACE at median FU 2.7-years	Perivascular fat attenuation index independently predicted MACE (highest vs. lowest quartiles HR 12.6, 95% CI 8.5–18.6, $p < 0.001$).
Ridker et al, 2024a	CLEAR-Outcomes		Statin-intolerant patients	hsCRP (observational)		MACE	hsCRP predicted MACE more strongly that LDL-C (HR 1.43 for highest vs. lowest hsCRP quartile, 95% CI 1.24–1.65).
Ridker et al, 2024b		USA	Healthy US women	hsCRP, LDL-C, Lp(a) measurements (observational)		1st MACE (MI, revascularisation, stroke, CV death)	hsCRP, LDL-C, and Lp(a) all predictive of CV events at 30-year FU.
Sidik et al, 2024		UK	CCS with unobstructed coronary arteries	Invasive endotyping available (n = 115)	Standard care (blinded to endotype) (n = 116)	Reclassification of initial diagnosis	Intervention more likely to diagnose vasomotor disorder (OR 4.05, 95% CI 2.32–7.24, $p < 0.001$) but no effect on angina burden.

STEMI, ST-segment elevation myocardial infarction; CTCA, computed tomography coronary angiography; MACE, major adverse cardiovascular events; FU, follow-up; HR, hazard ratio; CI, confidence interval; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); MI, myocardial infarction; CV, cardiovascular; CCS, chronic coronary syndrome; OR, odds ratio.

Methods

The New England Journal of Medicine (NEJM), The Lancet, The Journal of the American College of Cardiology (JACC), The European Heart Journal (EHJ), and circulation were searched using the term; "coronary artery" or "ischaemic heart disease" or "ischemic heart disease" or "myocardial infarction" or "acute coronary syndrome". Studies were included at the authors' discretion following assessment of impact of new information and likelihood of changing practice.

Assessment and Investigation

In 2024, key updates in CAD assessment came in electrocardiogram (ECG) interpretation and imaging. We learned that broadened ECG criteria for detecting coronary artery occlusion vastly outperform traditional ST-segment elevation myocardial infarction (STEMI) criteria (McLaren et al, 2024), artificial intelligence (AI) interpretation of ECGs can lead to earlier detection of coronary artery occlusion (Herman et al, 2024) and that coronary artery inflammation on computed tomography coronary angiography (CTCA) is an independent risk factors for major adverse cardiovascular events (MACE) (Chan et al, 2024). These will be discussed in greater detail below, and Table 1 shows a summary of important 2024 studies in this area.

The ECG is a vital tool in assessing the urgency of invasive coronary angiography (ICA) for patients with ACS. For many years the "STEMI-paradigm" has dominated practice, with patients whose ECGs display ST-segment elevation being candidates for emergency ICA. This year an influential review (McLaren et al, 2024) argued for broadening criteria and highlighted additional ECG features suggestive of coronary artery occlusion. A 2024 meta-analysis revealed STEMI criteria has only a 43.6% sensitivity for detecting an occlusion myocardial infarction (OMI) (de Alencar Neto et al, 2024) but this can be doubled by broadening ECG criteria without compromising specificity (Pendell Meyers et al, 2021). Broadened ECG criteria include ST elevation not meeting traditional criteria, hyperacute T-waves, ST depression maximal in leads V1–V4, acute Q-waves, ST elevation in inferior leads with either ST depression or T-wave inversion in aVL, terminal QRS distortion and modified sgarbossa criteria. Using AI can lead to earlier detection of OMI by up to 3 hours, in part by taking into account the broadened criteria (Herman et al, 2024; Lin et al, 2024). Limitations include being trained on retrospective data, albeit a large multicentre sample and prospective validation is required before adoption into clinical practice. In the meantime, further education may lead to reduced delays to reperfusion for patients with STEMI-negative OMI.

An emerging economical and accessible technique is the detection of acoustic murmurs for diagnosis of CAD. When validated against ICA, acoustic murmur detection had sensitivities of 81.9%, 83.3% and 85.7% for stenoses of 50%, 70%, and 90% respectively (Zhao et al, 2023). This point-of-care tool has also demonstrated excellent specificity. The CADScor® system is a portable ultrasensitive phonocardiographic device, offering non-invasive radiation-free assessment. It detects murmurs caused by turbulent flow in stenosed coronary arteries and a CADScor®

<20 has a negative predictive value of 95.4% (Rasmussen et al, 2021). This additional measure of risk-stratification may reduce costly and/or invasive investigation and be well-suited to low-resource settings.

In imaging, the multicentre UK-based Oxford risk factors and non-invasive imaging (ORFAN) study (Chan et al, 2024) demonstrated that perivascular fat attenuation (a marker of coronary artery inflammation) on CTCA was an independent predictor of MACE. This study included over 3000 participants across 2 UK centres and had median follow-up of 7.7 years. Higher fat attenuation index (FAI) scores were associated with MACE in all coronary artery territories, and this information was subsequently used to validate the AI-risk algorithm (Oikonomou et al, 2021) in a UK population. These findings support the hypothesis that active inflammation plays a significant role in unstable coronary plaques, regardless of degree of stenosis (Puchner et al, 2014), and may lead to future practice-changing developments such as more aggressive primary prevention in these patients, a lower threshold for ICA, or may help identify patients that respond to anti-inflammatory treatment. Limitations include reliance on high quality imaging, which may impact the scalability in low-resource settings. Clinical implementation will also be challenging as it is unclear how best to manage patients with high FAI.

Total plaque burden was another independent CTCA variable shown to be predictive of MACE. A sub-study of patients in the international study of comparative health effectiveness with medical and invasive approaches (ISCHEMIA; including patients with stable angina, stenosis >50% but excluding left mainstem disease) (Maron et al, 2020) demonstrated that total plaque volume is independently associated with cardiovascular death or myocardial infarction (MI) [adjusted hazard ratio (HR) 1.56, 95% confidence interval (CI) 1.25–1.97 per interquartile range increase, $p = 0.001$] (Nurmohamed et al, 2024). Adding total plaque burden to known risk factors improved the investigators' model (area under curve 0.654 vs. 0.608, $p = 0.002$).

The coronary artery inflammation hypothesis was strengthened as high-sensitivity C-reactive protein (hsCRP), a non-specific biomarker for inflammation, was shown to be a stronger predictor of MACE than low-density lipoprotein cholesterol (LDL-C) using data from the CLEAR-Outcomes trial (Nissen et al, 2023; Ridker et al, 2024a). A study by the same group found that a combined risk model of hsCRP, lipoprotein(a), and LDL-C was predictive of cardiovascular events in initially healthy women over 30 years (Ridker et al, 2024b).

A UK-based multi-centre study assessed the utility of invasive endotyping in patients with INOCA (Sidik et al, 2024). All 250 patients underwent invasive endotyping (including coronary flow reserve, index of microvascular resistance and an intracoronary infusion of acetylcholine), however it was randomised whether the results were made available to the patient and cardiologist. The diagnosis had a significant chance of changing if results were made available, namely there was a much higher incidence of diagnosis of vasomotor disorder in the unblinded group (odds ratio (OR) 4.05, 95% CI 2.32–7.24, $p < 0.001$), however this had no effect on symptom burden at 6 or 12 months, raising doubt over the benefit of invasive assessment. This is an important finding which reflects the current state of under-

standing of INOCA (covered later in the article) but is a pragmatic, real-world study showing that currently invasive endotyping does not improve patient quality of life. This will be important to re-visit in future if treatments emerge for specific subsets of INOCA.

