NICE National Institute for Health and Care Excellence

Medical Technologies Advisory Committee (MTAC)

Thursday 21 November 2024

GID-HTE10039 Drug-eluting coronary stents for treating coronary artery disease: Late-Stage Assessment (LSA)

This product class was selected for late stage assessment in 2023.

Clinical and economic evidence has been submitted to NICE by the companies in RFIs, and an external assessment group report has been completed by the EAG. Alongside this, a user preference report has been produced by NICE.

This pack presents the information required for the MTAC to make draft recommendations on this topic.

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Papers included in pack:

1. Front sheet
2. Final scope
3. External Assessment Report (EAR)
4. Assessment Report Overview (ARO)
5. EAR collated comments
6. User preference report
7. Register of Interests

Late-stage assessment

GID-HTE10039 Drug-eluting coronary stents for treating coronary artery disease: late-stage assessment

Final scope

1 Introduction

The topic has been identified for late-stage assessment (LSA) by NICE, in collaboration with the Department of Health and Social Care. LSA aims to assess technologies that are in established use in the NHS. Over time, technologies in use often undergo continuous or incremental innovation and adaptation. LSA will assess whether price variations between technologies are justified by the incremental differences and advancements, and which technologies represent value for money. It will support clinical practitioners, managers and commissioners in using NHS resources as effectively as possible and ensure that patient and system benefits are maximised.

The technologies identified for this assessment are drug-eluting coronary stents available in the NHS Supply Chain framework for use in the NHS. The evaluation will assess the clinical and economic benefits and user preferences of drug-eluting stents for treating coronary artery disease to justify price variation and inform procurement decisions.

Population

Around 2.3 million people in the UK have coronary artery disease (British Heart Foundation [BHF]). In coronary artery disease, the heart's blood supply gets interrupted by a build-up of fatty substances in the coronary arteries. A typical symptom of coronary artery disease is angina (chest pain that is exacerbated by exertion). A critical reduction of the blood supply to the heart may result in myocardial infarction (heart attack) or death. To restore the

blood flow, a stent may be inserted in coronary arteries during percutaneous coronary intervention (PCI).

In 2022/23, nearly 90,000 PCIs were done in in England and Wales (The National Institute for Cardiovascular Outcomes Research [NICOR] National Audit of Percutaneous Coronary Intervention [NAPCI] summary report). PCI and stents are used in both stable angina and acute coronary syndromes (ST-segment elevation myocardial infarction [STEMI], non-ST-segment elevation myocardial infarction [NSTEMI] and unstable angina). While the number of PCI procedures for the acute coronary syndromes has remained stable since 2019/20 (before COVID-19 pandemic), the number of elective procedures for stable conditions has fallen by 20% (NICOR NAPCI summary report). In 2022/23, most PCIs, around 72%, were done for acute indications (NICOR NAPCI summary report). The mean age of people having PCI was 66 years. Most, around 75%, were men (British Cardiovascular Intervention Society [BCIS] Audit).

Use of drug-coated balloons instead of stents for specific indications (such as re-narrowing of the vessel after stenting [restenosis]) and even as an alternative to stents in new lesions is increasing. However, drug-eluting stents were used in around 83% of PCI for STEMI (called primary PCI), 84% for NSTEMI and 80% of PCI for stable conditions in 2022/23 (BCIS Audit). Stents that are used are almost exclusively drug-eluting stents and bare metal stents are no longer used. There is regional variation in the choice using drug-eluting stents and drug-coated balloons. Many people find they can do more after the procedure, and their symptoms, such as chest pain and breathlessness, get better (BHF). For people having a heart attack, it can be life-saving.

Current management

In the NHS, the current management of coronary artery disease and using drug-eluting stents follows the NICE guideline on acute coronary syndromes (NG185), NICE stable angina guideline (CG126), European Society of Cardiology [ESC] guidelines for the management of acute coronary syndromes 2023 and the European Society of Cardiology [ESC] and

European Association for Cardio-Thoracic Surgery [EACTS] guidelines on myocardial revascularisation 2018.

A full list of related NICE guidance is listed in Appendix A of this document.

Coronary angiography and PCI

In STEMI, coronary reperfusion therapy should be delivered as quickly as possible. This is a medical emergency. NICE guideline on acute coronary syndromes (NG185) recommends coronary angiography and primary PCI (if indicated), as the preferred strategy over fibrinolysis (medicines to break down blood clots), if:

- the person presents within 12 hours of onset of symptoms, and
- if primary PCI can be delivered within 120 minutes of when fibrinolysis could have been given.

Primary PCI (if indicated) should also be offered to people who present within 12 hours of the onset of STEMI symptoms with cardiogenic shock. It should be considered for people who present more than 12 hours after the onset of symptoms and have cardiogenic shock, or when there is evidence of continuing myocardial ischaemia.

If fibrinolysis is done but ECG suggests this did not restore the blood flow in the blocked vessel, immediate coronary angiography with follow-on PCI should be offered.

For multivessel disease without cardiogenic shock, where appropriate, a complete revascularisation should be offered and doing this during the index hospital admission should be considered. Treating only the culprit vessel during index admission should be considered for people with multivessel disease and cardiogenic shock.

In unstable angina or NSTEMI, NICE guideline on acute coronary syndromes (NG185) recommends offering immediate coronary angiography when people are critically unwell. But most people with unstable angina or NSTEMI have an intermediate risk of adverse cardiovascular events (predicted 6-month

mortality above 3.0%, Global Registry of Acute Cardiac Events [GRACE] risk score). So for them, if there are no contraindications to angiography such as active bleeding or comorbidity, coronary angiography with follow-on PCI is considered within 72 hours of first admission. Coronary angiography with follow-on PCI should also be considered for people who are initially assessed to be at low risk of adverse cardiovascular events (predicted 6-month mortality 3.0% or less) if they subsequently have symptoms of ischaemia or this is demonstrated by ischaemia testing.

In stable angina, NICE stable angina guideline (CG126) recommends considering coronary revascularisation, by coronary artery bypass graft (CABG) or PCI, for people whose symptoms are not satisfactorily controlled with optimal medical treatment (one or two anti-anginal drugs as necessary, plus drugs for secondary prevention of cardiovascular disease). In these circumstances, PCI is usually a planned, elective procedure.

A PCI is done in a catheter lab under local anaesthesia. A guide wire is passed into the target coronary artery, most commonly through the radial artery in the wrist but sometimes through the femoral artery in the groin, under fluoroscopic image guidance. A balloon angioplasty catheter passed over the guide wire is used to dilate the coronary artery stenosis and then removed. If a stent is used, a drug-eluting stent mounted on a balloon catheter is then passed over the guide wire into the relevant segment of the artery. It is expanded by inflation of the balloon inside it. The balloon is then deflated and removed with the guide wire. The stent acts as a scaffold to hold the vessel open. Additional intracoronary imaging (such as intravascular ultrasound [IVUS] or optical coherence tomography [OCT]) is increasingly used to guide the procedure for complex lesions. This is to further optimise positioning and deployment of the stent in the target coronary artery. In 2022/23, intracoronary imaging was used in nearly 75% of PCI for left main stem lesions (level of use across hospitals varied) (NICOR NAPCI summary report).

A PCI procedure usually takes between 30 minutes and 2 hours. People are awake throughout the procedure. For elective, planned procedures, people having a stent are usually able to go home later the same day. After an

emergency procedure, the hospital stay is usually longer. PCI with stenting is generally a painless procedure. Some people temporarily experience mild chest pain when the balloon is inflated or the stent expanded. There may be some bruising and tenderness where the catheter tube was put in. People often feel tired after the procedure but most people after a non-emergency procedure find that this goes away after a few days. After a heart attack, it will take longer to recover (BHF). Getting information about the procedure and its risks, how long stents last, and how likely it is that they may need a repeat procedure is often important to people having a stent.

