Current concepts in coronary artery revascularisation

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Coronary artery revascularisation can be performed surgically or percutaneously. Surgery is associated with higher procedural risk and longer recovery than percutaneous interventions, but with long-term reduction of recurrent cardiac events. For many patients with obstructive coronary artery disease in need of revascularisation, surgical or percutaneous intervention is indicated on the basis of clinical and anatomical reasons or personal preferences. Medical therapy is a crucial accompaniment to coronary revascularisation, and data suggest that, in some subsets of patients, medical therapy alone might achieve similar results to coronary revascularisation. Most revascularisation data are based on prevalently White, non-elderly, male populations in high-income countries; robust data in women, older adults, and racial and other minorities, and from low-income and middle-income countries, are urgently needed.

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Introduction

Coronary artery revascularisation is a common procedure in current medical practice. Every year almost 800 000 patients in the USA,[1] 900 000 in China,[2] 250 000 in Japan,[1,3] and over 1·2 million in Europe[4] undergo revascularisation by either coronary artery bypass grafting (CABG) or percutaneous coronary interventions(PCI). In the past 20 years, PCI, CABG, and medical therapy for coronary artery disease have undergone very important changes and their relative results have been tested in numerous randomised controlled trials (RCTs).

In this Review, we evaluate the current evidence on coronary revascularisation with the aim of summarising key concepts to help to inform clinical decision making. We also highlight gaps in knowledge and future research directions.

Coronary artery bypass surgery

After almost three decades of attempts at indirect coronary surgery (through pericardial, sympathetic system, or thyroid gland interventions),[5] CABG was introduced in the early 1970s and rapidly adopted (figure 1). Currently, it is the most common heart operation, representing over 50% of all adult cardiac surgeries worldwide.[6,7]

During CABG, segments of arteries or veins are connected to the coronary arteries distal to flow-limiting obstructions. Most operations are performed through median sternotomy, with a cardiopulmonary bypass pump, grafting the left anterior descending coronary artery with the internal thoracic artery and bypassing the remaining target coronary arteries with segments of the great saphenous vein.[8] Operative mortality has progressively declined despite referral of older and more comorbid patients, currently ranging between 1% and 2% for elective cases, and with values in the low decimal range for cases without preoperative organ dysfunction.[7,8] Stroke is infrequent but is a serious complication of CABG, with a prevalence in modern series ranging between 0·5% and 1·5%.[8,9] Stroke can occur intraoperatively, mainly through embolism from aortic manipulation, or postoperatively from arrhythmias or hypotension.[10] Cognitive decline is a potential complication of CABG, but data are mixed and without solid evidence.[11,12] Some studies reported similar neuropsychological dysfunction after either PCI or CABG,[13,14] suggesting that cognitive decline in CABG patients might relate to ageing and systemic atherosclerotic disease rather than to the surgery itself. Other important complications are postoperative renal (occurring in 1–2% of cases)[15] and respiratory failure (occurring in approximately 10% of cases);[16] they are usually rapidly reversible in patients with preserved preoperative function.

Postoperative atrial fibrillation is the most common complication of CABG, affecting 20–25% of patients.[17] The arrhythmia is generally well tolerated, with most patients reverting to sinus rhythm within 1 or 2 days.[17] However, postoperative atrial fibrillation significantly increases length of in-hospital stay, costs, risk of subsequent heart failure and stroke, and even mortality, through mechanisms that are not entirely clear.[17,18] Postoperative atrial fibrillation also increases the risk of recurrent atrial fibrillation in the years after surgery.[19] β blockers or amiodarone and left posterior pericardiotomy are effective measures to prevent postoperative atrial fibrillation,[20,21] whereas the roles of rhythm versus rate control and of systemic anticoagulation are less clear.[22,23]

Surgical wound complications occur in 5–10% of CABG patients,[24,25] particularly in individuals with multiple risk factors (eg, female sex, obesity, and diabetes), affecting postoperative quality of life.[26] Sternal wound complications are associated with increased short-term and long-term

Search strategy and selection criteria

We searched PubMed from the site's inception to Dec 31, 2022 for references with the terms "coronary revascularisation", "percutaneous coronary intervention", "coronary bypass surgery", "medical therapy", or any combination of these terms in the title or abstract, and no language restrictions. We also identified relevant articles from the reference lists of selected articles. We prioritised RCTs and publications from the past 10 years, but we cited other references when relevant.

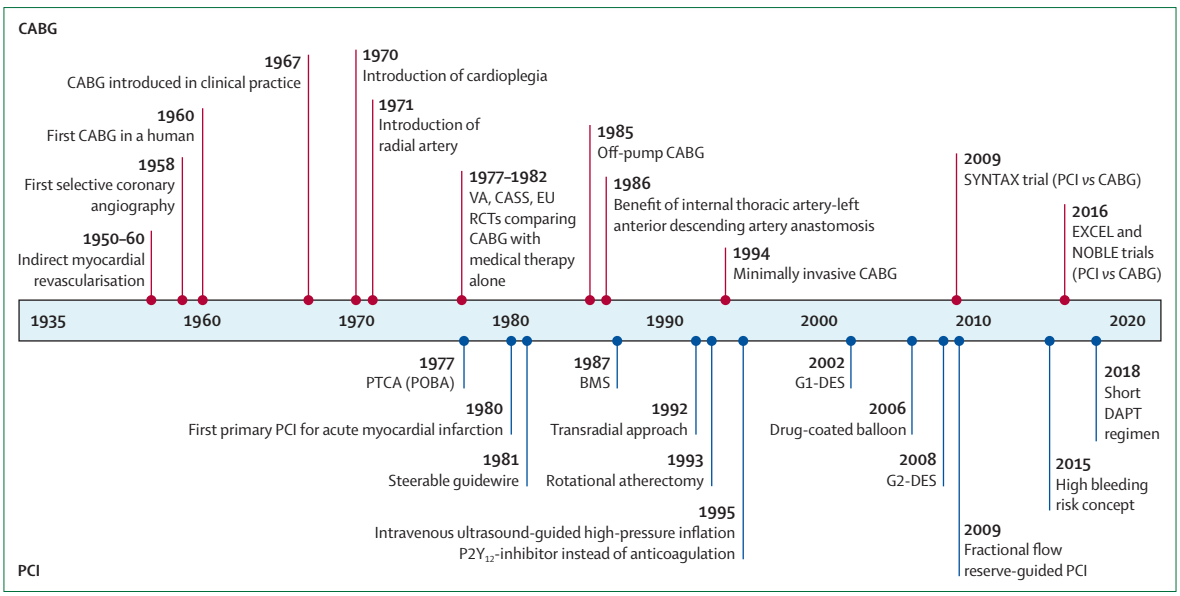

Figure 1: **Timeline of key advancements in surgical and percutaneous coronary revascularisation**
BMS=bare-metal stent. CABG=coronary artery bypass surgery. CASS=Coronary Artery Surgery Study. DAPT=dual antiplatelet. G1-DES=first-generation drug-eluting stent. G2-DES=second-generation drug-eluting stent. PCI=percutaneous coronary intervention. PTCA=percutaneous transluminal coronary angioplasty. POBA=plain old balloon angioplasty. RCTs=randomised clinical trials. SYNTAX=Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery. VA=Veterans Administration.

mortality[25] and with higher risk of graft failure (probably owing to mediastinal inflammation and hypercoagulability).[27] Hospital readmission after CABG is frequent, with reported rates of 10–15% at 30 days and 20–25% at 90 days.[28] The most common reasons are pericardial effusions, heart failure related to fluid overload, arrhythmias, and wound complications, whereas myocardial ischaemia and graft failure are less common.[28]

Patients generally recover from surgery within 2–3 months, with large variations based on age, preoperative comorbidity, and severity of heart disease. Adoption of Enhanced Recovery After Surgery (ERAS) protocols can reduce complications and accelerate return to healthy life.[29] Centre-based and home-based post-operative rehabilitation reduces hospital readmissions and shortens recovery time.[30] Depression and anxiety are common after surgery and behavioural, psychological, or pharmacological interventions might improve quality of life and even clinical outcomes postoperatively.[31]

Procedural aspects of CABG

Off-pump CABG is undertaken without the cardiopulmonary bypass pump, with the use of dedicated instruments to stabilise the target vessels and perform anastomoses on the beating heart.[32] Large RCTs have not reported significant benefits compared with traditional techniques,[33,34] and there have been concerns over less complete revascularisation and higher risks of graft failure when CABG is performed off-pump. Off-pump CABG is currently adopted routinely only by dedicated surgeons, although with important variations (in India and Japan, for example, most CABG procedures are performed off-pump).[8,35]

The use of arterial rather than saphenous venous grafts to revascularise non-left anterior descending coronary artery targets has been hypothesised to improve long-term CABG outcomes on the basis of the higher failure rate of venous grafts compared with arterial conduits.[36,37] Although observational series have generally reported better overall and event-free survival for patients operated upon with multiple versus single arterial grafts, RCTs have not shown significant differences between groups,[38] and treatment allocation and experience bias might be the reason for the reported differences in observational studies. The ongoing ROMA trial[39] should provide more definitive information.