Assessment and Investigation: Guideline Updates

Firstly, a note about the ESC guideline notation. Statements are assigned a class of recommendation and a level of evidence. The recommendation classes are I ("is recommended"), IIa ("should be considered"), IIb ("may be considered"), or III ("not recommended"). The level of evidence may be graded A ("data derived from multiple randomised clinical trials or meta-analyses"), B ("a single randomised clinical trial or large non-randomised trials"), or C ("consensus of the opinion of the experts and/or small studies, retrospective studies, or registries"). When discussing guideline recommendations in this article, the strength of recommendation and level of evidence will follow the statement in brackets.

The ESC 2024 CCS guidelines adopt a bayesian approach to diagnosis, with assessment of pre-test probability of obstructive CAD guiding whether to and how to investigate (Vrints et al, 2024). Use of the ESC risk factor-weighted clinical likelihood model is recommended to guide approach to investigation (IB). If pre-test probability is very low (≤5%) deferring further tests should be considered (IIaB). CTCA is recommended to diagnose obstructive CAD in patients with a low (>5–15%) or moderate (>15–50%) pre-test probability (IA). Functional tests (stress echocardiography, positron emission tomography (PET)/single photon emission computer tomography (SPECT) myocardial perfusion imaging, cardiac magnetic resonance (CMR) perfusion imaging) are recommended for patients with a moderate (>15–50%) or high (>50–85%) pre-test probability (IB). ICA remains the only investigation recommended for patients with a very high (>85%) probability (IC). During ICA, selective assessment of functional severity of intermediate diameter stenoses is recommended to guide revascularisation. Fractional flow reserve (FFR) ≤0.8, instantaneous wave-free ratio (iFR) ≤0.89 (IA) or quantitative flow ratio (QFR) ≤0.8 (IB) are graded as significant. Routine wire-based pressure assessment of all coronary vessels is not recommended (IIIA).

Additional new recommendations include broadening of anginal symptoms; "symptoms like chest pain triggered by emotional stress, dyspnoea or dizziness on exertion; pain in arms, jaw, neck, or upper back; or fatigue should be considered as potential angina equivalents" (IIaB) and testing hsCRP and/or fibrinogen (IIaB) to risk stratify.

Medical Treatment

In 2024, the most important medical developments arose in secondary prevention of CAD. Further evidence emerged supporting abbreviated dual antiplatelet therapy (DAPT) after PCI (Ge et al, 2024; Hong et al, 2024b; Watanabe et al, 2024b) and that clopidogrel is an alternative to aspirin beyond one year post PCI (Watanabe et al, 2024a). Two papers were published that seemed to conflict regarding the

role of beta-blockers after ACS with preserved LVEF; the REDUCE-AMI found no difference in outcomes between beta-blocker and placebo after ACS (Yndigegn et al, 2024) but the ABYSS study showed increased hospitalisation if beta-blockers are stopped once established on therapy in this population (Silvain et al, 2024). Finally, the EMPACT-MI study demonstrated empagliflozin lowers rate of heart failure hospitalisation post MI with new reduced LVEF but provides no mortality benefit (Butler et al, 2024). We explore these in more details in the following sections and Table 2 shows a summary of papers referenced in this chapter.

Medical Treatment: Antithrombotic Regimens

2024 brought evidence about optimal antithrombotic strategies after PCI, and abbreviated DAPT gained momentum. The ULTIMATE-DAPT (Ge et al, 2024) followed the IVUS-ACS (Li et al, 2024) and demonstrated that ticagrelor single antiplatelet therapy (SAPT) reduced major bleeding compared to DAPT (aspirin and ticagrelor) between 1 month and 1 year after PCI (4.6% vs. 2.1%, HR 0.45, 95% CI 0.30–0.66, $p < 0.0001$) without increasing MACE (3.6% vs. 3.7%, HR 0.98, 95% CI 0.69–1.39, $p_{\text{non-inferiority}} < 0.0001$). Limitations of this study include a narrow range of ethnicity (almost 90% Chinese ethnicity) but the results are in keeping with the TICO and T-PASS randomised controlled trials (RCTs) from South Korea (Kim et al, 2020; Hong et al, 2024b) and three individual patient meta-analyses that support abbreviated DAPT (stepping down to ticagrelor SAPT) after PCI for ACS (Baber et al, 2024; Lee et al, 2024; Valgimigli et al, 2024).

The short and optimal duration of dual antiplatelet therapy (STOPDAPT) trials, conducted in Japan, add further evidence. STOPDAPT-3 found prasugrel SAPT was non-inferior to prasugrel and aspirin DAPT for cardiovascular endpoints (4.12% vs. 3.69%, HR 1.12, 95% CI 0.87–1.45, $p_{\text{non-inferiority}} = 0.01$) without a change in bleed rate at 1 month post PCI (Natsuaki et al, 2024). The second phase of STOPDAPT-3 found no difference in bleeding or cardiovascular outcomes between 1 month and 1 year post PCI between clopidogrel SAPT and aspirin SAPT (Watanabe et al, 2024b). STOPDAPT-2 found that clopidogrel SAPT was superior to clopidogrel and aspirin DAPT between 1–12 months post PCI for composite endpoint of bleeding and thrombotic events (Watanabe et al, 2019). 5-year follow-up of this cohort compared clopidogrel SAPT versus aspirin SAPT beyond 1 year post PCI (Watanabe et al, 2024a). Clopidogrel was superior for cardiovascular outcomes (8.61% vs. 11.05%, HR 0.77, 95% CI 0.61–0.97, $p = 0.03$) and non-inferior for a bleeding/thrombosis composite outcome (11.75% vs. 13.57%, HR 0.85, 95% CI 0.70–1.05, $p_{\text{non-inferiority}} < 0.001$, $p_{\text{superiority}} = 0.13$). Table 2 illustrates the difference in antiplatelet trials discussed and trial populations.

The data discussed strongly suggest that abbreviated DAPT after PCI is safe and effective in South Korean, Chinese, and Japanese populations. There is a paucity of evidence in for abbreviated DAPT in European populations and this is reflected in the conservative recommendation in the 2023 ESC ACS guidelines; 12-month DAPT remains the default strategy but abbreviated DAPT (or de-escalation to less potent agents) should only be used if the patient is at high bleeding risk

(Byrne et al, 2023b). By contrast, the 2024 Korean ACS guidelines recommend abbreviated DAPT or de-escalation after 1–3 months for any patient not at high ischaemic risk (Kim et al, 2024). This illustrates the impact of ethnic and geographical factors on treatment strategies and abbreviated DAPT requires further assessment in European populations before changing practice.