Drug therapy for people having PCI

People having PCI should be offered dual antiplatelet therapy and anticoagulants. The dual antiplatelet therapy includes aspirin and a thienopyridine. The thienopyridine could be prasugrel (recommended for STEMI, the dose may be reduced for people aged 75 and over), ticagrelor (recommended for NSTEMI), or clopidogrel (recommended for stable angina and people with high bleeding risk including people taking oral anticoagulants) (NICE guideline on acute coronary syndromes [NG185], ESC guidelines for the management of acute coronary syndromes 2023, ESC/EACTS guidelines on myocardial revascularisation 2018).

In acute coronary syndromes, the dual antiplatelet therapy is usually for 12 months – in high bleeding risk (including people on oral anticoagulants), this may be abbreviated to 1, 3 or 6 months (ESC guidelines for the management of acute coronary syndromes 2023). In stable angina, dual antiplatelet therapy is usually for 1 to 12 months depending on individual bleeding and ischaemic risk benefit analysis (ESC/EACTS guidelines on myocardial revascularisation 2018).

The anticoagulant offered is unfractionated heparin. A glycoprotein IIb/IIIa inhibitor may be additionally given when clot burden is high, flow is poor or as a bailout (NICE guideline on acute coronary syndromes [NG185], ESC guidelines for the management of acute coronary syndromes 2023, ESC/EACTS guidelines on myocardial revascularisation 2018).

2 Technologies

This section describes the NHS market for drug-eluting stents as well as information on their purpose and properties. This section is based on information provided to NICE by companies, commissioning and clinical experts, and information available in the public domain.

2.1 Current NHS market for the technologies

According to NHS Spend Comparison Service data, in 2021, NHS spent over £21 million on nearly 86,000 drug-eluting coronary stents in England (GIRFT Programme National Specialty Report on Cardiology).

The cost of the drug-eluting coronary stents is covered by a set of healthcare resource group (HRG) codes and the associated NHS tariffs for PCI procedures (the HRG codes are listed in Appendix B). Therefore, they are indirectly reimbursed locally, by the integrated care boards (ICBs) for all other procedures except the primary PCI for STEMI. Primary PCI is commissioned by the NHSE Specialised Commissioning. So, the Specialised Commissioning indirectly funds the drug-eluting coronary stents used for primary PCI.

Drug-eluting coronary stents are not in the Specialised Services Devices programme and so there is no central, nationwide supply route for them in the NHS. The NHS Supply Chain holds a framework contract for interventional cardiology (Lot 1 of NHS Supply Chain framework for Interventional Cardiology, Interventional Radiology and Interventional Neuroradiology, Cardiac Rhythm Management and Electrophysiology). Drug-eluting stents within the framework are available to the NHS with agreed pricing to purchase without trusts having to go out to a full tender on the products. In 2023, around 65% of the drug-eluting stents spend within NHS went through the NHS Supply Chain. The current framework contract is valid until 26 February 2027 (considering all extension options). NHS trusts or groups of trusts joined for procurement purposes, either independently or supported by NHS Supply Chain or by external contract management organisations, may negotiate further contracts with stent suppliers. These contracts may include pricing based on for example the expected market share within the trust (centralising

suppliers) or bundling of stents with different types of PCI devices or larger capital equipment. These contracts typically include 2 to 3 drug-eluting stents that can be used across various types of lesions. Some room, for example 10% of the contract, may be left for more specialised stents. Interventional cardiologists are often involved in the purchasing decisions.

2.2 Description of the technologies

The technologies included in this evaluation are limited to drug-eluting coronary stents expected to be available on the NHS Supply Chain framework for at least the next 12 months. Table 1 lists these 29 stents. Drug-eluting stents with a bioresorbable scaffold (fully-bioabsorbable stent) on the framework are excluded from this evaluation because current guidance is that they should be used only in the context of research (NICE guidance on bioresorbable stent implantation [IPG732]) and are not commissioned for routine use.

Each drug-eluting stent has an instruction for use (IFU) document that includes the indications for which the device can be used. The indications for use vary and may or may not specify subpopulations or lesion types that are included in the indication for use. They often specify the sizes of vessels (diameter or length or both) the stent can be used for. Because of their specific subpopulation or lesion type indications or certain design features, in some hospitals they are purchased for or used in mainly those specific cases.

The following list of technologies included in this evaluation is not exhaustive. Other technologies may be available to the NHS currently or in the future.

Table 1 Drug-eluting stents in the NHS Supply Chain framework

Manufacturer	Technology	Scaffold material	Polymer type	Drug
Abbott Medical	XIENCE PRO 48	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE PRO S	Cobalt chromium	Durable	Everolimus
Abbott Medical	Skypoint	Cobalt chromium	Durable	Everolimus

Abbott Medical	XIENCE Skypoint 48	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE Skypoint LV	Cobalt chromium	Durable	Everolimus
B. Braun Medical	Coroflex ISAR NEO	Cobalt chromium	Polymer-free	Sirolimus
Biosensors International	BioFreedom	Stainless steel	Polymer-free	Biolimus A9
Biosensors International	BioMatrix Alpha	Cobalt chromium	Biodegradable	Biolimus A9
Biosensors International	BioFreedom Ultra	Cobalt chromium	Polymer-free	Biolimus A9
Biotronik	Orsiro Mission	Cobalt chromium	Biodegradable	Sirolimus
Biotronik	Synsiro Pro	Cobalt chromium	Biodegradable	Sirolimus
Boston Scientific	Promus ELITE	Platinum chromium	Durable	Everolimus
Boston Scientific	Synergy MEGATRON	Platinum chromium	Biodegradable	Everolimus
Boston Scientific	Synergy XD	Platinum chromium	Biodegradable	Everolimus
Cardionovum	XLIMUS	Cobalt chromium	Biodegradable	Sirolimus
IHT	ihtDEStiny BD	Cobalt chromium	Biodegradable	Sirolimus
iVascular	Angiolite	Cobalt chromium	Durable	Sirolimus
Medtronic	Onyx Frontier	Cobalt chromium, platinum-iridium core	Durable	Zotarolimus
Meril	BioMime	Cobalt chromium	Biodegradable	Sirolimus
Meril	BioMime Branch	Cobalt chromium	Biodegradable	Sirolimus
Meril	BioMime Morph	Cobalt chromium	Biodegradable	Sirolimus
Meril	EverMine 50	Cobalt chromium	Biodegradable	Everolimus
Microport	Firehawk	Cobalt chromium	Biodegradable	Sirolimus
Microport	Firehawk Liberty	Cobalt chromium	Biodegradable	Sirolimus
QualiMed	MAGMA	Stainless steel	Biodegradable	Sirolimus
Sahajanand Medical Technologies	Supraflex	Cobalt chromium	Biodegradable	Sirolimus
Sahajanand Medical Technologies	Supraflex Cruz	Cobalt chromium	Biodegradable	Sirolimus

Terumo	Ultimaster Nagomi	Cobalt chromium	Biodegradable	Sirolimus
Terumo	Ultimaster Tansei	Cobalt chromium	Biodegradable	Sirolimus

2.3 Technology features

Basic technology features

The features of a drug-eluting stent make the stent an implantable scaffold to open up the artery, while minimising the risk of the artery re-narrowing. Drug-eluting stents are made from metal such as stainless steel, platinum-chromium or cobalt-chromium (Table 1). They have a coating of a drug, usually a type of antiproliferative drug. The drug varies between the stents (Table 1). The drug prevents scar tissue growing between the gaps in the stent and the artery from re-narrowing.