Minimally invasive CABG through ministernotomy or small thoracotomies, often with the support of dedicated (port-access) or robotic technologies, has been proposed but not tested in adequately powered RCTs; it remains a niche for dedicated surgeons and highly selected patients.[40] Hybrid revascularisation (minimally invasive surgical grafting of the left anterior descending coronary artery or of few selected targets, complemented by PCI of the remaining vessels) has not been widely embraced in clinical practice and the available evidence is scarce.[41]

Percutaneous coronary interventions

The first PCI was reported by Andreas Gruentzig in 1977 to treat severe, discrete, non-calcified coronary artery stenoses.[42] PCI was subsequently applied to patients with acute myocardial infarction as early as 1980 (figure 1),[43]

becoming the first-choice reperfusion therapy in this setting, given the survival and safety benefits of PCI over intravenous thrombolytic therapy.[44] PCI involves a guiding catheter introduced under local anaesthesia from a peripheral artery and directed to the coronary artery orifice, through which a dilation catheter with a distensible tip (balloon) is advanced across the stenotic or occluded arterial site and inflated to compress and crack atherosclerotic or thrombotic material, thereby dilating the lumen.[42] Clinical outcomes of patients treated by PCI have progressively improved with technical and medical advances (figure 2).[45] A first landmark was the introduction of coronary stents that greatly reduced the risk of abrupt vessel closure.[46] A major drawback, however, was stent thrombosis within the first month, complicating 1–3% of elective procedures and 7–15% of emergency procedures, despite the use of intravenous heparin and oral anticoagulation.[47] A second landmark was replacing oral anticoagulation with a platelet $P2Y_{12}$-receptor inhibitor (each on a background of aspirin), with dual antiplatelet therapy (DAPT) substantially reducing stent thrombosis rates and contributing to widespread adoption of PCI.[48] A persistent major drawback of the procedure—although with lower rates after stenting than with plain balloon angioplasty—was restenosis, necessitating repeated interventions.[46,49] A third landmark was the introduction of drug-eluting stents that limited the prevalence of restenosis to single percent digits compared with bare-metal stenting.[50] Older drug-eluting stents (sirolimus or paclitaxel) have been largely superseded by second generation drug-eluting stents (everolimus or zotarolimus).[51] Thus, despite referral of increasingly comorbid patients with complex lesions, short-term and long-term cardiovascular mortality following PCI has declined over the decades.[45,52]

Early complications of PCI include periprocedural myocardial infarction (with highly variable prevalence depending on definitions and ascertainment, from 2% to 18%),[53] stroke (0·1–1%),[54] major bleeding (1–5%),[55] and acute kidney injury (4–7%),[56] all of which can adversely affect short-term and long-term survival. Midterm and long-term stent-related adverse events include stent thrombosis (0·1% per year) and restenosis requiring revascularisation (0·5–1% per year),[57] with little attenuation up to 10 years after PCI, even with new-generation drug-eluting stents.[58] Stent thrombosis is classified on the basis of timing after implantation as acute (0–24 h), subacute (24 h–30 days), late (30 days–1 year), or very late (>1 year).[59] Acute and subacute events are generally related to technical issues (inadequate stent expansion, residual dissection, and tissue prolapse) or inadequate platelet inhibition, whereas late and very late events are generally related to discontinuation of antiplatelet therapy, neoatherosclerosis, and delayed vessel healing.[60] Although new-generation drug-eluting stents and more potent platelet inhibitors have reduced the prevalence of stent thrombosis, it still affects 1–2·5% of PCI patients.[57,58] Stent-free PCI is a novel approach to avoid stent-related complications. Drug-coated balloons are reported to be non-inferior to drug-eluting stents for small vessel lesions[61]

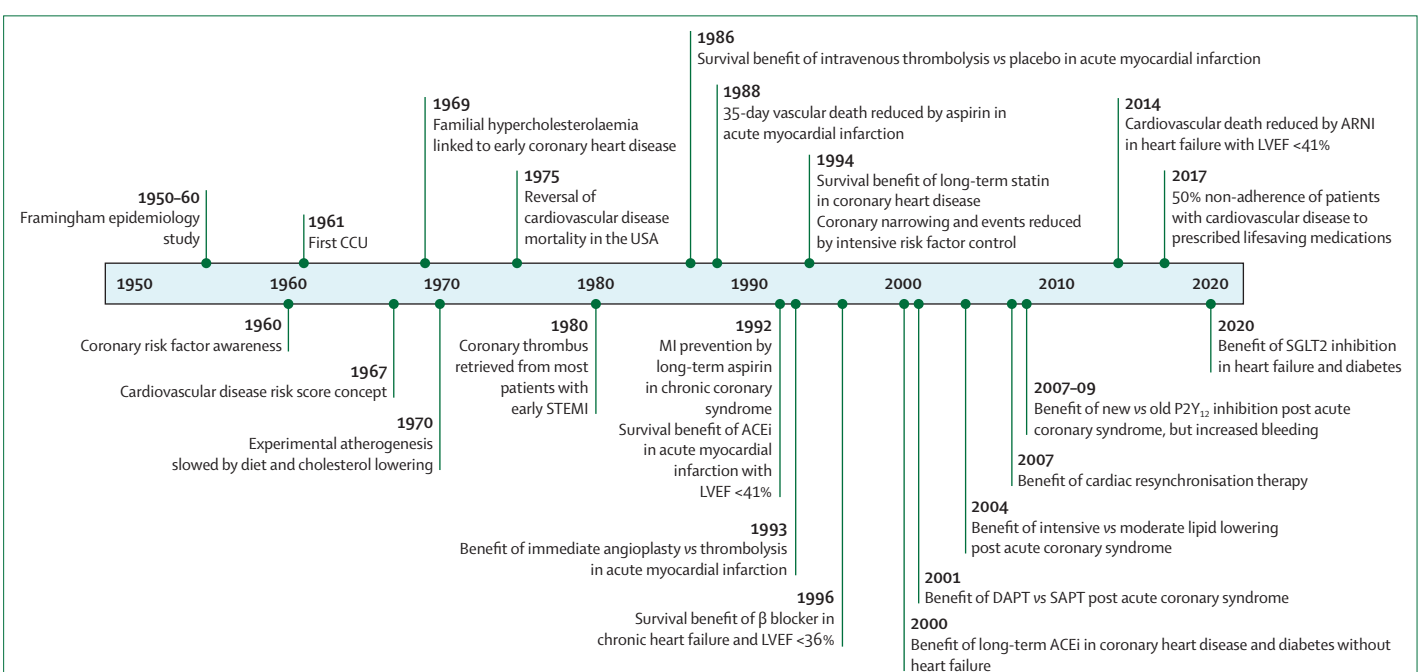

Figure 2: **Timeline of key advancements in medical therapy for coronary artery disease**
ACEi=angiotensin-converting enzyme inhibitor. ARNI=angiotensin receptor–neprilysin inhibitor. CCU=coronary care unit. DAPT=dual antiplatelet therapy. LVEF=left ventricular ejection fraction. SAPT=single antiplatelet therapy. SGLT2=sodium-glucose cotransporter-2. STEMI=ST-segment elevation myocardial infarction.

and are used for in-stent restenosis,[62] whereas bioresorbable stent scaffolds have so far not shown incremental benefits compared with drug-eluting stents.[63]

Procedural aspects of PCI

Radial artery access has become standard PCI practice, as trial findings and meta-analyses show lower rates of major bleeding, vascular complications, major adverse cardiovascular events, and mortality compared with the traditional femoral artery approach.[64,65]

Fractional flow reserve assessed by adenosine vasodilation or resting instantaneous wave-free ratio is recommended by current guidelines to assess the functional severity of intermediate epicardial artery