Having an indication for anticoagulation such as atrial fibrillation (AF) alongside CAD is a common clinical scenario. The EPIC-CAD trial assessed the efficacy of edoxaban monotherapy versus edoxaban plus clopidogrel (dual antithrombotic group) for patients with AF and stable CAD (Cho et al, 2024). The edoxaban monotherapy group had a lower incidence of bleeding (HR 0.34, 95% CI 0.22–0.53) without an increase in thrombotic events (HR 1.23, 95% CI 0.48–3.10). This trial strongly supports current guidelines, which advocate the use of anticoagulation monotherapy in this patient group (assuming greater than 1 year post PCI).

Medical Treatment: Beta-Blockers

2024 saw apparent conflicting evidence for beta-blockers after MI with preserved LVEF with the REDUCE-AMI (Yndigegn et al, 2024) and ABYSS (Silvain et al, 2024) trials reaching opposite conclusions. Both open-label trials, REDUCE-AMI randomised patients to beta-blocker or no beta-blocker after MI, whereas ABYSS randomised patients with a history of MI (>6 months prior) already established on a beta-blocker to either have the beta-blocker interrupted or continued. REDUCE-AMI found no difference in a composite outcome of death or acute MI over a median follow-up period of 3.5 years. Conversely, ABYSS concluded that beta-blocker interruption was inferior to continuation for a composite outcome of death, nonfatal myocardial infarction (MI), nonfatal stroke, or hospitalization for cardiovascular reasons. The results appear to be conflicting, however, the ABYSS outcome was entirely driven by an increase in cardiovascular hospitalisation in the beta-blocker interruption arm, specifically for ICA. Neither trial found significant difference in rates of cardiovascular death, stroke, or MI. The difference in trial conclusions may be explained by the difference in trial population; not starting a beta-blocker (REDUCE-AMI) is not the same as stopping it in patients established on treatment (ABYSS). The outcomes may reflect subtraction anxiety experienced by the beta-blocker interruption group in the ABYSS trial as the patients were aware a medication was being stopped but could suggest a deleterious effect of beta-blocker cessation. Considering these results, it seems reasonable to not start beta-blocker after MI and preserved LVEF, particularly if there are concerns about whether the patient will tolerate the medication, however it may not be worth de-prescribing beta-blockers for patients who tolerate them well and have been established on treatment for a long time. Should the latter patient develop issues with beta-blockers in future (for example bradycardia or postural hypotension) then these trials allow an evidence-based discussion around benefits and risks of stopping.

Table 2. Summary of 2024 articles in the medical management of coronary artery disease.

Authors	Acronym	Country	Population	Intervention	Comparator	Primary outcome	Result
Ge et al, 2024	ULTIMATE-DAPT	China, Pakistan, Italy, UK	ACS patients, no events after 1-month DAPT, median age 63, 74% male, 88% Chinese, 32% diabetic	Ticagrelor & placebo (n = 1700)	Ticagrelor & Aspirin (n = 1700)	(1) Bleeding (superiority). (2) MACE (non-inferiority) 1–12 months after PCI	Ticagrelor monotherapy had lower bleeding (HR 0.45, 95% CI 0.30–0.66, $p < 0.0001$) and non-inferior MACE (HR 0.98, 95% CI 0.69–1.39, $p_{\text{non-inferiority}} < 0.0001$).
Hong et al, 2024b	T-PASS	South Korea	ACS and DES, mean age 61, 84% male, 30% diabetic	Ticagrelor monotherapy <1 month after PCI (n = 1426)	Ticagrelor-based DAPT for 12 months (n = 1424)	Composite (all-cause death, MI, stent thrombosis, stroke, and major bleeding) at 1 year	Ticagrelor monotherapy superior to DAPT (HR 0.54, 95% CI 0.37–0.80, $p_{\text{non-inferiority}} < 0.001$, $p_{\text{superiority}} = 0.002$).
Watanabe et al, 2024a	STOPDAPT-2	Japan	Japanese patients with DES (38% ACS), mean age 69, 78% male, 39% diabetic	DAPT 1 month then clopidogrel lifelong (n = 1471)	DAPT 12 months then aspirin lifelong (n = 1486)	Composite (ischaemic & bleeding) between 1–5 years post PCI	Clopidogrel non-inferior but not superior to aspirin (HR 0.85, 95% CI 0.70–1.05, $p_{\text{non-inferiority}} < 0.001$, $p_{\text{superiority}} = 0.13$).
Natsuaki et al, 2024	STOPDAPT-3 (1 month FU)	Japan	Japanese patients with DES (75% ACS), mean age 72, 76% male, 41% diabetic	1-month SAPT (prasugrel) (n = 2894)	1-month DAPT (aspirin & prasugrel) (n = 2982)	Composite (CV death, MI, stent thrombosis, stroke) or bleeding at 1 month after PCI	SAPT not superior in reducing bleeding (HR 0.95, 95% CI 0.75–1.20, $p_{\text{superiority}} = 0.66$) but was non-inferior for CV events (HR 1.12, 95% CI 0.87–1.45, $p_{\text{non-inferiority}} = 0.01$) up to 1 month post PCI.
Watanabe et al, 2024b	STOPDAPT-3 (1 year FU)	Japan	Japanese patients with DES (75% ACS), mean age 72, 76% male, 41% diabetic	Month 1–12 aspirin monotherapy (n = 2920)	Month 1–12 clopidogrel monotherapy (n = 2913)	(1) MACE. (2) Bleeding between months 1–12 after PCI	No difference. (1) HR 1.00 (95% CI 0.77–1.30, $p = 0.97$). (2) HR 1.02 (95% CI 0.69–1.52, $p = 0.92$).
Lee et al, 2024	Meta-analysis		ACS with DES	Step down to ticagrelor SAPT after <3 months DAPT	12 months DAPT	Ischaemic and bleeding endpoints	Ticagrelor had lower bleeding (HR 0.54, 95% CI 0.40–0.72, $p < 0$ .001) but no increase ischaemic (HR 0.79, 95% CI 0.56–1.13, $p = 0.194$).
Valgimigli et al, 2024	Meta-analysis			De-escalation to tigarelor	DAPT	(1) Bleeding (superiority). (2) MACE (non-inferiority)	De-escalation is safe (MACE (HR 0.91, 95% CI 0.78–1.07, $p_{\text{non-inferiority}} = 0.0039$) and reduces bleeding (HR 0.43, 95% CI 0.34–0.54, $p_{\text{superiority}} < 0.0001$).

Table 2. Continued.