Additional features, adaptions, and potential innovations

In some stents, with the aim of controlling the release of the drug, the drug is applied on a polymer (Table 1). To try to reduce potential inflammatory reaction and optimise healing, the polymer coating and drug release may be over the entire surface of the stent (conformal) or on the surface in contact with the vessel wall (abluminal). Durable polymers may have characteristics that aim to encourage faster healing. For this same aim, some stents are polymer-free (these may have a substance like probucol as an excipient or vehicle for the antiproliferative drug). Some polymers are absorbable and disappear after all the drug has been released. The drug dose and the release or elution time vary between the stents. Some stents may be indicated with reduced 1-month dual antiplatelet therapy in specific populations, such as people with high bleeding risk.

The mechanical properties of the stent scaffold or matrix such as the thickness of the stent struts and the strut design or architecture may differ. These may affect, for example, the radial strength (dependent on number of crowns), longitudinal compressibility, elastic recoil (change in the stent outer diameter from the expanded stent on the delivery system under inflation

pressure to the stents relaxed diameter after deflating the balloon), foreshortening (change in stent length from its crimped state upon deployment, fracture resistance, side branch access (open vs closed cell design), cell size, overexpansion capability, crossing profile or flexibility and deliverability. The properties of the delivery system that is part of the stent (removed after insertion) may also affect how easy it is to get to the target vessel and lesion. The mechanical properties of the stent may affect how well the stent can be seen under fluoroscopy. In some stents, there may be features that aim to increase the visibility to help improve the accuracy of positioning the stent. The stent may be available for a wide range of diameters and lengths or across a narrower range (size matrix).

Some stents may have a wide range of indications and evidence of performance in specific populations, such as people with more arterial calcification (more common with age), people with diabetes, people with left main stem lesions, people with STEMI or people with high risk of bleeding.

Some features may affect how well the stent is suited for use in certain populations or for treating certain types of lesions. Some features may sometimes be the difference between being able to do a procedure or not.

3 Decision problem

Population	People having PCI (including primary PCI) and for whom drug-eluting stent is indicated for treating coronary artery disease (including stable angina, STEMI, unstable angina or NSTEMI) Where data permits, the following subgroups may be considered: • Women • Ethnicity (important subgroups are discussed in section 3.1) • People with left main stem lesions • People with bifurcation lesions • People with high bleeding risk • People with diabetes
Interventions	Drug-eluting coronary stents: • XIENCE PRO 48 • XIENCE PRO S • Skypoint

	• XIENCE Skypoint 48 • Xience Skypoint LV • Coroflex ISAR NEO • BioFreedom • BioMatrix Alpha • BioFreedom Ultra • Orsiro Mission • Synsiro Pro • Promus ELITE • Synergy MEGATRON • Synergy XD • XLIMUS • ihtDEStiny BD • Angiolite • Onyx Frontier • BioMime • BioMime Branch • BioMime Morph • EverMine 50 • Firehawk • Firehawk Liberty • MAGMA • Supraflex • Supraflex Cruz • Ultimaster Nagomi • Ultimaster Tansei
Comparator(s)	A drug-eluting stent or stents or a type or types of drug-eluting stent that is considered the current standard of care in the NHS (for example the drug-eluting stent is widely being used as the comparator in non-inferiority trials on drug-eluting stents). The comparator may differ between subgroups.
Healthcare setting	Secondary care, tertiary care
Outcomes	Outcome measures for consideration may include but are not limited to: Intermediate outcomes: • Accurate stent positioning (related to visibility under fluoroscopy) • Ability to deliver the stent • Acute procedural success • Procedure and fluoroscopy time • Amount of contrast used Patient reported outcomes:

	• Health-related quality of life • Symptom relief (for example angina relief) Costs and resource use: • Cost of technologies • Cost of staff training • Cost of further diagnostic tests (for example pressure wire and IVUS or OCT guided PCI) • Cost of treatment (including costs of any adverse events, retreatment and for example lesion modifying therapy such as rotational and orbital atherectomy or intravascular lithotripsy) Clinical outcomes: • Intervention related adverse events • Major Adverse Cardiac Events (MACE) • Bleeding • Target lesion or vessel failure • Acute and chronic stent failure • Target lesion and target vessel revascularisation • Restenosis • Stent thrombosis • Myocardial infarction • Patient orientated cardiovascular events (POCE, a composite of ischemic and bleeding events, see Academic Research Consortium for definition) • All-cause mortality • Cardiac mortality Outcomes and criteria that users consider important when making decisions on which technology to use will be based on the principles of multi-criteria decision analysis if considered appropriate for the assessment.
Economic analysis	A health economic model will be developed, where possible, comprising a cost-comparison or cost utility analysis. Costs will be considered from an NHS and Personal Social Services perspective. Sensitivity and scenario analysis should be done to address the relative effect of parameter or structural uncertainty on results. The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared.
Existing UK registries	• A registry that is potentially relevant and may help inform this assessment is the National Institute for Cardiovascular Outcomes Research (NICOR) collects data and produces analysis to enable hospitals and healthcare improvement

	bodies to monitor and improve the quality of care and outcomes of cardiovascular patients. • BCIS collects and analyses annual survey data from PCI centres in the UK. • Registry data may not capture all the population or lesion characteristics that are important for consideration of clinical effectiveness, these may be more fully recorded in trial data. • Some drug-eluting coronary stent manufacturers may have large registries or cohorts in the UK. These would include only the manufacturer's stents.
Other considerations	• Key evidence on the included technologies may be on their previous versions (not included in the scope if they are no longer available through the NHS Supply Chain framework), this evidence should be considered where clinical equivalence between versions is claimed. • Where no evidence is available on a technology comparing it to another drug-eluting stent, key evidence that includes another comparator could be considered.

3.1 Potential equality issues or considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Prevalence rates of coronary artery disease are higher in men and older people (aged over 65 years). But women are underdiagnosed, may have different symptoms to men, and are less likely to receive heart treatments such as PCI (National Heart, Lung and Blood Institute). Some underlying risk factors for coronary artery disease are more common in some ethnic groups, such as people with type 2 diabetes in South Asian, African Caribbean or Black Asian groups and hypertension in Black African or Black Caribbean groups. Clinical experts noted that they see people from Black African, Black Caribbean and East Asian groups with symptoms of coronary artery disease that tend to be 5 to 10 years younger than people from European groups. Prevalence and mortality of coronary artery disease is higher in people from lower socioeconomic groups. People with advanced coronary artery disease may be covered under disability legislation in the Equality Act 2010 if symptoms substantially affect the ability to carry out day to day activities for

longer than 12 months. Many may have a co-existing long-term condition. PCI outcomes for women may be worse because they tend to have smaller vessels. Women are also underrepresented in clinical trials of stents.

PCI outcomes for women may be worse because they tend to have smaller vessels. Women are also underrepresented in clinical trials of stents. Some underlying risk factors for coronary artery disease are more common in some ethnic groups, such as people with type 2 diabetes in South Asian, African Caribbean or Black Asian groups and hypertension in Black African or Black Caribbean groups. PCI outcomes for people from South East Asian groups may be worse because they tend to have smaller vessels. Stent failure in people with type 2 diabetes is more common. There is also limited data to support decision making in different ethnic groups. For example, in the NICOR data, only 70% of the people have their ethnicity recorded (BCIS Audit). Stent failure in people with type 2 diabetes is more common. Prevalence and mortality of coronary artery disease is higher in people from lower socioeconomic groups.