	Participants (N [medical therapy; revascularisation])	Patient population	Sex of participants (%)	Mean age of participants (years)	Modality of revascularisation (%)	Follow-up period	Primary outcome (revascularisation *vs* medical therapy)
AVERT (1999) PMID: 10395630	341 (164; 177)	Patients with coronary artery disease and negative stress test	Female 15·9%	58·5	PCI 100%	1·5 years	Composite of cardiac death, myocardial infarction, stroke, resuscitation after cardiac arrest, repeat revascularisation, or angina requiring hospitalisation: PCI 37%, medical therapy 13%; p=0·048
MASS (1999) PMID: 10567287	214 (72; 142 [PCI 72, CABG 70])	Patients with coronary artery disease	Female 18%	57·0	PCI 51%, CABG 49%	5·0 years	Composite of cardiac death, acute myocardial infarction, or refractory angina requiring revascularisation: CABG 8·6%, PCI 40·3%, medical therapy 23·9%; p=0·001
TIME (2001) PMID: 11583747	305 (150; 155)	Patients older than 75 years and chronic coronary syndrome	Female 42·9%	80·0	PCI 71%, CABG 29%	6 months	Composite of death, myocardial infarction, or hospitalisation for acute coronary syndrome: invasive 19·0%, medical therapy 49·0%; p<0·0001
RITA-2 (2003) PMID: 14522473	1018 (514; 504)	Patients with coronary artery disease and angina	Female 18%	58·0	PCI 100%	7·0 years	Composite of death or myocardial infarction: PCI 14·5%, medical therapy 12·3%; difference +2·2% (95% CI –2·0 to 6·4; p=0·21)
COURAGE (2007) PMID: 17387127	2287 (1138; 1149)	Patients with coronary artery disease	Female 15%	62·6	PCI 100%	4·6 years	Composite of death or myocardial infarction: PCI 19·0%, medical therapy 18·5%; HR 1·05 (95% CI 0·87 to 1·27; p=0·62)
COURAGE (2015) PMID: 26559572	1211 (598; 613)	Patients with coronary artery disease	Female 8·5%	63·0	PCI 100%	11·9 years	Death: PCI 25%, medical therapy 24%; HR 1·03 (95% CI 0·83 to 1·21; p=0·76)
BARI 2D (2009) PMID: 19502645	2368 (1192; 1172 [PCI 798, CABG 378])	Patients with diabetes and coronary artery disease	Female 29·6%	62·4	PCI 67%, CABG 33%	5·3 years	Death: Revascularisation 11·7%, medical therapy 12·2%; p=0·97; PCI 10·8%, medical therapy 10·2%; p=0·48; CABG 13·6%, medical therapy 16·4%; p=0·33
MASS II (2010) PMID: 20733102	611 (203; 405 [PCI 205, CABG 203])	Patients with multivessel coronary artery disease	Female 31%	60·0	PCI 50%, CABG 50%	11·4 years	Composite of death, Q-wave myocardial infarction, or angina requiring revascularisation: CABG 33·0%, PCI 42·4%, medical therapy 59·1%; p<0·001
STICH (2011) PMID: 21463150	1212 (602; 610)	Patients with coronary artery disease and left ventricular ejection fraction ≤35%	Female 12·2%	59·0	CABG 100%	4·6 years	Death: CABG 36%, medical therapy 41%; HR 0·86 (95% CI 0·72 to 1·04; p=0·12)
STICHES (2016) PMID: 27040723	1212 (602; 610)	Patients with coronary artery disease and left ventricular ejection fraction ≤35%	Female 12·2%	59·0	CABG 100%	9·8 years	Death: CABG 58·9%, medical therapy 66·1%; HR 0·84 (95% CI 0·73 to 0·97; p=0·02)
FAME-II (2018) PMID: 29785878	888 (441; 447)	Patients with functionally significant lesions (fractional flow reserve ≤0·80)	Female 21·2%	63·7	PCI 100%	5 years	Composite of death, myocardial infarction, or urgent revascularisation: PCI 13·9%, medical therapy 27·0%; HR 0·46 (95% CI 0·34 to 0·63; p<0·001)
ORBITA (2018) PMID: 29103656	200 (95; 105)	Patients with 1-vessel coronary artery disease	Female 26·5%	66·0	PCI 100%	6 weeks	Exercise time increment (s): PCI 28·4, medical therapy 11·8; Difference 16·6 (95% CI –8·9 to 42·0; p=0·200)

(Table 1 continues on next page)

	Participants (N [medical therapy; revascularisation])	Patient population	Sex of participants (%)	Mean age of participants (years)	Modality of revascularisation (%)	Follow-up period	Primary outcome (revascularisation *vs* medical therapy)
(Continued from previous page)							
DECISION-CTO (2019) PMID: 30813758	834 (398; 417)	Patients with chronic total occlusion lesions	Female 21·8%	62·6	PCI 100%	4·0 years	Composite of death, myocardial infarction, stroke, or repeat revascularisation: PCI 22·4%, medical therapy 22·3%; HR 1·03 (95% CI 0·77 to 1·37; p=0·86)
ISCHEMIA (2020) PMID: 32227755	5179 (2591; 2588 [PCI 1915, CABG 673])	Patients with moderate-severe ischaemia	Female 22·6%	64·0	PCI 74%, CABG 26%	3·2 years	Composite of cardiovascular death, myocardial infarction, hospitalisation for unstable angina, heart failure, or resuscitated cardiac arrest: invasive 16·4%, conservative 18·2%; difference −1·8% (95% CI −4·7 to 1·0)
ISCHEMIA-CKD (2020) PMID: 32227756	777 (389; 388)	Patients with chronic kidney disease and moderate-severe ischaemia	Female 31·1%	62·7	PCI 85%, CABG 15%	2·2 years	Composite of cardiovascular death or myocardial infarction: Invasive 36·4%, conservative 36·7%; HR 1·01 (95% CI 0·79 to 1·29; p=0·95)
REVIVED (2022) PMID: 36027563	700 (353; 347)	Patients with extensive coronary artery disease, left ventricular ejection fraction ≤35%, and demonstrable myocardial viability	Female 13%	69·3	PCI 100%	3·4 years	Composite of death or hospitalisation for heart failure: PCI 37·2%, medical therapy 38·0%; HR 0·99 (95% CI 0·78 to 1·27; p=0·96)

CABG=coronary artery bypass grafting. HR=hazard ratio. LVEF=left ventricular ejection fraction. PCI=percutaneous coronary intervention.

Table 1: **Main outcomes of randomised trials comparing revascularisation and medical therapy in patients with coronary artery disease**

stenoses.[66,67] In the FAME trial, PCI guided by fractional flow reserve significantly reduced the composite endpoint of death, myocardial infarction, and repeat revascularisation in patients with multivessel coronary artery disease compared with PCI guided by angiography only (13·2% *vs* 18·3%).[68] Two subsequent trials showed PCI guided by instantaneous wave-free ratio to be non-inferior to PCI guided by fractional flow reserve.[69,70] PCI guided by intravascular ultrasound has been associated with fewer ischaemic events than has PCI guided by angiography only.[71] More recently, PCI guided by optical coherence tomography was found to be non-inferior to PCI guided by intravascular ultrasound.[72] Despite the benefits suggested by the data, haemodynamic and imaging guidance are seldom used in clinical practice.[1]

With declining rates of ischaemic cardiovascular events after PCI, growing concerns have emerged over midterm and long-term bleeding related to prolonged DAPT therapy. Recent data show that short-term DAPT (1–3 months) followed by $P2Y_{12}$-inhibitor monotherapy reduces major bleeding events compared with standard 12-month DAPT, without significantly increasing ischaemic events.[73,74]

PCI of chronic total occlusion is burdened by technical challenges, low procedural success, and high complication rates,[75] but recent advances have improved patient outcomes after chronic total occlusion-PCI undertaken by experienced operators.[75] Complex high-risk indicated PCI is performed in patients with a clinical indication for coronary revascularisation who are at high procedural risk related to comorbidities, complex coronary anatomy, or unstable haemodynamics.[76] Many of these patients have anatomical indications for CABG but a prohibitive surgical risk.

Medical therapy

In the 1970s and 1980s, atherogenesis in animals was found to revert with changes in diet and serum cholesterol.[77] Progression of coronary narrowing in humans was found to slow down with changes in diet, smoking cessation, exercise, and control of blood pressure, bodyweight, and lipid profile.[77,78] Since then, cardiovascular medical therapy has made great progress (figure 2). In the 1990s, statins,[79] aspirin,[80] and angiotensin-converting enzyme inhibitors[81] were found to benefit patients with chronic coronary syndromes. Cardiovascular events were reduced by fibrinolysis in patients with ST-elevation myocardial infarction,[82] and by higher intensity statins,[83] or by DAPT in patients with acute coronary syndromes.[84] In patients with chronic heart failure, cardiovascular events were reduced by β blockade,[85] angiotensin receptor–neprilsyn inhibitors,[86] and sodium-glucose cotransporter-2 inhibition (figure 2).[87] Yet a major limitation of medical therapy is the suboptimal long-term compliance rate of approximately 50% reported in multiple studies, including revascularisation trials.[88,89]

Numerous randomised trials have compared the efficacy and safety of revascularisation strategies against medical therapy alone in non-acute patients with

obstructive coronary artery disease not involving the left main stem (table 1). The COURAGE trial randomly assigned 2287 patients with coronary artery disease with preserved left ventricular ejection fraction to initial PCI or medical therapy alone and found no difference between groups at 4·6 years in the primary outcome of death and myocardial infarction (19·0% *vs* 18·5%).[90] The largest and most recent ISCHEMIA trial randomly assigned 5179 patients with moderate or severe inducible ischaemia and preserved ejection fraction to either an initial invasive strategy (74% by PCI, 26% by CABG) or to medical therapy alone. At 3·2 years, the primary endpoint of cardiovascular death, myocardial infarction, stroke, or hospitalisation for unstable angina or resuscitated cardiac arrest did not differ significantly between groups (16·4% and 18·2%, respectively).[91] Spontaneous myocardial