Authors	Acronym	Country	Population	Intervention	Comparator	Primary outcome	Result
Baber et al, 2024	Meta-analysis			3 months DAPT then ticagrelor SAPT	12 months DAPT	Bleeding, MACE	Significantly reduced bleeding in ticagrelor SAPT group, no increased ischaemic risk.
Cho et al, 2024	EPIC-CAD	South Korea	AF and stable CAD	Edoxaban monotherapy (n = 524)	Edoxaban & SAPT (n = 516)	Composite (death, MI, stroke, embolism, revascularisation, bleeding)	Edoxaban lower primary outcome (HR 0.44, 95% CI 0.30–0.65, $p < 0.001$).
Yndigegn et al, 2024	REDUCE-AMI	Sweden, Estonia, New Zealand	MI, angiography, LVEF ≥50%	Beta-blocker (Bb) (n = 2508)	No Bb (n = 2512)	Composite (all-cause death, MI)	No difference (median FU 3.5 years) (HR 0.96, 95% CI 0.79–1.16, $p = 0.64$)
Silvain et al, 2024	ABYSS	France	Previous MI, LVEF >40%, on Bb	Stop Bb (n = 1846)	Continue Bb (n = 1852)	MACE (death, non-fatal MI/stroke, CV hospitalisation)	Non-inferiority criteria not met (HR 1.16, 95% CI 1.01–1.33, $p_{\text{non-inferiority}} = 0.44$). Mainly driven by hospitalisation.
Butler et al, 2024	EMPACT-MI	22 countries	MI and at risk of HF	Empagliflozin (n = 3260)	Placebo (n = 3262)	Composite (HF hospitalisation or all-cause death)	No difference (HR 0.90, 95% CI 0.76–1.06, $p = 0.21$).
Udell et al, 2024	EMPACT-MI (substudy)	22 countries	ACS, LVEF <45%	Empagliflozin (n = 3260)	Placebo (n = 3262)	Composite (death, HF hospitalisation)	Empagliflozin reduced HF hospitalisation across range of LVEF. Lower LVEF associated with worse outcomes.
Hernandez et al, 2024	EMPACT-MI (substudy)	22 countries	MI with LVEF <45%	Empagliflozin (n = 3260)	Placebo (n = 3262)	HF hospitalisation	HF hospitalisation reduced in empagliflozin group.
Patel et al, 2024	Meta-analysis			SGLT2-inhibitors	Placebo	MACE	SGLT2-inhibitors reduced MACE across wide range of patient groups (driven by CV death/HF hospitalisation).
Rosenson et al, 2024		4 countries	Mixed hyperlipidaemia	Zodasiran (n = 153)	Placebo (n = 51)	Triglyceride level at week 24	Triglycerides lower with zodasiran.
Ballantyne et al, 2024		Multi-national	Mixed hyperlipidaemia	Plozasiran (n = 200)	Placebo (n = 87)	Triglyceride level at week 24	Triglycerides lower with plozasiran.
Miyauchi et al, 2024	RESPECT-EPA	Japan	Stable CAD, low EA:AA ratio, on a statin	Icosapent ethyl (n = 1249)	Control group (n = 1257)	MACE	No significant difference (HR 0.79, 95% CI 0.62–1.00, $p = 0.055$).

Table 2. Continued.

Authors	Acronym	Country	Population	Intervention	Comparator	Primary outcome	Result
Szarek et al, 2024	REDUCE-IT (substudy)	11 countries	Established CV disease or >50 with risk factors	Icosapent ethyl (n = 3515)	Placebo (n = 3511)	1st MACE	Baseline Lp(a) prognostic for MACE. Icosapent ethtyl consistently reduced MACE across Lp(a) levels ($p_{interaction}$ > 0.10).
Lincoff et al, 2024	CLEAR-Outcomes	32 countries	Statin-intolerant	Bempedoic acid (n = 6992)	Placebo (n = 6978)	MACE reduction normalised to LDL-C reduction	MACE risk with bempedoic acid is similar to statin when normalised for LDL-C reduction.
Gibson et al, 2024b		49 countries	MI, multi-vessel CAD, and RFs	ApoA-1 infusion (n = 9112)	Placebo (n = 9107)	MACE	No difference at 90, 180, or 365 days (HR 0.93, 95% CI 0.85–1.02).
Povsic et al, 2024	AEGIS-II (substudy)	49 countries	High risk MI	ApoA-1 infusion (n = 9112)	Placebo (n = 9107)	CV death/recurrent MI	No significant difference at day 365 (HR 0.89, 95% CI 0.79–1.01, p = 0.07).
Huet et al, 2024	COLD-MI	France	STEMI patients	Colchicine	No colchicine	%LV showing sympathetic denervation	Denervation less in colchicine group.
Yu et al, 2024	COLOCT (substudy)	Canada	ACS, lipid-rich plaque on OCT	Colchicine (n = 2366)	Placebo (n = 2379)	Change in minimal fibrous cap thickness on repeat OCT at 12 months	OCT features improved with colchicine (minimal fibrous cap change 34.2 µm, 95% CI 9.7–58.6 µm, p = 0.006).

ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention; DES, drug-eluting stent; SAPT, single antiplatelet therapy; HF, heart failure; SGLT2, sodium-glucose cotransporter 2; AF, atrial fibrillation; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; Bb, beta-blocker; RFs, risk factors; EA, eicosapentaenoic acid; AA, arachidonic acid; ApoA-1, apolipoprotein A-1; LV, left ventricle; OCT, optical coherence tomography.

Table 3. Summary of 2024 studies on the topic of coronary artery intervention.

Authors	Acronym	Country	Population	Intervention	Comparator	Primary outcome	Result
Erlinge et al, 2024	INFINITY-SWEDEHEART	Sweden	ACS/CCS	Bioadaptor (n = 1201)	DES (n = 1198)	Target lesion failure at 12 months	Bioadaptor non-inferior to DES at 1 year.
Gao et al, 2024	REC-CAGEFREE I	China	De novo CAD with indication for stent	DCB (n = 1133)	DES (n = 1139)	Composite: CV death, target vessel MI, target vessel revascularisation	DCB inferior to DES (6.4% vs. 3.4%, $p_{non\text{-}inferiority}$ = 0.65).

Table 3. Continued.