Dual antiplatelet therapy is needed for some time following a coronary stent implantation. People with mental health problems, or learning difficulties, or people who do not speak English (if translation is not available) may find it difficult to take the medication regularly or to understand how to follow the therapy.

Safety and effectiveness of stents has not been established for pregnant women, women nursing or for children. But clinical experts noted that PCI involving drug-eluting stents or drug-coated balloons would likely still be used in pregnant or breastfeeding women following myocardial infarction.

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Appendix A Related NICE Guidance

- Acute coronary syndromes (2020). NICE guideline 185.
- Acute coronary syndromes in adults (2014, last updated 2020) NICE quality standard 68.
- Bioresorbable stent implantation to treat coronary artery disease (2022). NICE interventional procedures guidance 732.
- Coronary artery stents (2003, last updated 2020). NICE technology appraisal guidance 71.
- Drug-eluting stents for the treatment of coronary artery disease (2008, last updated 2020). NICE technology appraisal guidance 152.
- Stable angina (2011, last updated 2016). NICE clinical guideline 126.
- Stable angina (2012, last updated 2017) NICE quality standard 21.

Appendix B HRG codes for procedures that may include drug-eluting stents

HRG code	HRG name
EY40A	Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 12+
EY40B	Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11
EY40C	Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7
EY40D	Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3
EY41A	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 12+
EY41B	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11
EY41C	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7
EY41D	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3
EY42A	Complex Cardiac Catheterisation with CC Score 7+
EY42B	Complex Cardiac Catheterisation with CC Score 4-6
EY42C	Complex Cardiac Catheterisation with CC Score 2-3
EY42D	Complex Cardiac Catheterisation with CC Score 0-1
EY43A	Standard Cardiac Catheterisation with CC Score 13+
EY43B	Standard Cardiac Catheterisation with CC Score 10-12
EY43C	Standard Cardiac Catheterisation with CC Score 7-9
EY43D	Standard Cardiac Catheterisation with CC Score 4-6
EY43E	Standard Cardiac Catheterisation with CC Score 2-3
EY43F	Standard Cardiac Catheterisation with CC Score 0-1
EY44A	Very Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 12+
EY44B	Very Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11
EY44C	Very Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7
EY44D	Very Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3

Appendix C Abbreviations

CABG	Coronary artery bypass graft
ESC	European Society of Cardiology
EACTS	European Association for Cardio-Thoracic Surgery
ICB	Integrated care board
LSA	Late-stage assessment
NAPCI	National Audit of Percutaneous Coronary Intervention
NICOR	The National Institute for Cardiovascular Outcomes Research
NSTEMI	non-ST-segment elevation myocardial infarction
PCI	Percutaneous coronary intervention
STEMI	ST-segment elevation myocardial infarction

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Late-stage assessment
GID-HTE10039 Drug-eluting coronary stents for treating coronary artery disease
External assessment report

Produced by: CEDAR (Centre for Healthcare Evaluation, Device Assessment, and Research)

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Contains confidential information: Yes.

Number of attached appendices: 11.

Purpose of the late-stage assessment report

The late-stage assessment report is part of the late-stage guidance process described in the late-stage assessment interim process and methods statement. The purpose of the external assessment report is to review and synthesise the relevant evidence in order to evaluate the value of the different outcomes and features of technologies under assessment. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Committee when it is making decisions about the late-stage assessment.

Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

None.

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Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Confidential information

Summary table of all confidential information and its source in report

Brief description	AIC/CIC	Page numbers	Source
Cost of technologies	CIC	101	NHS Supply Chain
Details of cost for no further event	CIC	102	[redacted]
Resource use and cost parameters	CIC	102-104	[redacted]
Results of EAG economic modelling	CIC	14, 107-125	EAG analysis.
Company training information	CIC	227	Companies.

Post-MTAC Corrections

Summary table of corrections made in the report

The discounting rate was corrected in the cost calculation for all economic analyses. Changes to the results are very minor, and apply to all devices, with no change in the overall economic findings. There is very slight reduction in total costs, leading to a small increase in NMB for all devices.

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Contents

Abbreviations

Term	Definition
ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
BES	Bioliums eluting stent
BMS	Bare metal stent
BP-DES	Bioabsorbable polymer-drug eluting stent
BPP	Bayesian posterior probability
BSI	British Standards Institution
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CD-TLR	Clinically driven-target lesion revascularisation
CEAC	Cost-effectiveness acceptability curve
CI	Confidence interval
CoCr	Cobalt chromium
CrI	Credible interval
CV	Cardiovascular
DAPT	Dual antiplatelet therapy
DCB	Drug-coated balloon
DES	Drug eluting stent
DHSC	Department of Health and Social Care
DIC	Deviance Information Criterion
DM	Diabetes mellitus
DOCE	Device-oriented composite endpoint
DP-DES	Durable polymer-drug eluting stent
EAG	External Assessment Group
EES	Everolimus-eluting stent
FE	Fixed effects
GI	Gastrointestinal
HBR	High bleeding risk
HealthTech	Health Technologies Evaluation Programme
HES	Hospital Episodes Statistics
HN	Half normal
HR	Hazard ratio
HRG	Healthcare Resource Group
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
ID-TLR	Ischaemia driven-target lesion revascularisation
IHD	Ischaemic heart disease
IQR	Interquartile range
ISR	In-stent restenosis
ITT	Intention-to-treat
IVUS	Intravascular ultrasound
JBI	Joanna Briggs Institute

Term	Definition
LAD	Left anterior descending
LLL	Late lumen loss
LM	Left main
LSA	Late stage assessment
LY	Life year
MACE	Major adverse coronary event
MAUDE	Manufacturer and User Facility Device Experience
MCDA	Multi-criteria decision analysis
MHRA	Medicines & Healthcare products Regulatory Agency
MI	Myocardial infarction
NAPCI	National Audit of Percutaneous Coronary Interventions
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
NICE HTE	NICE health technology evaluation
NICE QS	NICE quality standard
NICOR	National Institute for Cardiovascular Outcomes Research
NMA	Network meta-analysis
NMB	Net monetary benefit
NSTEMI	Non-ST elevated myocardial infarction
OAC	Oral anticoagulant
ONS	Office for National Statistics
OR	Odds ratio
PCI	Percutaneous coronary intervention
PCL	Polycaprolactone
pD	Effective number of parameters
PDLLA	Poly(d,l-lactide)
PES	Percutaneous endovascular stent
PLA	Polylactic acid
PLCL	Poly(l-lactide-co-ε-caprolactone)
PLGA	Poly(lactic-co-glycolic acid)
PLLA	Poly(l-lactide) acid
POCE	Patient-oriented composite endpoint
PP-DES	Permanent polymer-drug eluting stent
PSA	Probabilistic sensitivity analysis
PSSRU	Personal Social Services Research Unit
PVDF-HFP	Poly(vinylidene fluoride-co-hexafluoropropylene)
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
RE	Random effects
RFI	Request for information (from NICE to companies)
SCAAR	Swedish Coronary Angiography and Angioplasty Registry
SD	Standard deviation

Term	Definition
SE	Standard error
SES	Sirolimus-eluting stent
SRMA	Systematic review and meta-analysis
ST	Stent thrombosis
STEMI	ST-elevated myocardial infarction
TA	Technology Appraisal
TLF	Target lesion failure
TLR	Target lesion revascularisation
TVMI	Target vessel-related myocardial infarction
TVF	Target vessel failure
TVR	Target vessel revascularisation
UK	United Kingdom
UME	Unrelated mean effects
USA	United States of America
WDHR	Western Denmark Heart Registry
WTP	Willingness to pay
ZES	Zotarolimus-eluting stent

Executive summary

Background

Drug-eluting stents (DES) are implantable devices used in the treatment of coronary artery disease. Further information regarding the use of DES and the clinical context can be found in the published scope. The aim of this late stage assessment (LSA) is to assess whether there is evidence of superior clinical effectiveness for any of the devices that justify a higher cost. A total of 29 devices, from 14 companies, were included in this assessment.