	ESC/EACTS 2018 guidelines PMID: 30165437	ACC/AHA/SCAI 2021 guidelines PMID: 34882436	JCS/JSCVS 2018 guidelines PMIDs: 35095031 and 30930428
Stable coronary artery disease			
One-vessel coronary artery disease	No proximal LAD stenosis: PCI* (COR: I; LOE: C); proximal LAD stenosis: CABG or PCI (COR: I; LOE: A)	No proximal LAD stenosis: no revascularisation (COR: III-no benefit; LOE: B-R); proximal LAD stenosis: coronary revascularisation uncertain to improve survival (COR: IIb; LOE: B-R)	No proximal LAD stenosis: PCI* (COR: I; LOE: C); proximal LAD stenosis: CABG* (COR: I; LOE: C)
Two-vessel coronary artery disease	No proximal LAD stenosis: PCI* (COR: I; LOE: C); proximal LAD stenosis: CABG (COR: I; LOE: B); PCI (COR: I; LOE: C)	No proximal LAD stenosis: no revascularisation (COR: III-no benefit; LOE: B-R); proximal LAD stenosis: coronary revascularisation uncertain to improve survival (COR: IIb; LOE: B-R)	SYNTAX score 0–22: CABG (COR: I; LOE: A) PCI (COR: I; LOE: B); SYNTAX score 23–32: CABG* (COR: I; LOE: A); SYNTAX score ≥33: CABG (COR: I; LOE: A)
Three- or multivessel coronary artery disease	SYNTAX score 0–22: CABG or PCI (COR: I; LOE: A); SYNTAX score >22: CABG* (COR: I; LOE: A)	CABG and PCI (COR: IIb; LOE: B-R to improve survival and COR: IIa; LOE B-R to reduce the risk of cardiovascular events); SYNTAX score >33: CABG to improve survival (COR: IIa; LOE: B-R)	SYNTAX score 0–22: CABG (COR: I; LOE: A) PCI (COR: I; LOE: B); SYNTAX score 23–32: CABG* (COR: I; LOE: A); SYNTAX score ≥33: CABG (COR: I; LOE: A)
Left main coronary artery disease	SYNTAX score 0–22: CABG or PCI (COR: I; LOE: A); SYNTAX score 23–32: CABG* (COR: I; LOE: A); SYNTAX score ≥33: CABG* (COR: I; LOE: A)	CABG (COR I; LOE: B-R); if PCI can provide equivalent revascularisation: PCI acceptable (COR: IIa; LOE: B-NR)	Bifurcation lesions requiring <2 stents, and SYNTAX score 0–22: CABG (COR: I; LOE: A) PCI (COR: I; LOE: B); bifurcation lesions requiring <2 stents, and SYNTAX score 23–32: CABG* (COR: I; LOE: A); bifurcation lesions requiring 2 stents: CABG* (COR: I; LOE: A); SYNTAX score ≥33: CABG (COR: I; LOE: A)
Diabetes			
Two-vessel coronary artery disease:	NA	NA	SYNTAX score 0–22: CABG* (COR: I; LOE: A); SYNTAX score 23–32: CABG* (COR: I; LOE: A); SYNTAX score ≥33: CABG (COR: I; LOE: A)
Three-vessel or multivessel coronary artery disease	CABG (COR: I; LOE: A)	Involvement of LAD and appropriate surgical candidate: CABG (COR: I; LOE: A); poor surgical candidate: PCI (COR: IIa; LOE: B-NR)	SYNTAX score 0–22: CABG* (COR: I; LOE: A); SYNTAX score 23–32: CABG* (COR: I; LOE: A); SYNTAX score ≥33: CABG (COR: I; LOE: A)
Left main stenosis	NA	Low-to-intermediate complexity in remaining coronary anatomy: PCI (COR: IIb; LOE: B-R)	NA
Low ejection fraction			
One-vessel or two-vessel coronary artery disease	If complete revascularisation possible: consider PCI (COR: IIa; LOE: C)	NA	CABG (COR: I; LOE: B)
Multivessel coronary artery disease	If acceptable surgical risk: CABG (COR: I; LOE: B)	Ejection fraction <35%: CABG (COR: I; LOE: B-R); ejection fraction 35–50%: CABG (COR: IIa; LOE: B-NR)	CABG (COR: I; LOE: B)
Acute coronary syndrome			
Non-ST-elevation	Revascularisation according to same principles for stable coronary artery disease (COR: I; LOE: B)	Revascularisation by PCI or CABG (the mode of revascularisation should be based on the acuity of the patient's condition, the angiographic characteristics of the culprit lesion, and the complexity of the patient's anatomy and, when appropriate, include a Heart Team discussion; COR: I; LOE: A); failed PCI and ongoing ischaemia, haemodynamic compromise, or threatened occlusion of an artery with substantial myocardium at risk: CABG (COR: IIa; LOE: B-NR)	The revascularisation strategy should be discussed within the Heart Team as needed (COR: I; LOE: C); failed PCI or technical difficulty, persistent ischaemic attacks and haemodynamic instability refractory to medical treatment, or frequent ischemic attacks refractory to medical treatment and a large risk area (severe stenosis in left main stem or proximal LAD): CABG (COR: I; LOE: C)

ACC=American College of Cardiology. AHA=American Heart Association. BMS=bare-metal stents. B-NR=B-non-randomised. B-R=B-randomised. CABG=coronary artery bypass graft. COR=class of recommendation (I, IIa, IIb, or III). DES=drug-eluting stents. ESC/EACTS=European Society of Cardiology and European Association for Cardio-Thoracic Surgery. JCS=Japanese Circulation Society. JSCVS=Japanese Society of Cardiovascular Surgeons. LAD=left anterior descending artery. LIMA=left internal mammary artery. LOE=level of evidence (A, B , or C). PCI=percutaneous coronary intervention. SCAI=Society of Cardiovascular Angiography & Interventions. SYNTAX=Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery. *For categories with more than one revascularisation strategy recommended, we listed the one with the higher class of recommendation.

Table 2: **Summary of current practice guidelines' recommendations for coronary revascularisation**

infarction, hospitalisation for unstable angina, and cardiac health deterioration were less frequent in the revascularisation group.[91,92] Follow-up extension to 7 years showed no mortality difference between the groups (12·7% initial invasive strategy *vs* 13·4% initial medical therapy), but fewer cardiovascular deaths and more non-cardiovascular deaths in the invasive group.[93] The BARI 2D trial[94] in patients with coronary artery disease and diabetes with preserved ejection fraction also found no difference between initial revascularisation (PCI or CABG) or medical therapy alone at 5 years follow-up. By contrast, in the FAME-II trial the composite of death, myocardial infarction, or urgent revascularisation was significantly reduced in the fractional flow reserve-guided PCI group (13·9%) versus medical therapy alone (27·0%).[95]

Comprehensive meta-analyses of trials comparing revascularisation (CABG, PCI, or both) to medical therapy alone in patients with non-acute coronary artery disease and without left main disease or severely reduced left ventricular ejection fraction have found no significant difference in overall survival between strategies,[96,97] but reductions in cardiac deaths[97] and spontaneous myocardial infarction, at the consequence of more frequent procedural myocardial infarctions with revascularisation.[97]

Two trials, STICH[98,99] and REVIVED BCIS2,[100] have compared revascularisation to medical therapy alone in patients with non-acute multivessel coronary artery disease and reduced left ventricular ejection fraction (≤35%). The STITCH trial found no difference in all-cause deaths at 4·6 years, but fewer deaths with CABG after 9·8 years.[98,99] In REVIVED BCIS2, the primary endpoint of all-cause death or hospitalisation for heart failure did not differ between PCI and medical therapy.[100]

An individual patient data analysis of 2523 patients with and without severely reduced ejection fraction derived from four trials comparing CABG with medical therapy alone found significantly lower 10-year mortality with CABG (45% *vs* 52%), with the CABG survival benefit becoming significant after the fourth postoperative year.[101] Chronic total occlusion-PCI compared with medical therapy alone has been found to improve angina and physical performance, but whether it reduces hard clinical outcomes remains unestablished.[75] The available evidence on complex high-risk indicated-PCI compared with medical therapy alone is limited to a few registry studies.[76]

In summary, medical therapy should be used in all patients with coronary artery disease, with efforts focused on long-term compliance. Some patients might experience long-term reduction of cardiovascular events and anginal symptoms with revascularisation on top of medical therapy and lifestyle changes. For other patients, revascularisation might not be necessary, or the periprocedural risks might outweigh the potential long-term revascularisation benefits, and medical therapy alone could be the treatment of choice (table 2).