Authors	Acronym	Country	Population	Intervention	Comparator	Primary outcome	Result
Foley et al, 2024	ORBITA-COSMIC	UK	CCS on maximal therapy	Coronary sinus reducer (CSR, n = 25)	Placebo procedure (n = 26)	(1) Myocardial blood flow in ischaemic segments on CMR. (2) Number of daily angina episodes	(1) No change in myocardial blood flow (difference 0.06 mL/min/g 95% CI –0.09–0.20, Pr(Benefit) = 78.8%). (2) CSR reduced daily angina episodes (OR 1.40; 95% CI 1.08–1.83; Pr(Benefit) = 99.4%).
Li et al, 2024	IVUS-ACS	China, Pakistan, Italy, UK	ACS	IVUS-guided PCI (n = 1753)	Angiography-guided PCI (n = 1752)	Target vessel failure at 12 months	IVUS superior to angio-guided (HR 0.55, 95% CI 0.41–0.74, $p = 0.0001$).
Hong et al, 2024a	OCCUPI	South Korea	≥1 complex coronary lesions	OCT-guided PCI (n = 803	Angiography-guided PCI (n = 801)	MACE at 12 months	OCT superior (5% vs. 7%, HR 0.62, 95% CI 0.41–0.93, $p = 0.023$).
Stone et al, 2024	Meta-analysis			IVUS/OCT	Angiography-guided PCI	Target lesion failure	Reduced target lesion failure with intravascular imaging (RR 0.71, 95% CI 0.63–0.80, $p < 0.0001$).
Kunadian et al, 2024	SENIOR-RITA	UK	ACS, Age ≥75	Angiography ± PCI	Medical management	Composite (CV death/nonfatal MI)	No difference at median 4.1 years FU (HR 0.94, 95% CI 0.77–1.14, $p = 0.53$).
Cocco et al, 2024	FIRE (substudy)	Italy, Spain, Poland	Age >75, MI and multivessel disease	Complete revascularisation (n = 720)	Culprit PCI only (n = 725)	Composite (death, MI, stroke, unplanned revascularisation) analysed by MI type	Composite outcome reduced with full revascularisation across spectrum of ACS.
Böhm et al, 2024	FULL REVASC	7 countries	STEMI/high risk NSTEMI with multivessel disease	PCI to non-culprit lesions with FFR <0.8 (n = 764)	Culprit PCI only (n = 778)	MACE (death, MI, unplanned revascularization)	No difference at 4.8-year FU (HR 0.93, 95% CI 0.74–1.17; $p = 0.53$).
Reddy et al, 2024	Meta-analysis		ACS with multivessel disease	Complete revascularisation	Culprit PCI only	All-cause mortality	Complete revascularisation reduces all-cause mortality (RR 0.85, 95% CI 0.74–0.99, $p = 0.04$).
Ezad et al, 2024	REVIVED-BCIS2 (substudy)	UK	Severe ischaemic cardiomyopathy	Revascularisation (anatomical or viability-guided)	Incomplete revascularisation/medical therapy only	Composite (death/HF hospitalisation)	No change in event-free survival (anatomical-guided HR 0.90, 95% CI 0.62–1.32, viability-guided HR 0.95, 95% CI 0.66–1.35).
Campo et al, 2024	Meta-analysis		Older patients with STEMI-longer-term FU	Full revascularisation	Culprit PCI only	Death, MI, ischaemic-driven revascularisation	Primary endpoint reduced in full revascularisation group up to 4 years post MI.

DCB, drug-coated balloon; CSR, coronary sinus reducer; CMR, cardiac magnetic resonance; IVUS, intravascular ultrasound; RR, relative risk; FFR, fractional flow reserve; NSTEMI, non-ST-segment elevation myocardial infarction; Pr, probability.

Medical Treatment: Sodium-Glucose Cotransporter 2 Inhibitors

After the recent success of sodium-glucose cotransporter 2 (SGLT2) inhibitors in heart failure with reduced and preserved LVEF (McMurray et al, 2019; Packer et al, 2020; Packer et al, 2023; Anker et al, 2021; Solomon et al, 2022; Doehner et al, 2024), the eagerly anticipated results of the EMPACT-MI study, investigating the efficacy of empagliflozin after MI, were published in 2024 (Butler et al, 2024). EMPACT-MI randomised patients with acute MI and LVEF <45% or signs of congestion to receive empagliflozin or a matching placebo. After median follow-up of 17.9 months, there was no difference in rates of first hospitalisation for heart failure or death between groups. The empagliflozin group did, however, have a lower rate of hospitalisation for heart failure (HR 0.77, 95% CI 0.60–0.98, $p = 0.031$). Prespecified subgroup analyses confirmed that this effect persisted across a range of LVEF and presence or absence of congestion (Hernandez et al, 2024; Udell et al, 2024).

Medical Treatment: Lipid-Lowering Therapies

Lipid reduction was hot topic in 2024. Two phase 2b trials for Ribonucleic Acid interference agents (Zodasiran and Plozasiran) were positive for reducing triglycerides at 24 weeks in patients with mixed hyperlipidaemia (Ballantyne et al, 2024; Rosenson et al, 2024). Important negative results include the Study to Investigate CSL112 in Subjects With Acute Coronary Syndrome (AEGIS-II) that demonstrated that infusions of apolipoprotein A-1 after high-risk MI did not reduce cardiovascular events at 90 days, however this may be effective for patients with LDL-C ≥100 mg/dL (Gibson et al, 2024a; Gibson et al, 2024b; Povsic et al, 2024). Post-hoc analysis of a study of AMR101 to evaluate its ability to reduce cardiovascular events in high-risk patients with hypertriglyceridemia and on statin (REDUCE-IT) found icosapent ethyl reduced MACE across a range of lipoprotein(a) levels for patients with established cardiovascular disease, or diabetic and with an additional risk factor (Bhatt et al, 2019; Szarek et al, 2024). The RESPECT-EPA trial, however did not show any statistically significant reduction in cardiovascular events with icosapent-ethyl in patients with chronic coronary artery disease, a low eicosapentaenoic acid:arachidonic acid ratio and on statin treatment over a median period of 5 years (Miyauchi et al, 2024). Both RESPECT-EPA and REDUCE-IT noted an increased incidence of AF in the intervention arm (3.1% vs. 1.6%; $p = 0.017$) (Olshansky et al, 2023).

Medical Treatment: Colchicine

Colchicine continued to gain traction as a potential treatment for CAD in 2024. The COLOCT (Yu et al, 2024) follows the COLCOT (Tardif et al, 2019) and the randomised controlled trial on the effect of LoDoCo2 (Nidorf et al, 2020) trials that have provided evidence of benefit in ACS in recent years. COLOCT randomised 128 patients with ACS to colchicine or placebo then repeated ICA with optical co-

herence tomography (OCT) at 12 months. The colchicine group had an increase in the minimal fibrous cap thickness as well as other features of plaque stability at 1 year. The COLD-MI found reduced LV denervation post STEMI with colchicine as assessed by ^{123}I-metaiodobenzylguanidine single-photon emission computed tomography (^{123}I-MIBG SPECT) at 6-month follow-up (Huet et al, 2024). The trial was small (46 included in final analysis), however adds a potential mechanism to explain benefits of colchicine after ACS.

Medical Treatment: Guideline Updates

The 2024 ESC CCS guidelines include new recommendations on all medical aspects of CAD (Vrints et al, 2024). Clopidogrel is recommended as an alternative to aspirin for patients with prior MI or PCI (IA), whilst aspirin is recommended lifelong after coronary artery bypass grafting (CABG) (IA). Aspirin is also recommended for patients with CCS with significant obstructive CAD even without prior MI or revascularisation (IB).

New recommendations around anti-anginal therapy include "Ivabradine should be considered as an add-on anti-anginal therapy for patients with LVEF $<$40% and inadequate symptom control" (IIaB). However, ivabradine is not recommended for patients with LVEF $>$40% and no clinical heart failure (IIIB) or in combination with non-dihydropyridine calcium channel blockers or other strong Cytochrome P450 3A4 (CYP3A4) inhibitors (IIIB).

Lipid targets are set at LDL-C $<$1.4 mmol/L and a $\geq$50% reduction in baseline (IA). Adding bempedoic acid to ezetimibe is recommended for statin-intolerant patients who do not meet target LDL-C (IB), and it should be considered for patients taking a statin and ezetimibe (IIaC).

SGLT2 inhibitors are recommended for patients with type 2 diabetes mellitus and CCS, regardless of haemoglobin A1c level (IA) and semaglutide (a glucagon-like peptide-1 agonist) should be considered for patients with overweight or obesity to reduce cardiovascular risk (IIaB).