Clinical evidence

The EAG identified 22 key RCTs which compared two devices (or accepted clinically equivalent predecessors) with each other. Of the 22 key RCTs, 21 were designed as non-inferiority studies and so were only able to demonstrate that one device was not worse than a comparator device. The one superiority trial identified (BIOSTEMI) demonstrated significantly lower rates of TLF in the Orsiro Mission group in comparison to Xience, in a population of people with STEMI. (Section 5.1)

The EAG identified a large volume of non-RCT evidence, which has been summarised in Section 6 and Appendix H. The EAG accepts that results of these studies may provide evidence of clinical efficacy and safety for a large proportion of devices in the scope of this assessment. However, the EAG has prioritised comparative evidence from RCTs as the best available evidence to demonstrate whether there were any differences in clinical outcomes that may justify price variation.

The most frequently used comparator in the non-inferiority RCTs was Xience, with non-inferiority being demonstrated against Xience for the following devices: Orsiro Mission, Ultimaster Nagomi/Tansei, Synergy XD, Promus Elite, Supraflex and Firehawk. However, the EAG notes that the outcome(s) used in each study to assess non-inferiority varied. Additionally, the populations included in each study differed, with some trials including an 'all-comer' population and others focusing on a more specific subset of participants. The table below summarises the comparisons made in the 22

RCTs identified, and indicates the 14 RCTs which were deemed eligible for the network meta-analysis (NMA) as per criteria described by the EAG in Section 4.3.

Trial name	Intervention (n)	Comparator (n)	Included in NMA
ANGIOLITE	Angiolite (110)	Xience Xpedition (Pro 48) (113)	N
BIODEGRADE	Orsiro (1175)	BioMatrix (1166)	Y
BIOFLOW-DAPT	Orsiro Mission (969)	Resolute Onyx (979)	N
BIOFLOW IV	Orsiro (385)	Xience Prime/Xpedition (Pro 48) (190)	Y
BIOFLOW V	Orsiro (884)	Xience (450)	Y
BIOFREEDOM QCA	BioFreedom Ultra (97)	BioFreedom (97)	N
BIONYX	Resolute Onyx (1243)	Orsiro (1245)	Y
BIO-RESORT	Synergy (1172)	Orsiro (1169)	Y
BIOSCIENCE	Orsiro (1063)	Xience Prime (1056)	Y
BIOSTEMI	Orsiro (649)	Xience Prime/Xpedition (Pro 48) (651)	N
CASTLE	Orsiro (722)	Xience Sierra (Pro S)/Xpedition (Pro 48) (718)	Y
CENTURY II	Ultimaster (562)	Xience (557)	Y
EVOLVE II	Synergy (846)	Promus Element Plus (838)	Y
IDEAL-LM	Synergy (410)	Xience (408)	N
MERIT-V	BioMime (170)	Xience V (86)	N
ONYX ONE	Resolute Onyx (1003)	BioFreedom (993)	N
PLATINUM	Promus (768)	Xience V (762)	Y
SORT OUT IX	BioFreedom (1572)	Orsiro (1579)	Y
SORT OUT VIII	BioMatrix (1379)	Synergy (1385)	Y
TALENT	Supraflex (720)	Xience family (715)	Y
TARGET	Firehawk (823)	Xience family (830)	Y
XLIMIT	Xlimus (117)	Synergy (60)	N

No RCTs drawing comparisons against another device in scope were identified for the following devices: BioMime Branch, BioMime Morph, Coroflex ISAR NEO, EverMine 50, Firehawk Liberty, ihtDEStiny BD, MAGMA and Synergy Megatron.

The EAG acknowledge that there are some subgroups which could potentially benefit from the choice of a particular stent over another, due to factors other than the outcomes considered in the EAG analysis (such as lesion characteristics and presence of co-morbidities). Overall, there was a lack of evidence to suggest differences in outcomes between any stents in the subgroups identified in the scope. Where RCTs reported results for particular subgroups, or where subgroup analyses were reported, no significant differences in between-stent clinical outcomes were observed within that subgroup (Section 5.1.2).

Network meta-analyses within a Bayesian framework using the random-effect model were performed to estimate the relative treatment effect of Target lesion revascularisation (TLR) and Target vessel-related myocardial infarction (TVMI) between devices at the first-year and long-term follow-up. A total of 14 trials comparing 10 devices contributed to the NMA.

Given the data sparsity issue in the NMA, the uncertainty with relative treatment effects prevented any firm conclusions being made, particularly for the long-term estimates.

The NMA at the first year demonstrated some evidence that Promus Elite may have meaningful effect in reducing TVMI rate at 1 year compared to Xience [hazard ratio (HR) 0.59, 95% credible interval (CrI) 0.31 to 1.03]. It was found that BioFreedom had a higher rate of TLR compared to Xience (HR 3.70, 95%CrI 1.83 to 6.80). Compared to Xience, there was some weak evidence suggesting Firehawk and Supraflex may result in lower TLR rate, whereas Synergy and Orsiro may reduce TVMI rate, although these estimates were very uncertain with wide 95%CrI.

Given the very sparse data in the long-term NMA, the estimates were very unreliable and uncertain, as indicated by the much wider 95%CrI. At long-term

follow-up, the NMA results using 12 trials with long-term data found no evidence for meaningful differences in TLR and TVMI rates between devices. Although there was some weak evidence suggesting a beneficial effect on TLR or TVMI for three devices, the estimates were uncertain due to the wide 95%CrI. These devices are Resolute Onyx and Promus Element with respect to TLR, and Supraflex with respect to TVMI.

The relative effects are sensitive to the prior heterogeneity distribution used, despite overall conclusions on the relative treatment effect in the first year remaining the same. The sensitivity analysis, achieved by fitting a higher prior heterogeneity distribution, indicated more uncertainty in terms of treatment effect and high posterior between-study heterogeneity in longer term NMA than the first-year NMA. This is because the data is sparse and from very few studies, particularly in the longer-term analysis, resulting in wider 95% CrIs. Therefore, the relative effect was too uncertain to establish any conclusions. Detailed NMA findings are presented in Section 5.2.4.

Economic evidence

The EAG conceptualised and developed an economic model based on clinical expert opinion, published literature and the NMA output. A Markov model was developed with a yearly cycle length including seven health states: no further event, TLR, TVMI, TVMI-repeat revascularisation, post-revascularisation, post-MI and death. The base case analysis in a 1-year time horizon was undertaken using the NHS and Personal Social Services perspective. Based on company information regarding clinical equivalence for some devices, a total of 18 devices were compared in the economic analysis. Total costs, total QALYs and net monetary benefit (NMB) of each device were estimated. Probabilistic sensitivity analysis (PSA) and a series of scenario analyses were conducted to explore the impact of uncertainty on the cost-effectiveness findings. Additionally, a cost-comparison analysis was performed, where all 29 devices in the scope were assumed to be clinically equivalent.

The economic analyses (both deterministic and probabilistic) demonstrate that there is a lot of uncertainty surrounding the NMB findings, which outweigh the small NMB difference between devices.