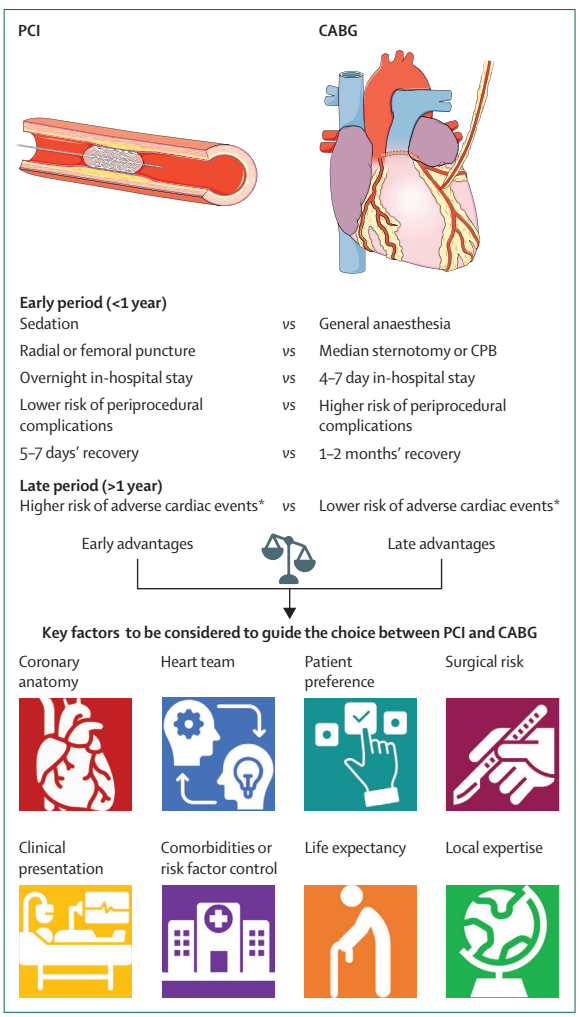

Figure 3: **Comparison of key aspects of surgical and percutaneous coronary revascularisation**
Parts of the figure were drawn with pictures from Flaticon.com (https://flaticon.com) and Servier Medical Art (https://smart.servier.com/). Servier Medical Art by Servier is licensed under a CC BY 3.0 licence. CABG=coronary artery bypass grafting. CPB=cardiopulmonary bypass. PCI=percutaneous coronary intervention. *In particular, myocardial infarction and the need for repeat revascularisation.

PCI versus CABG

PCI and CABG are mechanistically and clinically very different interventions (figure 3). PCI treats only the flow-limiting stenosis and increases flow downstream; its technical complexity depends on the lesion characteristics (location, calcification, and length).[102] Surgery, given its more distal anastomoses, restores distal flow while protecting against potential progression of proximal plaques that were not flow-limiting at the time of intervention, and its technical complexity is independent from lesion characteristics. Periprocedural deaths are very low for both interventions, but non-fatal procedural complications and rehospitalisation rates are higher, and recovery periods longer, with surgery. In the years after the procedure, however, PCI requires more frequent

reinterventions than does surgery (mostly for disease progression in untreated areas),[103] with a higher risk of acute coronary events. In clinical practice, most patients have clinical or anatomical characteristics (such as older age, diabetes, comorbidities, complex coronary anatomy, or frailty) or strong preferences that make one or the other intervention more indicated. Published comparative trials refer to patients where equipoise between PCI and CABG existed for both the treating physicians and the patient. In the early 2000s, several RCTs compared the relative effects of PCI and CABG. These trials are not representative of current practice and are mainly of historical interest. Table 3 shows the trials that inform current decision-making.

The SYNTAX trial in patients with multivessel disease or left main disease[104,105] found the composite outcome including death, myocardial infarction, stroke, or repeat revascularisation occurred significantly more frequently in the PCI group than the CABG group. No significant difference between groups was found in patients with low coronary artery disease complexity (expressed by a SYNTAX anatomical disease score <23), although the trial was underpowered for subgroup analysis on the basis of SYNTAX score strata. At 10 years, deaths between the two groups did not differ (28% for PCI *vs* 24% for CABG), but at 11·2 years, deaths were significantly higher with PCI.[106] The anatomical extent of coronary artery disease was a significant treatment effect modifier, with patients with triple-vessel, but not those with left main, disease having better survival with CABG.

The BEST trial[107] compared new-generation everolimus-eluting stents to CABG in patients with multivessel but not left main coronary artery disease and found the composite of death, myocardial infarction, and repeat revascularisation was significantly higher in the PCI group at 4·6 years, but found no difference at 11·8 years of follow-up, although spontaneous myocardial infarction and revascularisations were significantly more common with PCI than with CABG.[108]

In an individual patient data analysis of 11 PCI versus CABG trials including more than 11 000 patients, there were fewer deaths with CABG (11·2% *vs* 9·2%), but eight trials used old PCI technology (bare-metal stenting and first-generation drug-eluting stents in four trials each).[109] In the FAME-III trial,[110] despite the use of fractional flow reserve guidance and current generations stents in the PCI group, the incidence of the primary composite outcome including death, myocardial infarction, stroke, or repeat revascularisation was significantly higher in the PCI group than the CABG group (10·6% *vs* 6·9%). The EXCEL[111] and NOBLE[112] trials found seemingly different results when comparing PCI with CABG in patients with left main coronary disease, but this contradiction in results was due to differences in the studies' primary outcome definitions; myocardial infarction and re-revascularisation during follow-up were more frequent in the PCI group in both trials, while mortality was lower with CABG in the EXCEL trial, but not in the NOBLE trial. An individual patient-data analysis of four PCI versus CABG trials in patients with left main coronary disease found 5-year deaths were similar for PCI and CABG (11·2% *vs* 10·2%).[113] Spontaneous myocardial infarction was more common with PCI (6·2% *vs* 2·6%), whereas there was no difference in the overall risk of stroke (2·7% *vs* 3·1%), although in the first year after randomisation the risk of stroke was lower with PCI.[113]

Prespecified subanalyses of trials have reported overall similar improvement in patients' quality of life after PCI and CABG, although the PCI group showed faster recovery and less physical limitations in the first months and the surgery group showed better symptom relief at late follow-up.[114,115]

No RCT has directly compared PCI and CABG in patients with reduced left ventricular ejection fraction. A network meta-analysis of 23 studies involving 23 633 patients (including four small RCTs) found that PCI and medical therapy were associated with more deaths than was CABG, but treatment allocation bias might have favoured surgery.[116] The ongoing STICH3C trial (NCT05427370) will provide new information.

Overall, the evidence suggests a higher rate of periprocedural complications with CABG versus higher rates of myocardial infarction and re-revascularisation during follow-up with PCI. Current guidelines recommend CABG for patients with complex coronary artery disease, especially with diabetes or reduced ejection fraction, whereas PCI is preferred for patients with less extensive or less complex coronary artery disease and for those at high surgical risk (table 2).[66,67] All guidelines, however, specify that patient preference should be key in informing treatment decisions.

Coronary revascularisation for acute coronary syndromes

The aim of revascularisation in acute coronary syndromes is to salvage ischaemic myocardium and prevent adverse events, including short-term death, while revascularisation in chronic coronary syndromes has the scope of improving symptoms and reducing the risk of long-term cardiac events, particularly myocardial infarctions.

In patients hospitalised with ST-segment-elevation myocardial infarction, early PCI of the culprit lesion (primary PCI) reduces the rates of death, myocardial infarction, stroke, and major bleeding compared with fibrinolysis,[44] and is a class I recommendation in the current American, European, and Japanese guidelines (fibrinolytic therapy is recommended when primary PCI is not available).[66,67,117–119] In RCTs, complete revascularisation, even as a staged procedure, reduced cardiac events compared with culprit lesion-only PCI.[120–122]

In patients with non-ST-segment-elevation acute coronary syndromes, early revascularisation is recommended in patients at high risk, and PCI is often the chosen modality; however, in patients with complex coronary anatomy, CABG should be considered.[66,67,117,123]