Low-dose colchicine should be considered in patients with atherosclerotic CAD to reduce MI, stroke, and need for revascularisation (IIaA).

Intervention: PCI

There were many exciting developments in PCI in 2024, with new technology and evidence about optimal approaches using existing techniques. Table 3 provides a summary of important 2024 papers in this field. Key updates include invasive management of elderly patients with non-ST-elevation MI (NSTEMI) does not reduce mortality but does reduce incidence of non-fatal MI (Kunadian et al, 2024), FFR-guided full revascularisation after index PCI for ACS was not shown to reduce death, MI or unplanned revascularisation over culprit-only PCI (Böhm et al, 2024), and intravascular imaging lowering death, MI and unplanned revascularisation compared to angiographically-guided PCI (Hong et al, 2024a; Li et al, 2024). These are discussed in greater detail below.

The INFINITY-SWEDEHEART trial demonstrated that a new design of stent, the DynamX bioadaptor was non-inferior to a zotarolimus drug-eluting stent (DES) for target lesion failure at 1 year for patients with ACS or CCS (Erlinge et al, 2024). The bioadaptor is an intracoronary device that provides radial support to the vessel upon insertion, however the cobalt-chromium strands are held together by a bioresorbable polymer, which absorbs after 6 months, allowing the device to "uncage" (Verheye et al, 2023). After this, the device can transmit radial and torsional motion and is theorised to allow more normal physiological function of the vessel. The 2399 patients across 20 sites in Sweden will be followed up for 5 years to investigate whether the bioadaptor out-performs DES over a longer period. This remains an exciting area to watch.

The coronary sinus reducer for the treatment of refractory angina (ORBITA-COSMIC), a double-blind RCT conducted across 6 UK sites investigated whether a coronary sinus reducer (CSR) was effective for patients with refractory angina with no further treatment options (Foley et al, 2024). The CSR is an hourglass-shaped device that is placed percutaneously into the coronary sinus, aiming increase venous resistance and thereby recruit collateral vessels and improve flow to the ischaemic endocardium (Verheye et al, 2015). 50 patients were included in the final analysis and the number of daily angina events was reduced in the CSR group (OR 1.40, 95% CI 1.08–1.83, Probability of benefit = 99.4%), however there was no difference in quantitative ischaemia on adenosine-stress perfusion CMR. Worryingly, there were 2 CSR embolization events in the intervention arm (n = 24). The CSR remains a IIb B recommendation in the 2024 ESC CCS guidelines for patients with refractory angina (Vrints et al, 2024). Ongoing trials (COSIMA; NCT04606459 and COSIRA-II; NCT05102019) aim to assess CSR's efficacy in microvascular angina and again in refractory angina, respectively.

The REC-CAGEFREE I (Gao et al, 2024), a multicentre randomised open-label non-inferiority study conducted in China, compared drug-coated balloon (DCB) and DES for de novo coronary artery lesions. DCB involves inflating a balloon inside the lesion, creating dissection in the atheromatous plaque and allowing delivery of anti-proliferative drugs which coat the balloon (in REC-CAGEFREE 1 this was paclitaxel) (Kenny and Sharif, 2024). The DCB strategy was inferior to DES as measured by a device-orientated composite endpoint (cardiovascular death, target vessel MI, target vessel revascularisation). This was primarily driven by an increase in target vessel revascularisation, however cardiovascular death was close to reaching statistical significance (DEB 2.3% vs. DES 1.2%, 95% CI 0.02–2.15%, $p = 0.053$).

The randomised trial of invasive versus conservative strategy in older patients with non-ST elevation myocardial infarction (SENIOR-RITA) (Kunadian et al, 2024) provided evidence to address a gap in knowledge identified in the 2023 ESC ACS guidelines (Byrne et al, 2023b); management of NSTEMI in older/frail adults. SENIOR-RITA was a prospective multi-centre RCT comparing conservative versus invasive management of patients aged ≥75 admitted with NSTEMI, 32.4% of whom had frailty. Over median follow-up 4.1 years, there was no mortality difference between groups, however non-fatal MI was lower in the invasive group (HR 0.75,

95% CI 0.57–0.99). Reassuringly, the complication rate was low in the invasive arm (<1%). The cohort included in SENIOR-RITA represents a large group of patients seen in daily clinical practice; however this group has rarely been included in research. This study allows informed discussions to be held regarding coronary artery intervention in the elderly and represents a significant step towards developing evidence-based practice for patients with frailty.

Intravascular imaging has been a hot topic in recent years, and 2024 provided more evidence of benefit. IVUS-ACS (Li et al, 2024) and OCCUPI (Hong et al, 2024a) were multi-centre RCTs investigating intravascular ultrasound (IVUS) and OCT respectively. Both trials shared a composite primary outcome (cardiac death, myocardial infarction, or target-vessel revascularisation) assessed at 1 year post PCI. IVUS-ACS included 3505 patients with ACS whilst OCCUPI included any patient with an indication for PCI and a complex coronary lesion (n = 1604, roughly half ACS and half CCS). Both trials showed a similar magnitude of reduction in the primary outcome (absolute risk reduction; IVUS-ACS 3.3%, OCCUPI 2.8%), suggesting a number needed to treat of 30–36. These findings are supported by a meta-analysis published earlier in the year (Stone et al, 2024) which found intravascular imaging reduced the relative risk of cardiac death, target lesion failure, and stent thrombosis. IVUS and OCT yielded similar outcomes in this meta-analysis. A sub-study of the optical coherence tomography guided coronary stent implantation compared to angiography: a multicenter randomized trial in PCI (known as ILLUMIEN-IV) may help narrow the population most likely to benefit. ILLUMIEN-IV was a negative study for OCT in patients with diabetes or a complex coronary lesion, however the sub-study showed that OCT reduced MACE for those with a complex coronary lesion (HR 0.63, 95% CI 0.40–0.99, $p = 0.04$), as well as giving a larger minimal stent area (Ali et al, 2023; Ali et al, 2024). The benefits may therefore be limited to those with complex coronary lesions although IVUS-ACS suggests there may be a role in the acute setting regardless of lesion complexity. Nonetheless, one must consider limitations of wide-spread implementation of intravascular imaging given the disparity of access to these technologies and additional operator training required. In resource-limited settings, this is unlikely to be cost-effective given improvements in medical therapy and standard PCI have lowered event rate significantly.