In the base case, there is a small NMB variation of [redacted] among 18 devices, which is [redacted] of the highest NMB. Across all 18 devices, the NMB ranged from [redacted] to [redacted], costs between [redacted] to [redacted] (difference [redacted]) and QALYs between [redacted] to [redacted] (difference [redacted]). Although Promus Elite appeared to yield the highest NMB at the WTP of £20,000 per QALY, there was only a modest NMB difference between Promus Elite and Firehawk (Table 24). In addition, the probabilistic sensitivity analysis results suggested there was substantial uncertainty in the NMB findings, driven by the uncertainty in relative treatment effect between devices. It was noted that the NMB 95%CrI for all devices were overlapping, as illustrated in Figure 8. From the cost-effectiveness acceptability curves (Figure 9), no device had more than 30% probability of achieving the highest NMB. It showed that at WTP £20,000, Firehawk and Promus Elite had the highest chance of achieving the highest NMB ([redacted]). The position of Firehawk and Promus Elite were very close in both base case and probabilistic sensitivity analyses.

In all scenarios in Section 10.3, the NMB differences between devices at the predefined WTP were small (2.2-3.1% of the highest NMB), however Promus Elite appeared to yield the highest NMB. The scenario analysis showed that the results were sensitive to long-term treatment effect, however the substantial uncertainty with the long-term NMA estimates has serious implications on the result validity. Significant change in the NMB profile for most devices was noted when the time horizon increased to 5 years using relative effects derived from a higher prior heterogeneity. When the maximum stent price was used for all devices, Firehawk was estimated to generate the highest NMB due to its low cost.

When all devices were assumed to clinically equivalent in the cost-comparison analysis, Firehawk appeared to yield the highest NMB (Table 27). This indicates that Firehawk may offer the cheapest option when only the cost per device is considered.

Key points for decision makers

The EAG believes the following issues should be considered by decision makers:

- Data sparsity in NMA.
- Insufficient prior information to enable NMA model to estimate relative treatment effect reliably.
- NMA using long-term data is highly dependent on the prior distribution, meaning the reliability of the estimate is a concern.
- Some relevant clinical outcomes are not captured in the NMA, thus limiting a comprehensive assessment of treatment effect between devices.
- Economic findings are impacted by the underlying issues in the NMA, and this key source of uncertainty prevented a firm conclusion from being drawn.
- Trial data used to inform baseline event risk and relative treatment effect limits the generalisability of the findings to an NHS setting.
- The economic model structure and model inputs are guided by the trial data. The nature and quality of trial reporting would impact the accuracy of the model results.
- Evidence used in this assessment is based on previous generations of devices, and not those in scope, which introduces further uncertainty when interpreting results.

Summary

There is evidence of non-inferiority for some devices against another device in scope, most commonly Xience.

The NMA found that any evidence at 1 year was weak and had considerable uncertainty. However, there was some indication that Promus Elite may reduce TVMI rates at 1 year and BioFreedom has increased TLR rates at 1 year, when both are compared to Xience. In long-term follow-up, there is no meaningful difference found between devices in terms of TLR and TVMI.

A robust economic finding could not be established, given the uncertainty with respect to treatment effect. This has therefore prevented firm conclusions on cost-effectiveness being drawn. From the base case economic analysis, there were small NMB differences between devices. However, these differences are outweighed by the uncertainty surrounding the NMB findings.

The EAG recognises that a full systematic review of published literature may help to improve robustness of the NMA and subsequent economic analyses,

as data from comparing devices in scope with devices out of scope may strengthen any indirect comparisons drawn in the NMA. However, the key issues of heterogeneity of the study populations and a lack of long-term follow-up data, and the consequent inconsistency and sparsity of data, would likely still be present and this would impact on the validity of comparisons being drawn. Additionally, participants included in RCTs may not reflect the patient population in the NHS. Real-world data could hypothetically provide additional information including treatment effect and long-term outcomes to compliment data from published RCTs. However, there are significant issues with real-world data that is currently collected for percutaneous coronary intervention (PCI) procedures in the NHS, such as incomplete data recording and confounding, that preclude its use for this purpose. This is discussed in detail in Section 4.1.1.

1 Decision problem

The decision problem is described in the scope, published 09 July 2024.

During the assessment process, information was received from the manufacturer of the Supraflex and Supraflex Cruz devices (Sahajanand Medical Technologies) which indicated that the Supraflex device was no longer available for purchase on NHS Supply Chain. As a result, the Supraflex device was removed as an intervention in scope, and the Supraflex Cruz Nevo device was added as an intervention in scope.

2 Technologies

Drug-eluting stents are implantable devices used in the treatment of coronary artery disease. Further information regarding the use of drug-eluting stents can be found in the published scope and the clinical context is described in Section 3 of this report.

Drug-eluting stents (DES) have three key components: a metal scaffold, a polymer (or alternative) coating and an antiproliferative drug. In DES with a polymer coating, the purpose of the polymer is to control release of the drug. These polymers can either be durable or absorbable, where they degrade after all of the drug has been released. Some DES are ‘polymer-free’ where an alternative substance such as probucol may act as a vehicle for the drug.

A range of diameters and lengths of drug-eluting stents are available to meet the varying anatomical requirements present in individuals undergoing percutaneous coronary intervention (PCI). Lesion and vessel characteristics are key factors in stent choice, in addition to other clinical considerations such as the presence of co-morbidities. Clinical experts highlighted the importance of considering dual-anti platelet therapy (DAPT) requirements associated with stents, which is given to prevent clotting, as individuals with a high-bleeding risk would benefit from shorter DAPT regimens. Operator preference and the range of devices available to the operator at the time of the procedure also influence choice. Clinical experts have indicated that the majority of stents in

scope would be considered appropriate for any given individual considered suitable for PCI.

Multiple generations of drug-eluting stents have been developed over time, with changes to key features and components aiming to improve device-related outcomes and deliverability for the user. Only 2nd and 3rd generation drug-eluting stents are considered in this LSA. Table 1 describes the claimed benefits of potentially innovative features commonly identified in modern drug-eluting stents. The EAG will aim to assess clinical evidence for each DES device as a whole and will not seek to demonstrate whether each potentially innovative feature works as intended.

Table 1: Potentially innovative features of drug-eluting stents.

Potentially innovative feature	Intended benefit
Polymer-free	Avoids polymer-related complications such as the triggering an inflammatory response which may lead to impaired tissue healing (endothelialisation).
Faster drug elution time	Promotes faster endothelialisation which can shorten the required length of post-PCI DAPT.
Thinner struts (under 100μm)	Reduces inflammation and accelerates endothelialisation by providing less contact surface area between the stent and the artery walls.
Bioabsorbable polymer	Decreased risk of polymer-related complications such as vascular inflammation and reduced risk of stent thrombosis.
Alternative metal alloy to stainless steel in stent scaffold e.g. cobalt chromium, platinum chromium	Increased biocompatibility reduces risk of immunological response. Improved strength and elasticity facilitates thinner struts and higher radial strength. Higher density of the metals increase radiopacity.

Abbreviations: *DAPT: dual antiplatelet therapy; PCI: percutaneous coronary intervention.*

This Late Stage Assessment (LSA) includes 29 drug-eluting stents from 14 companies. A brief overview of the technologies can be found in Table 2, including information on scaffold material, the drug eluted, polymer coatings, strut thickness and drug elution time. This information was sourced from company information submitted to NICE, company websites or through direct contact between NICE and the company. Information regarding innovative features of each of the 29 devices is summarised in Appendix A.