	Participants (N [PCI; CABG])	Patient population	Sex of participants (%)	Mean age of participants (years)	Follow-up period	Primary outcome (PCI *vs* CABG)
ARTS (2001) PMID: 11297702	1205 (600; 605)	Patients with multivessel disease	Female 23·5%	61·0	1 years	Composite of death, myocardial infarction, repeat revascularisation, stroke, or transient ischaemic attack: PCI 26·2%, CABG 12·2%; log-rank p<0·001
AWESOME (2001) PMID: 11451264	454 (222; 232)	Patients with medically refractory myocardial ischaemia	Not reported	67·0	4·8 years	Death: PCI 22·0%, CABG 27·0%; p>0·46
ERACI-II (2001) PMID: 11153772	450 (225; 225)	Patients with coronary artery disease	Female 20·6%	61·95	30 days	Composite of death, Q-wave myocardial infarction, stroke, or repeat revascularisation: PCI 1·8%, CABG 11·4%; p=0·0002
ERACI-II (2005) PMID: 16098419	450 (225; 225)	Patients with coronary artery disease	Female 20·6%	61·95	5 years	Death: PCI 7·1%, CABG 11·5%; p=0·182
Stent or Surgery (2002) PMID: 12383664	988 (488; 500)	Patients with multivessel disease	Female 21·9%	61·5	2 years	Repeat revascularisation: PCI 21%, CABG 6%; HR 3·85 (95% CI 2·56 to 5·79; p<0·0001)
OCTOstent (2005) PMID: 25696506	280 (138; 142 off-pump CABG)	Patients with coronary artery disease	Female 31·5%	61·5	1 year	Composite of death, myocardial infarction, stroke, or repeat revascularisation: PCI 14·5%, CABG 8·5%; difference –6·0% (95% CI –13·5 to 1·5)
CARDia (2010) PMID: 20117456	510 (256; 254)	Patients with multivessel or complex 1-vessel coronary artery disease and diabetes	Female 25·9%	64·0	1 year	Composite of death, myocardial infarction, or stroke: PCI 13%, CABG 10·5%; HR 1·25 (95% CI 0·75 to 2·09; p=0·39)
PRECOMBAT (2011) PMID: 21463149	600 (300; 300)	Patients with left main disease	Female:23·5%	62·3	2 years	Composite of death, myocardial infarction, stroke, or ischaemia-driven TVR: PCI 12·2%, CABG 8·1%; HR 1·50 (95% CI 0·90 to 2·52; p=0·12)
PRECOMBAT (2020) PMID: 32223567	600 (300; 300)	Patients with left main disease	Female 23·5%	62·3	11·3 years	Composite of death, myocardial infarction, stroke, or ischaemia-driven TVR: PCI 29·8%, CABG 24·7%; HR 1·25 (95% CI 0·93 to 1·69)
FREEDOM (2012) PMID: 23121323	1900 (953; 947)	Patients with diabetes and multivessel disease	Female 28·7%	63·1	3·8 years	Composite of death, myocardial infarction, or stroke: PCI 26·6%, CABG 18·7%; p=0·005
FREEDOM (2019) PMID: 30428398	943 (478; 465)	Patients with diabetes and multivessel disease	Female 31·0%	63·2	7·5 years	Death: PCI 23·7%, CABG 18·7%; HR 1·32 (95% CI 0·97 to 1·78; p=0·076)
VA CARDS (2013) PMID: 23428214	198 (101/97)	Patients with diabetes and multivessel or isolated proximal LAD disease	Female 1·1%	62·5	2 years	Composite of death or myocardial infarction: PCI 31%, CABG 53%; HR 0·89 (95% CI 0·47 to 1·71)
SYNTAX (2013) PMID: 23439102	1800 (903; 897)	Patients with 3-vessel or left main disease	Female 22·4%	65·1	5 years	Composite of death, myocardial infarction, stroke, or repeat revascularisation: PCI 32·1%, CABG 28·6%; HR 1·13 (95% CI 0·83 to 1·53; p=0·43)
SYNTAXES (2019) PMID: 31488373	1689 (841; 848)	Patients with 3-vessel or left main disease	Female 21·9%	65·1	11·2 years	Death: PCI 27·0%, CABG 24·0%; HR 1·17 (95% CI 0·97 to 1·41; p=0·092)
BEST (2015) PMID: 25774645	880 (438; 442)	Patients with multivessel disease and Euroscore <8	Female 28·6%	64·6	4·6 years	Composite of death, myocardial infarction, or TVR: PCI 15·3%, CABG: 10·6%; HR 1·47 (95% CI 1·01 to 2·13; p=0·04)
BEST (2022) PMID: 36121700	880 (438; 442)	Patients with multivessel disease and Euroscore <8	Female 28·6%	64·6	11·8 years	Composite of death, myocardial infarction, or TVR: PCI 34·5%, CABG 30·3%; HR 1·18 (95% CI 0·88 to 1·56; p=0·26)
EXCEL (2019) PMID: 31562798	1905 (948; 957)	Patients with left main disease and SYNTAX score ≤32	Female 23·1%	66·0	5 years	Composite of death, myocardial infarction, or stroke: PCI 22·0%, CABG 19·2%; event rate difference 2·8% (95% CI –0·9 to 6·5; p=0·13)
NOBLE (2020) PMID: 31879028	1201 (598; 603)	Patients with left main disease	Female 22%	66·2	4·9 years	Composite of death, myocardial infarction, stroke, or repeat revascularisation: PCI 28%, CABG 19%; HR 1·58 (95% CI 1·24 to 2·01; p=0·0002)
FAME-III (2022) PMID: 34735046	1500 (757; 743)	Patients with 3-vessel disease	Female 17·7%	65·2	1 year	Composite of death, myocardial infarction, stroke, or repeat revascularisation: PCI 10·6%, CABG 6·9%; HR 1·5 (95% CI 1·1 to 2·2; p=0·35 for non-inferiority)

CABG=coronary artery bypass grafting. HR=hazard ratio. LVEF=left ventricular ejection fraction. PCI=percutaneous coronary intervention. SYNTAX=Synergy between PCI with Taxus and Cardiac Surgery. TVR=target vessel revascularisation.

Table 3: **Main outcomes of randomised trials comparing PCI and CABG**

Information on the relative effectiveness of PCI and CABG in patients with acute coronary syndromes is scarce, but in the pooled analysis of left main disease trials, clinical presentation was a significant treatment effect modifier and patients with acute coronary syndromes had lower mortality with PCI, whereas patients with chronic coronary artery disease had better outcomes with surgery.[113]

Antiplatelet therapy after PCI differs in patients with acute coronary syndromes or chronic coronary artery disease: ticagrelor or prasugrel for 3–12 months are recommended in patients with acute coronary syndromes, whereas clopidogrel for 1–6 months is recommended in patients with chronic coronary artery disease. Similarly, after CABG, aspirin alone is recommended long term for chronic coronary artery disease, whereas 12 months of DAPT is recommended for acute coronary syndromes.[66,67,117]

Coronary revascularisation in women and older adults

Women with coronary artery disease are at higher risk than men given their smaller body size, average 4-year to 10-year older patient age, more frequent comorbidities (diabetes, hypertension, heart and renal failure), more atypical symptoms leading to delayed diagnoses,[124–126] lower adherence to medications,[127] and lower socioeconomic status[128] than men.[124,125] Medical attention is on average delayed in women, recommended drugs and interventions underused, and revascularisation more often incomplete with lesser use of arterial grafts when CABG is undertaken.[124,125] Women have higher rates of adverse events, including bleeding, renal dysfunction, vascular or device complications, and early and late mortality after coronary revascularisation, even after adjustment for baseline characteristics.[124,125]

The prevalence of coronary artery disease constantly increases with age, and up to 80% of older individuals are estimated to have asymptomatic coronary artery disease.[128] Advanced age is a risk-enhancer among patients with coronary artery disease, given atypical disease presentation and delayed diagnosis, more extensive coronary artery disease compared with younger patients, more frequent frailty and comorbidity (particularly renal failure), polypharmacy and poor compliance with medical therapy with cognitive impairment, social dependency, and shorter life expectancy driving second-line care strategies.[129] The ISCHEMIA-CKD trial randomly assigned patients with advanced chronic kidney disease and moderate or severe inducible myocardial ischaemia to an initial invasive strategy or to medical therapy alone.[130] After 2·2 years, the composite primary outcome of death or myocardial infarction did not differ in the two groups, but the risks of stroke and of death or dialysis were significantly increased with revascularisation.

Treatment effects for women and older adults are derived from underpowered subgroup analyses. In most revascularisation trials, women accounted for 20–30% of the enrolled population (tables 1 and 3). On the basis of available data, the benefits of several coronary artery disease therapies seem to be extendable to women, including fibrinolysis,[82] antiplatelet regimens,[80,125] renin-angiotensin-aldosterone inhibitors,[81,125] statins,[79,124,125] β blockers[85] and angiotensin receptor–neprilysin inhibitor,[86] SGLT2-inhibitors,[87] radial arterial access,[65] primary PCI,[131] PCI in acute coronary syndromes,[132] revascularisation for ischaemic cardiomyopathy,[98] drug-eluting stents,[133] and radial arteries for CABG.[134,135]

In most revascularisation trials, patient age at baseline was approximately 65 years (tables 1 and 3). Most effects of revascularisation and medical therapies also seem applicable to older adults, provided age adjustments are made for drug doses, especially for prasugrel, fibrinolysis, certain direct oral anticoagulants, and enoxaparin.[129] History of stroke and a high-bleeding risk profile influence the choice and duration of antiplatelet therapy.[129] Although procedural complications increase exponentially with age, so do the expected benefits of treatment.[129] The SENIOR-RITA trial (NCT03052036) is comparing revascularisation (PCI or CABG) versus medical therapy alone in patients aged 75 years or older with acute non-ST elevation myocardial infarction.

Coronary revascularisation in low-income and middle-income countries

Approximately 84% (ie, 6·6 billion people) of the world's current population live in low-income or middle-income countries (LMICs).[136] Since 1990, age-standardised[137] annual mortality from cardiovascular diseases has decreased by 43% (from 283 to 160 cases per 100 000 people) in high-income countries (HICs), largely thanks to improved lifestyles, diets, medical therapy, and access to health care, but mortality has decreased by only 13% (from 381 to 332 per 100 000 people) in LMICs.[136,137] The PURE cohort study,[138] evaluating 156 424 people from the general population of 17 countries between 2003 and 2009, found substantially higher rates of cardiovascular disease and death in LMICs versus HICs, despite a lower risk factor burden in LMICs,[139] suggesting important differences across countries in terms of access to recommended medical therapies and appropriate revascularisation.