The extent of revascularisation is another gap in evidence (Byrne et al, 2023b). It is common for patients with ACS or CCS to have multiple-vessel CAD, however it is unclear whether to address all lesions (full revascularisation) and, if so, when to do this. The FULL REVASC trial assessed whether physiology-guided full revascularisation using fractional flow reserve (FFR ≤0.80 deemed significant stenosis) was superior to culprit-only PCI for patients presenting with STEMI or high-risk NSTEMI (Böhm et al, 2024). After median follow-up 4.8 years, there was no significant difference in the composite primary outcome of death, MI, or unplanned revascularisation. This contrasts to the Complete vs Culprit-only Revascularization to Treat Multi-vessel Disease After Early PCI for STEMI (COMPLETE) which concluded that angiographically-guided full revascularisation reduced the primary endpoint of cardiovascular death or new MI at median follow-up of 3 years (HR

0.74, 95% CI 0.60–0.91, $p = 0.004$), driven entirely by reduction in MI (Mehta et al, 2019). We will explore potential explanations; study cohorts, approach to revascularisation, timing of revascularisation, and validity of FFR in ACS. The demographics of FULL REVASC and COMPLETE cohorts are similar (median age 65 vs. 62, 76% vs. 80% male, 16% vs. 20% diabetic, 91% vs. 100% STEMI respectively) and most likely predominantly Caucasian although this is not specified. Crucially, the severity of bystander disease was lower in FULL REVASC (16.6% had stenosis $\geq$90%, compared to 23.1%) and may reflect a group of patients less likely to benefit from full revascularisation. Furthermore, FULL REVASC ended recruitment early due to feasibility and was only 74% powered for the event rate observed. Regarding approach to bystander lesions, FULL REVASC mandated FFR on all lesions graded 50–89% angiographically (FFR optional if $\geq$90%) and revascularisation if FFR $\leq$0.8 (or angiographically $\geq$90% and no FFR done), whereas COMPLETE mandated revascularisation if angiographic stenosis $\geq$70% or 50–69% with FFR $\leq$0.8. The more restrictive approach in FULL REVASC predictably reduced stenting (only 18.8% of non-culprit vessels were stented) which may contribute to the lack of difference between groups. Concerningly, there remained a significantly higher incidence of stent thrombosis in the full revascularisation arm. Thirdly, timing; FULL REVASC conducted bystander PCI a median 2 days after index PCI, which was sooner than in COMPLETE (randomisation occurred $<$72 hours after index PCI, roughly two-thirds underwent bystander PCI during the index admission (median 1 day after randomisation), and one-third as a separate admission (median 23 days after randomisation)). It may be that the longer interval between index PCI and full revascularisation seen in COMPLETE contributed to better outcomes. Finally, it has been suggested that microvascular dysfunction induced by ACS can cause false-negative FFR in culprit and non-culprit vessels (Uren et al, 1994; Tamita et al, 2002; Claessen and van Wijk, 2020), however one study comparing FFR during index PCI and 1 month later found no difference whilst another found FFR was only 0.02 higher during index PCI, which is unlikely to change decision making in many patients (Ntalianis et al, 2010; van der Hoeven et al, 2019). We therefore do not believe that false-negative FFR explains the discrepancy between FULL REVASC and COMPLETE: instead, it may be that FFR is the incorrect technology to use given it provides no detail of plaque characteristics, such as instability. An ongoing trial (COMPLETE-2; NCT05701358) includes a sub-group assigned to OCT which should test this hypothesis. To muddy the waters further, the functional versus culprit-only revascularization in elderly patients with myocardial infarction and multivessel disease trial (FIRE) published in 2023 assessed physiologically-guided full revascularisation in an elderly population (median age 80) and this led to a reduction in the primary composite of death, MI, stroke, or ischaemia-driven revascularisation and a reduction in all-cause death at 1 year (19.2% vs. 12.8%, HR 0.70, 95% CI 0.61–0.96) (Biscaglia et al, 2023). The discrepancy between FULL REVASC and FIRE may be explained by follow-up duration or the higher event-rate in FIRE.

PCI: Guideline Updates

Three key new IA level recommendations in the 2024 ESC CCS guidelines regarding PCI are:

- "Intracoronary imaging guidance by IVUS or OCT is recommended for performing PCI on anatomically complex lesions, in particular left mainstem, true bifurcations and long lesions."

- "Intracoronary pressure measurement (FFR or iFR) or computation (QFR) is recommended to guide lesion selection in patients with multivessel disease."

- "For patients with significant left main coronary stenosis of low complexity (SYNTAX score $\leq$22), in whom PCI can provide equivalent completeness of revascularisation to that of CABG, PCI is recommended as an alternative to CABG, given its lower invasiveness and non-inferior survival." (Vrints et al, 2024).

Intervention: CABG

In both ACS and CCS, surgical revascularisation by CABG remains appropriate management in selected patients, reflected in both American (Lawton et al, 2022) and European (Byrne et al, 2023a; Byrne et al, 2023b; Vrints et al, 2024) guidance. This includes patients with left mainstem disease, complex multisegment disease (Syntax score >32), diabetes mellitus, and ischaemic cardiomyopathy who have an LVEF <35%. 2024 showed left mainstem disease treated with CABG had a lower re-admission rate over 5 years than PCI (Kosmidou et al, 2024), whilst women with multi-vessel CAD may gain a greater benefit with CABG over PCI (An et al, 2024), although both studies used non-randomised retrospective data. Furthermore, there is a role for CABG in management of STEMI when PCI is not feasible or is unsuccessful. Predominantly this is in the setting of cardiogenic shock where 70% of cases have complex multi-vessel CAD (Byrne et al, 2023b).

Recent developments and future directions in CABG focus on reducing length of admission and periprocedural complications without compromising long-term survival. A 2024 development includes proven feasibility of operative planning with CTCA rather than ICA for low-risk cases (Serruys et al, 2024). In the safety and feasibility evaluation of planning and execution of surgical revascularization solely based on coronary computed tomography angiography and fractional flow reserve derived from CT in patients with complex coronary artery disease trial (FAST TRACK CABG), operative planning using CTCA was feasible in 99.1% (95% CI 95.2–100%) of cases, with 82.9% concordance in plan between the ICA-blinded and unblinded teams. Another reduction in complications comes from minimally invasive coronary surgery (MICS). MICS involves off-pump ("beating heart") CABG performed via left thoracotomy incision. This reduces complications associated with aortic cross-clamping and sternotomy. MICS may be used in both single and multivessel disease. The minimally invasive coronary surgery compared to sternotomy coronary artery bypass grafting trial (MIST, NCT03447938) will compare quality of life and recovery of MICS and conventional CABG up to 12 months. Study completion is expected in 2028.

In multivessel CAD, hybrid revascularisation presents another treatment option. This involves PCI of non-left anterior descending (LAD) vessels combined with left mainstem/LAD MICS. This benefits from the improved prognosis associated with left internal mammary artery grafting of diseased left mainstem/LAD and a less invasive procedure. Emergence of hybrid revascularisation reflects lower restenosis rates with modern PCI compared to saphenous vein graft conduits, which have 8–25% failure at 1 year, and only 50–60% patency at 10 years (Xenogiannis et al, 2021).

Another trend in CABG is increased multi-arterial grafting, with the latest data from the Society of Thoracic Surgeons showing an increase from 10.9% in 2020 to 14.9% in 2021 (Kim et al, 2023). This technique was demonstrated as far back as 1999 when bilateral internal mammary artery grafting was shown to be superior to single mammary artery grafting (Lytle et al, 1999) but remains a minority procedure. This may be an area to watch for 2025.