Eight of the 14 companies, covering 18 of the 29 technologies, provided responses to NICE's requests for information. All of these 18 technologies have valid CE certification as a Class III implantable device. The EAG made no attempt to verify the certification status of the technologies where this information was not submitted to NICE. As all technologies included in the LSA process are established technologies that are available through NHS Supply Chain and have been approved for use in the NHS, the EAG has assumed that all devices in scope have the relevant regulatory certifications.

Table 2: Description of devices included in the assessment.

Company	Device name	Scaffold material	Drug	Polymer coating	Strut thickness	Drug elution time
Abbott Medical	Xience Pro 48	Cobalt chromium	Everolimus	Durable (PVDF-HFP)	81 µm	Approximately 80% within 30 days and 100% after 120 days.
	Xience Pro S	Cobalt chromium	Everolimus	Durable (PVDF-HFP)		
	Skypoint	Cobalt chromium	Everolimus	Durable (PVDF-HFP)		
	Xience Skypoint 48	Cobalt chromium	Everolimus	Durable (PVDF-HFP)		
	Xience Skypoint LV	Cobalt chromium	Everolimus	Durable (PVDF-HFP)		
B.Braun Medical	Coroflex ISAR Neo	Cobalt chromium	Sirolimus	Polymer-free (probucol mimics polymer)	55/65 µm	100% at 90 days.
Biosensors International	BioFreedom Ultra	Cobalt chromium	Biolimus A9	Polymer-free	84–88 µm	98% at 28 days.
	BioFreedom	Stainless steel	Biolimus A9	Polymer-free	120 µm	Approx. 50 hours.
	BioMatrix Alpha	Cobalt chromium	Biolimus A9	Bioabsorbable (PLLA)	84-88 µm	98% at 28 days.
Biotronik	Orsiro Mission	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA)	60-80 µm	Majority within 3 months, near-complete elution achieved within 1 year.
	Synsiro Pro	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA)	60-80 µm	Majority within 3 months, near-complete elution achieved within 1 year.
Boston Scientific	Promus Elite	Platinum chromium	Everolimus	Durable (PVDF-HFP)	81-86 µm	100% at 120 days.
	Synergy XD	Platinum chromium	Everolimus	Bioabsorbable (PLGA)	74 µm	Approximately 3 months.
	Synergy MEGATRON	Platinum chromium	Everolimus	Bioabsorbable (PLGA)	89 µm	Approximately 3 months.

Company	Device name	Scaffold material	Drug	Polymer coating	Strut thickness	Drug elution time
Cardionovum	Xlimus	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA)	71 µm	70% at 30 days.
IHT	ihtDEStiny BD	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA)	73 µm	Unknown.
iVascular	Angiolite	Cobalt chromium	Sirolimus	Durable (fluoroacrylate)	Unknown	>75% a 1 month, 100% at 2 months.
Medtronic	Onyx Frontier	Cobalt chromium, platinum-iridium core	Zotarolimus	Durable (BioLinx™)	81 µm	180 days.
Meril	BioMime Branch	Cobalt chromium	Sirolimus	Bioabsorbable	65 µm	Unknown.
	BioMime Morph	Cobalt chromium	Sirolimus	Bioabsorbable	65 µm	
	BioMime	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA & PLGA)	65 µm	
	EverMine 50	Cobalt chromium	Everolimus	Bioabsorbable (PLLA & PLGA)	50 µm	
Microport	Firehawk Liberty	Cobalt chromium	Sirolimus	Bioabsorbable PLA	86-96.5 µm	Unknown.
	Firehawk	Cobalt chromium	Sirolimus	Bioabsorbable PLA	86-96.5 µm	
QualiMed	MAGMA	Stainless steel	Sirolimus	Bioabsorbable (50% polylactide, 50% polyglycolid)	Unknown	Less than 3 months.
Sahajanand Medical Technologies	Supraflex Cruz	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA, PLCL, PVP)	60µm	80% at 1 month, 100% at 3 months.
	Supraflex Cruz Nevo	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA, PLCL, PVP)	60µm	Unknown.
Terumo	Ultimaster Tansei	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA polymer & PCL)	80 µm	3-4 months.
	Ultimaster Nagomi	Cobalt chromium	Sirolimus	Bioabsorbable (PLLA & PCL)	80 µm	3-4 months.

***Abbreviations**: PCL: Polycaprolactone; PLGA: Poly(lactic-co-glycolic acid); PLCL: Poly(l-lactide-co-ε-caprolactone); PLLA: Polylactic acid; PVDF-HFP: Poly(vinylidene fluoride-co-hexafluoropropylene); PVP: Polyvinylpyrrolidone*

3 Clinical context

3.1 *Clinical pathways*

Drug-eluting stents (DES) implanted via percutaneous coronary intervention (PCI) are used to treat people with stable angina and acute coronary syndromes (including ST-elevated myocardial infarction (STEMI), non-ST elevated myocardial infarction (NSTEMI) and unstable angina). Figures 1-3 below briefly outline where PCI and DES fit into the care pathways for each condition, as outlined by relevant NICE guidelines (CG126 and NG185). These diagrams are simplified to highlight the role of PCI and DES for the purposes of understanding the clinical context of this assessment, full details of recommendations for managing these conditions, including contraindications and alternative approaches, can be found in the NICE guidelines.

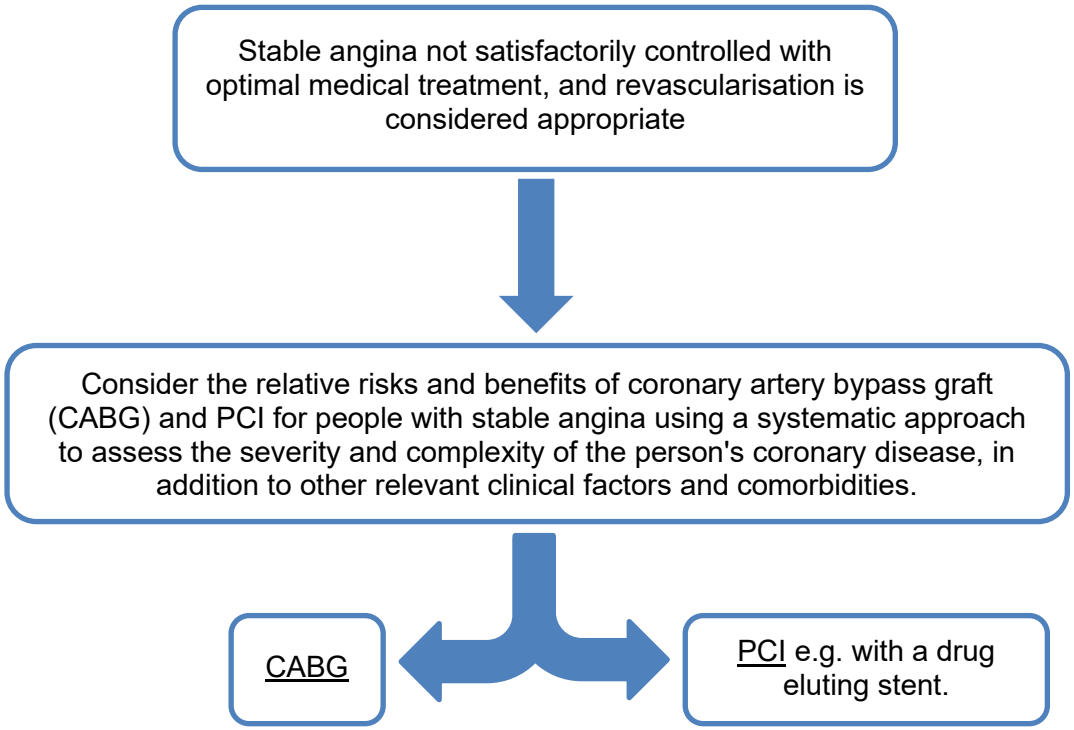


Figure 1: Simplified stable angina clinical pathway.