Compared with HICs, patients with coronary artery disease in LMICs are generally younger and have fewer risk factors (although the latter might be due to less efficient screening and reporting),[140] with significantly higher fatality rates related to coronary artery disease.[139,141,142] Coronary artery disease is a more frequent cause of heart failure[143] and prevention, and revascularisation procedures are substantially underused in LMICs compared with HICs.[141,142] The total number of PCI per million people is positively correlated with gross national income per capita (Kimura T, Kyoto University, Kyoto, Japan;

	Sample (n)	Leading institution	Interventions	Primary aim
CABG *vs* PCI				
PROVERB (NCT05532631)	1040	Assistance Publique–Hôpitaux de Paris, France	Intervention: CABG with total arterial revascularisation; comparator: PCI	Assess whether total arterial CABG *vs* PCI reduces MACCE at 3-year follow-up
STICH3C (NCT05427370)	754	Sunnybrook Health Sciences Centre, University of Toronto, Canada	Intervention: CABG; comparator: PCI	Assess whether CABG *vs* PCI in patients with multivessel or left main coronary artery disease and reduced LVEF reduces MACCE at 5-year follow-up
MILESTONE (NCT01311323)	1000	American Heart of Poland, Poland	Intervention: CABG; comparator: PCI	Assess whether CABG *vs* PCI in patients with multivessel or left main disease and NSTE-ACS reduces MACCE at 1-year follow-up
Coronary Artery Bypass Grafts or Percutaneous Coronary Intervention for Revascularization in Moderate- to High-Risk Patients With Ischemic Heart Disease and Reduced Left Ventricular Ejection Fraction (NCT05534698)	1550	Danish Study Group, Denmark	Intervention: CABG; comparator: PCI	Assess whether CABG *vs* PCI in high-risk patients with severe coronary artery disease reduces MACCE at 5-year follow-up
Minimally invasive surgery, hybrid revascularisation				
Hybrid Revascularization Versus Coronary Artery Bypass Grafting (NCT05504031)	1048	Copenhagen University Hospital, Denmark	Intervention: hybrid coronary revascularisation (MID-CAB using LIMA-LAD with PCI to ≥1 non-LAD lesion); comparator: CABG	Assess whether hybrid coronary revascularisation *vs* CABG reduces a composite outcome of MACCE or unplanned hospitalisation
EDGE (NCT05121610)	2864	Beijing Anzhen Hospital, China	Intervention: CABG; Comparator 1: PCI; comparator 2: hybrid coronary revascularisation	Assess whether CABG *vs* PCI *vs* hybrid coronary revascularisation in multivessel coronary disease (SYNTAX score >22) reduces MACCE at 1-year follow-up
HCR-EAST (NCT04811586)	200	Shanghai East Hospital, China	Intervention: one-stop hybrid coronary revascularisation (off-pump MID-CAB using LIMA-LAD with PCI to 1 or more non-LAD lesions); comparator: PCI	Assess whether hybrid coronary revascularisation *vs* PCI in multivessel or left main coronary artery disease reduces MACCE at 2-year follow-up
Efficacy and Safety of Minimal Invasive Coronary Surgery in Patients With Complex Coronary Artery Lesions (NCT04795193)	200	Peking University Third Hospital, China	Intervention: MICS-CABG; comparator: off-pump CABG	Assess whether MICS-CABG *vs* off-pump CABG improves physical quality of life and recovery (physical component score of SF-36) at 30-day follow-up
MIST (NCT03447938)	176	University of Ottawa Heart Institute, Canada	Intervention: MICS-CABG; comparator: CABG	Assess whether MICS-CABG *vs* CABG improves physical quality of life and recovery (physical component score of SF-36) at 30-day follow-up.
CABG—conduits				
ROMA (NCT03217006)	4300	Weill Cornell-New York Presbyterian, New York, USA	Intervention: CABG with multiple arterial grafts; comparator: CABG with single arterial graft	Assess whether multiple arterial grafting reduces postoperative MACCE in comparison with single arterial grafting
ROMA: Women (NCT04124120)	1310	Weill Cornell-New York Presbyterian, New York, USA	Intervention: CABG with multiple arterial grafts; comparator: CABG with single arterial graft	Assess whether multiple arterial grafting reduces postoperative MACCE in comparison with single arterial grafting in women
CABG—medical therapy				
TOP-CABG (NCT05380063)	2300	Fuwai Hospital, China	Intervention: de-escalated DAPT (ticagrelor 90 mg BID and 100 mg aspirin daily) for 3 months, then aspirin 100 mg daily + placebo) for 9 months; comparator: DAPT (ticagrelor 90 mg BID and 100 mg aspirin daily) for 12 months	Assess whether de-escalated DAPT *vs* DAPT for 12 months following elective CABG reduces SVG total occlusion (on cardiac CTA or coronary angiography) or bleeding events at 1-year follow-up
BEEFBURGER (NCT04788186)	200	Royal University Hospital, University of Saskatchewan, Canada	Intervention: de-prescription of β blockers (half-dose for 3 days, then quarter-dose for 3 days, then discontinuation); comparator: continued β blockers per usual clinical care	Assess whether β blockers deprescription *vs* continuation reduces MACCE, heart failure hospitalisations, cardiac arrhythmia, syncope or permanent pacemaker, or recurrent myocardial ischemia at 3-year follow-up following uncomplicated CABG in patients with LVEF ≥45% and no atrial fibrillation or flutter

(Table 4 continues on next page)

	Sample (n)	Leading institution	Interventions	Primary aim
(Continued from previous page)				
PACES (NCT04045665)	3200	Icahn School of Medicine at Mount Sinai, USA	Intervention: SAPT (aspirin or $P2Y_{12}$ inhibitor); comparator: OAC and SAPT (vitamin K antagonist [INR 2–3] or DOAC and aspirin or P2Y12 inhibitor)	Assess whether OAC plus SAPT *vs* SAPT reduces a composite of MACCE or systemic arterial or venous thromboembolism at 180 days after randomisation. Assess whether OAC plus SAPT *vs* SAPT reduces BARC type 3 or 5 bleeding at 90 days after randomisation
NEWTON-CABG (NCT03900026)	766	Unity Health Toronto, University of Toronto, Canada	Intervention: evolocumab; comparator: placebo	Assess whether evolocumab compared with placebo reduces SVG disease rate (proportion of vein grafts with significant stenosis [≥50%] or total occlusion on cardiac CTA or coronary angiography) at 2-year follow-up
TACSI (NCT03560310)	2200	Vastra Gotaland Region, Uppsala University, Sweden	Intervention: DAPT (ticagrelor 90 mg twice a day and 75–100 mg aspirin daily); comparator: aspirin 75–160 mg daily.	Assess whether DAPT *vs* SAPT reduces MACCE at 1-year follow-up after CABG in patients with acute coronary syndrome
PCI *vs* Sham				
ORBITA-2 (NCT03742050)	400	Imperial College London, UK	Intervention: PCI; comparator: sham procedure	Assess whether PCI *vs* sham procedure in patients with symptoms of stable angina without background anti-anginal therapy reduces symptoms of angina at 3-month follow-up.
DANANGINA (NCT04496648)	450	Herlev and Gentofte Hospital, Denmark	Intervention: PCI; comparator: sham procedure	Assess whether PCI *vs* sham procedure in patients with symptoms of stable angina reduces symptoms of angina or myocardial infarction at 3-month follow-up
PCI—drug-coated balloon *vs* drug-eluting stents in native coronary artery disease				
Long-term efficacy of drug-coated balloon versus drug-eluting stent in large de novo coronary lesions (NCT05101005)	400	Shanghai Songjiang Central Hospital, China	Intervention: PCI with drug-coated balloon; comparator: PCI with sirolimus-eluting sten	Assess whether PCI with drug-coated balloon compared with PCI with drug-eluting stent reduces target lesion failure
DEBATE (NCT04814212)	546	North Karelia Central Hospital, Finland	Intervention: PCI with drug-coated balloon; comparator: PCI with drug-eluting stent	Assess whether PCI with drug-coated balloon compared with PCI with drug-eluting stent reduces net clinical benefit (a composite of MACE and bleeding)
TRANSFORM II (NCT04893291)	1325	Clinica Polispecialistica San Carlo, Italy	Intervention: PCI with drug-coated balloon; comparator: PCI with everolimus-eluting stent	Assess whether PCI with drug-coated balloon compared with PCI with everolimus-eluting stent reduces target lesion failure
PCI—haemodynamic support strategies				
CHIP-BCIS3 (NCT05003817)	250	Guy's and St Thomas' NHS Foundation Trust, UK	Intervention: percutaneous temporary LVAD; comparator: standard of care	Assess whether percutaneous temporary LVAD *vs* usual care in high-risk PCI reduces a composite outcome of MACCE, periprocedural myocardial infarction, or cardiovascular hospitalisation at 1-year to 4-year follow-up
PIONEER Trial (NCT04045873)	306	Xijing Hospital, China	Intervention: VA-ECMO with IABP; comparator: IABP	Assess whether haemodynamic support combining VA-ECMO with IABP compared with IABP support alone in patients undergoing elective high-risk PCI reduces MACCE at 30-day follow-up
PCI—antithrombotic, PCSK9 inhibition and gastroprotective strategies				
STOPDAPT-3 (NCT04609111)	6000	Kyoto University, Graduate School of Medicine, Japan	Intervention: reduced dose prasugrel SAPT; comparator: DAPT (reduced dose prasugrel and aspirin)	Assess whether reduced dose prasugrel SAPT compared with DAPT reduces bleeding events and is non-inferior for cardiovascular events after PCI in acute coronary syndrome patients with high bleeding risk at 30-day follow-up
NEOMINDSET (NCT04360720)	3400	Hospital Israelita Albert Einstein, Brazil	Intervention: prasugrel or ticagrelor SAPT; comparator: DAPT (prasugrel or ticagrelor and aspirin)	Assess whether prasugrel or ticagrelor SAPT compared with DAPT reduces bleeding events and is non-inferior for MACE after PCI in patients with acute coronary syndrome at 1-year follow-up
SMART-CHOICE 3 (NCT04418479)	5000	Samsung Medical Center, Korea	Intervention: clopidogrel SAPT; comparator: aspirin SAPT	Assess whether clopidogrel SAPT compared with aspirin SAPT beyond 12 months after PCI reduces MACCE at 1-year follow-up
ETACS (NCT05457582)	1212	Nanjing First Hospital, Nanjing Medical University, China	Intervention: PCSK9 inhibitor with high intensity statin; comparator: placebo with high intensity statin	Assess whether PCSK9 inhibitor with high intensity statin compared with placebo with high intensity statin reduces MACCE at 1-year follow-up in patients with acute coronary syndrome and multiple lesions