Finally robotic CABG, either endoscopic or via a small incision, has shown promise in reducing complication rates. Recent evidence has shown low perioperative mortality rate of 0.8% and lower morbidity compared to conventional surgery (Göbölös et al, 2019). The graft patency rate of 93.2% beyond 5 years is also encouraging (Kitahara et al, 2019). Downsides include greater procedural time, cost and specialised operator training. Currently, only 1% of CABG in the USA is done robotically, although this is expected to increase as costs reduce and availability increases (Whellan et al, 2016).

CABG: Guideline Updates

New IA recommendations in the 2024 ESC CCS guidelines around CABG include:

"In CCS patients at low surgical risk with significant left main coronary stenosis, CABG

- is recommended over medical therapy alone to improve survival
- is recommended as the overall preferred revascularisation mode over PCI, given the lower risk of spontaneous myocardial infarction and repeat revascularisation."

Additional new recommendations are made regarding revascularisation for patients with CCS either with or without heart failure. The guidelines recommend Heart Team discussions for complex cases or where PCI and CABG hold the same level of evidence (IC). It is recommended that all decisions are patient-centred and consider preferences, health literacy, cultural circumstances, and social support (IC) (Vrints et al, 2024).

Special Cases: Cardiogenic Shock

2024 marked the publication of a trial over a decade in the making: the danish–german cardiogenic shock trial: microaxial flow pump in infarctrelated cardiogenic shock (DanGer Shock) (Møller et al, 2024). This multicentre RCT assessed the effect of routine use of the microaxial flow pump (mAFP), a form of mechanical cir-

culatory support (MCS), in patients with STEMI and cardiogenic shock. Inclusion criteria were STEMI and all the following: systolic blood pressure <100 mmHg (or ongoing need for vasopressor support), arterial blood lactate level ≥ 2.5 mmol.L^{-1}, and LVEF $<45\%$. Out-of-hospital cardiac arrest, poor neurological status or overt right ventricular failure were exclusion criteria. One should note the strict inclusion criteria and avoid extrapolating results. 355 patients were included in the final analysis with median age 67. Mortality at 180 days was high in both groups but there was a significant reduction in those managed using mAFP (45.8% vs. 58.5%, HR 0.74, 95% CI 0.55–0.99, $p = 0.04$). It should be noted that there was a higher incidence of adverse events in the mAFP group. Specifically the composite safety endpoint (severe bleeding, limb ischemia, haemolysis, device failure, and worsening of aortic regurgitation, 24.0% vs. 6.2%, HR 4.74, 95% CI 2.36–9.55), moderate or severe bleeding (21.8% vs. 11.9%, HR 2.06, 95% CI 1.15–3.66), limb ischaemia (5.6% vs. 1.1%, HR 5.15, 95% CI 1.11–23.84), renal replacement therapy (41.9% vs. 26.7%, HR 1.98, 95% CI 1.27–3.09), and sepsis with positive blood culture (11.7% vs. 4.5%, HR 2.79, 95% CI 1.20–6.48) all had higher incidence in the mAFP group, however crucially this did not translate to a higher overall mortality. Being aware of these complications of the mAFP may lead to earlier recognition and treatment, or future development of the device and techniques. This could further improve the mortality benefit. Additional supporting evidence comes from an individual patient meta-analysis which reviewed 6-month mortality data across 9 RCTs for patients with acute MI-related cardiogenic shock requiring MCS (of any device) (Thiele et al, 2024). Patients with STEMI-related cardiogenic shock deemed not at risk of hypoxic brain damage were the only group to derive a mortality benefit from MCS. This aligns with the inclusion criteria for DanGer Shock and should prompt clinicians to be selective in decision-making around MCS.

These trials represent a paradox: they are ground-breaking and yet advocate a device that has been used for over a decade. This reinforces the need for high quality evidence prior to marketing approval and should embolden researchers to assess devices against standard care if there is such an evidence gap.

Special Cases: INOCA

The ESC 2024 CCS guidelines talked in depth about INOCA (Vrints et al, 2024). This follows the emerging concept of coronary microvascular dysfunction; functional or structural abnormalities of the microcirculation that may lead to transient ischaemia and angina. This heterogenous group of patients has historically not been researched heavily.

Regardless of underlying endotype, the guidelines advocate lifestyle modification (namely nutrition, exercise, weight management, smoking cessation and coping with stress) and addressing other conventional risk factors as part of a holistic approach to management of INOCA. Patients may also require psychological support given the chronic nature of symptoms.

The new guidelines include an IA recommendation for the use of calcium channel blockers as treatment for isolated vasospastic angina. Nitrates should be con-

sidered to prevent recurrent episodes of this (IIaB). Additional IIa recommendations include basing medical therapy on coronary functional testing, prescribing ACE-inhibitors for symptom control in endothelial dysfunction, and prescribing beta-blockers for microvascular angina with reduced coronary flow reserve.

We predict that INOCA will be a focus of research in the coming years as there remain significant evidence gaps. As discussed in the assessment and investigation chapter, knowledge of the patient's endotype often changes diagnosis but not patient quality of life (Sidik et al, 2024). This may change if specific therapies are developed but we first need large scale RCTs which include endotyping. Additionally, development of non-invasive assessment methods is needed in this cohort but will only change practice if effective, evidence-based therapies are available.

Conclusion

This article has covered ground-breaking RCTs in important areas, however it should be noted that many publications in 2024 were sub-group analyses of previous RCTs. Excessive sub-group analyses lead to a greater chance of false positive findings, which highlights the ongoing need for long-term, large-scale RCTs to address specific research priorities. Nonetheless, the developments made in 2024 across all facets of the diagnosis, treatment, and prevention of CAD will have a real impact in patients seen in daily practice. 2025 promises to be no different. In the upcoming year, we can expect the publication of the new AHA ACS guidelines. It is a fool's errand to attempt to predict the future, however it can also be enjoyable. For this reason, the authors speculate that 2025 may yield further developments in lipid-lowering therapy, a greater understanding of treatment for INOCA, and greater advancement of AI ECG interpretation in ACS. In the era of big data and AI, we expect to see further progress towards individualised risk assessment and tailored management for prevention of and treatment of CAD Whether right or wrong, we look forward to finding out.

Key Points

- 2024 has yielded practice-changing evidence in the field of coronary artery disease and addressed gaps in evidence identified in the ESC guidelines.
- SENIOR-RITA gives clinicians evidence to shape management discussions with elderly patients with ACS: invasive management reduces recurrence of acute coronary syndrome but no mortality benefit over medical care.
- REDUCE-AMI showed no benefit of beta-blockers after ACS with preserved LVEF, but ABYSS found increased hospitalisation if beta-blocker was discontinued in the same population.
- DanGer Shock showed that the micro-axial flow pump reduces mortality in certain patients with STEMI-related cardiogenic shock.

Availability of Data and Materials

All the data of this study are included in this article and its references.

Author Contributions

TS and AD contributed to the conception of the manuscript. TS drafted the manuscript. DOS jointly contributed to the design of the manuscript and wrote several sections. All authors contributed to editorial changes of important content in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

Fig. 1 was created using BioRender. The authors have no financial or personal relationship with BioRender, and the use of this tool does not imply any endorsement.

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