(Table 4 continues on next page)

	Sample (n)	Leading institution	Interventions	Primary aim
(Continued from previous page)				
PROTECT-HBR (NCT04416581)	3000	Asan Medical Center, Korea	Intervention: potassium-competitive acid blocker; comparator: proton-pump inhibitor	Assess whether potassium-competitive acid blocker compared with proton-pump inhibitor in patients with cardiovascular disease receiving antiplatelet or OAC therapy who are at high gastrointestinal bleeding risk reduces gastrointestinal bleeding at 6-month follow-up
Intravascular ultrasound-guided left main PCI				
OPTMAL (NCT04072003)	800	John Radcliffe Hospital, Oxford University Hospitals, UK	Intervention: intravscular ultrasound-guided PCI; comparator: QCA-guided PCI	Assess whether intravscular ultrasound-guided PCI compared with qualitative angiography-guided PCI in patients with unprotected left main disease reduces MACCE at 2-year follow-up
Follow-up after coronary revascularisation				
ARCACHON (NCT04566497)	2664	Pitié-Salpêtrière, France	Intervention: no stress testing strategy; comparator: systematic stress testing strategy	Assess whether no stress testing strategy compared with systematic stress testing strategy is non-inferior for cardiovascular events in asymptomatic patients after coronary revascularisation
Acute myocardial infarction				
BETAMI (NCT03646357)	10 000	Oslo University Hospital, Norway	Intervention: β blockers; comparator: no β blockers	Assess whether β blockers in patients with acute myocardial infarction without heart failure or left ventricular systolic dysfunction reduces MACE at ≥2-year follow-up
DANBLOCK (NCT03778554)	3570	Bispebjerg Hospital, Denmark	Intervention: β blockers; comparator: no β blockers	Assess whether β blockers in patients with acute myocardial infarction without heart failure or left ventricular systolic dysfunction reduces MACCE at 2-year follow-up
REDUCE-SWEDEHEART (NCT03278509)	7000	Karolinska Institutet, Sweden	Intervention: β blockers; comparator: no β blockers	Assess whether β blockers in patients with acute myocardial infarction without left ventricular systolic dysfunction reduces MACE at 1-year follow-up
REBOOT (NCT03596385)	8468	Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III, Spain	Intervention: β blockers; comparator: no β blockers	Assess whether β blockers in patients with acute myocardial infarction without heart failure or left ventricular systolic dysfunction reduces MACCE at a median 2·75-year follow-up
SMART- DECISION (NCT04769362)	2540	Samsung Medical Center, Korea	Intervention: discontinuation of β blockers; comparator: continuation of β blockers	Assess whether discontinuation of β blockers after at least 1 year of β blockers compared with continuation of β blockers in patients with acute myocardial infarction without heart failure or left ventricular systolic dysfunction is non-inferior to MACE at 2-year follow-up
AβYSS (NCT03498066)	3700	Assistance Publique–Hôpitaux de Paris, France	Intervention: discontinuation of β blockers; comparator: continuation of β blockers	Assess whether discontinuation of β blockers after at least 6 months of β blockers compared with continuation of β blockers in patients with acute myocardial infarction without left ventricular systolic dysfunction is non-inferior to MACE at 2-year follow-up
SENIOR-RITA (NCT03052036)	2300	Newcastle-upon-Tyne Hospitals, UK	Intervention: coronary angiography; comparator: optimal medical therapy	Assess whether an initial invasive strategy of coronary angiography in older patients with NSTE-ACS compared with optimal medical therapy reduces death or myocardial infarction at 5-year follow-up

BARC=Bleeding Academic Consortium. CABG=coronary artery bypass grafting. CTA=computed tomography angiography. DAPT=dual antiplatelet therapy. DOAC=direct oral anticoagulant. IABP=intra-aortic balloon counterpulsation. INR=international normalised ratio. LAD=left anterior descending artery. LIMA-LAD=left internal mammary artery to left anterior descending artery grafting. LVAD=left ventricular assist device. LVEF=left ventricular ejection fraction. MACCE=major adverse cardiovascular and cerebrovascular events. MACE=major adverse cardiac events. MICS-CABG=minimally invasive cardiac surgery coronary artery bypass grafting. MID-CABG=minimally invasive direct coronary artery bypass grafting. NSTE-ACS=non ST-elevation acute coronary syndrome. OAC, oral anticoagulation. PCI=percutaneous coronary intervention. PCSK9=proprotein convertase subtilisin–kexin type 9. QCA=qualitative coronary angiography. SAPT=single antiplatelet therapy. SF-36=short form 36-item physical and mental health questionnaire. SVG=saphenous vein graft. SYNTAX=Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery. VA-ECMO=veno-arterial extracorporeal membrane oxygenation.

Table 4: **Summary of ongoing randomised trials on coronary revascularisation**

personal communication). When emergency reperfusion is recommended, patients with ST-segment elevation myocardial infarction are mainly given fibrinolytic therapy in LMICs, and primary PCI in HICs.[139,140]

Most published data on the effects of PCI, CABG, and medical therapy come from high income populations and might not apply to LMICs.[144] Many cardiovascular trials have shown important geographical differences in treatment effects between HICs and LMICs.[144,145] Although the available evidence suggests that in patients with coronary artery disease CABG is more cost-effective than PCI in the long-term,[146] this finding is based on procedural outcomes and postoperative survival that might not be applicable to some LMICs. Differences in demographics,

resources, insurance systems, and health policies between LMICs and HICs make general considerations for revascularisation choices in LMICs difficult. In general, the choice of coronary revascularisation method should be based on resource availability and local expertise. Given that the costs and technical challenges associated with procedural complications can be very high (potentially overwhelming fragile health systems[147,148]), the likelihood of procedural success should drive the choice of revascularisation method.

Future directions and gaps in knowledge

More than five decades after the introduction of CABG and four decades after the introduction of PCI into clinical practice, the procedural and long-term outcomes of the two revascularisation methods are now well characterised. Although technological improvements will continue to increase their safety and efficacy, the relative advantages and disadvantages of the two interventions will probably remain substantially unchanged (for a summary of key ongoing trials on coronary revascularisation see table 4).

A limitation of available data is that they are from prevalently young, White, male, HIC populations. The results of coronary revascularisation in women, non-White racial and ethnic groups, older adults, and LMICs require further and urgent investigation.[124]

All trials comparing medical therapy, PCI, or CABG aimed at assessing superiority or non-inferiority of one or other strategy in relation to a short list of cardiovascular outcomes (typically death, myocardial infarction, stroke, and repeat revascularisation). Advances in diagnostic techniques have enabled detection of minor non-fatal cardiovascular events, often neither associated with symptoms nor affecting quality of life. There is uncertainty on the definition of clinically relevant non-fatal events (in particular myocardial infarction and stroke) and on how to account for the competing risk of death,[149] and this uncertainty has generated confusion and disagreement in the interpretation of the available evidence. Other events that are very important for patients—such as renal, pulmonary, and neuro-psychological outcomes, as well as quality of life and the ability to work and interact socially—have been largely ignored or relegated to secondary analyses. Additionally, trials have generally used a time-to-first-event analysis, ignoring recurrent events and methods to adjust for multiplicity. At this stage of knowledge, the use of a superiority or non-inferiority approach seems outdated, as the interventions used to treat coronary artery disease clearly have very different early and late risk profiles and are complementary rather than antagonistic. The new generation of coronary revascularisation trials should provide adequately powered estimates of the results of the two techniques in heterogenous groups of patients and for a larger number of holistic outcomes, which should not be limited to the cardiovascular system or to the first event only. This information will allow accurately informed treatment decisions based on clinical status and personal expectations and goals to be made by individual patients and their treating physicians.

Finally, some of the classic concepts regarding coronary revascularisation and its role compared with medical therapy might have to be revisited. Future indications for the treatment of coronary artery disease could shift towards less invasive treatments and towards prevention rather than intervention, as generally happens with evolution in medicine.

Contributors

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