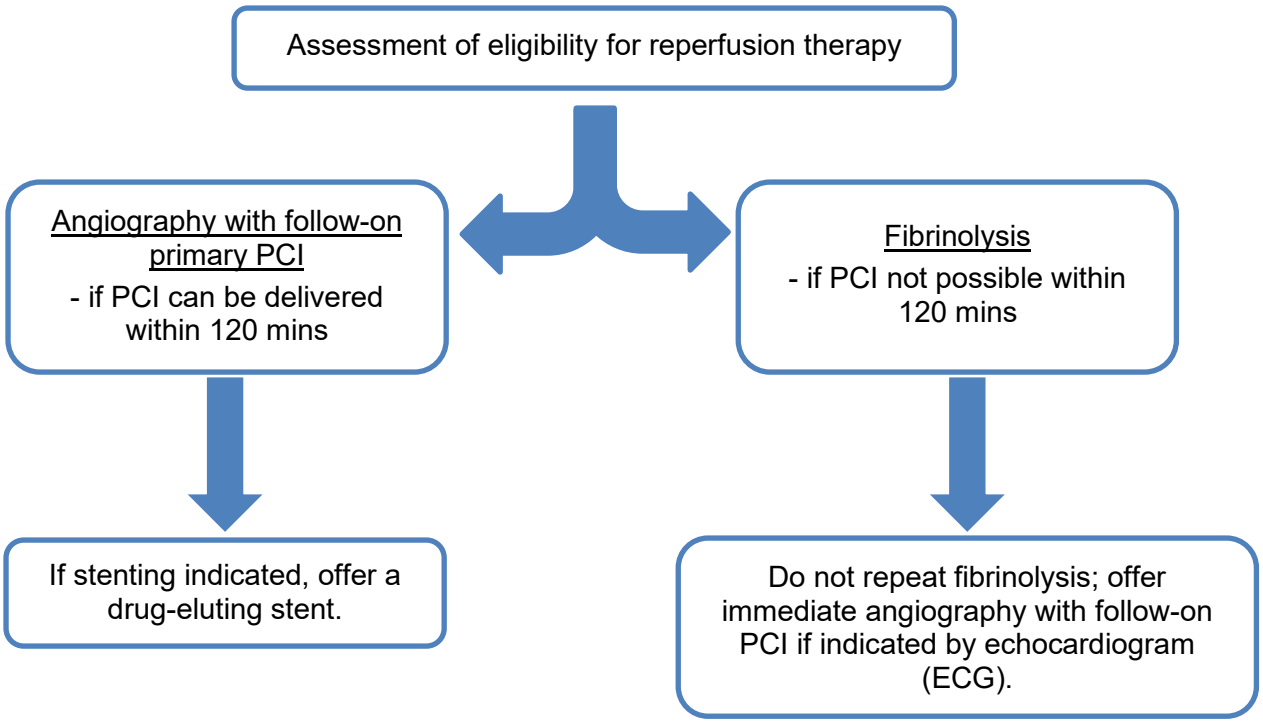


Figure 2: Simplified STEMI clinical pathway.

NSTEMI/unstable angina

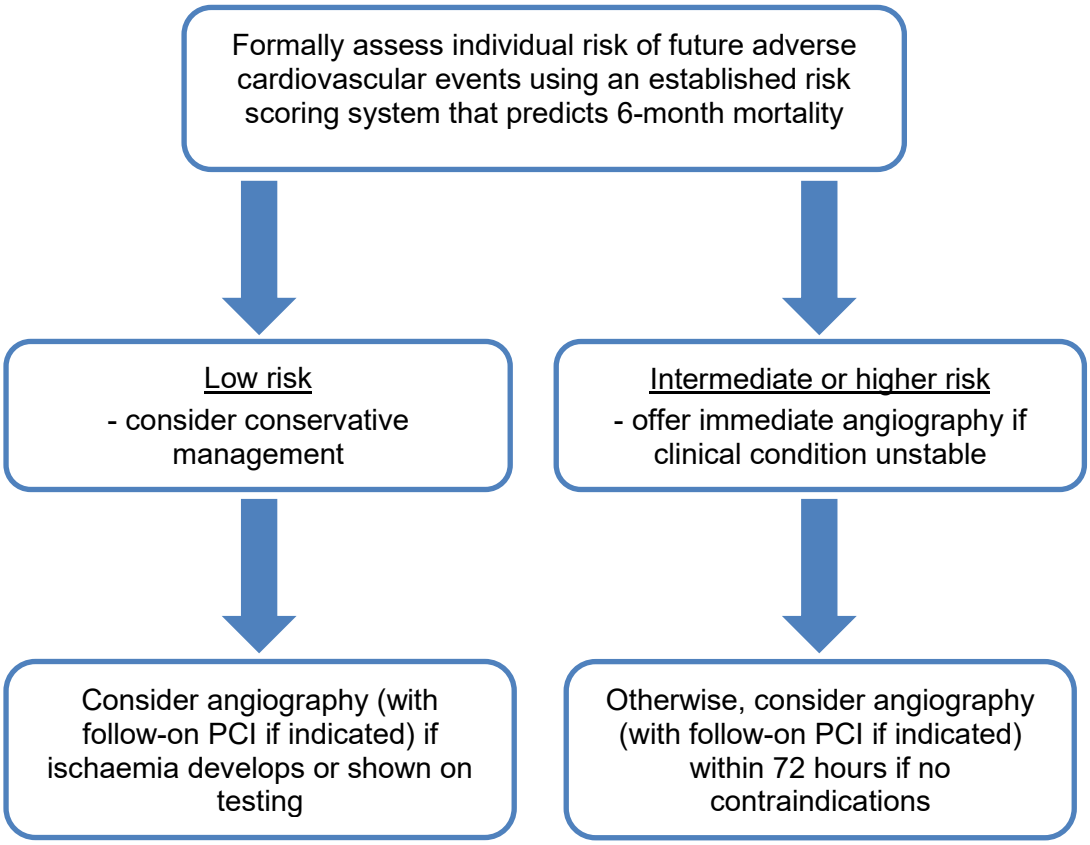


Figure 3: Simplified NSTEMI/unstable angina clinical pathway.

3.2 *PCI clinical outcomes*

There are numerous outcomes which are measured to determine clinical success of PCI in clinical trials and in practice, including patient-oriented composite end points, device-oriented composite end points, safety end points and effectiveness endpoints. A detailed description of these endpoints and their recommended definitions can be found in the Academic Research Consortium-2 Consensus Document.

The EAG sought guidance from clinical experts on which clinical outcomes should be the focus of this assessment, where the purpose is to identify differences in clinical efficacy between drug-eluting stent devices. Clinical experts advised that clinical endpoints (or 'clinically meaningful' endpoints) should be prioritised (e.g. mortality, myocardial infarction (MI), target lesion revascularisation (TLR) and stent thrombosis (ST)) over short-term outcomes measured via angiography such as late lumen loss, minimal luminal diameter and neointimal healing. This influenced the pragmatic study selection criteria used by the EAG, which is described in Section 4.1.3.

3.3 *Equality issues*

Equality issues and considerations for this LSA are described in the equality impact assessment published alongside the scope.

No additional equality issues have been identified during the assessment.

4 Clinical evidence evaluation methods

4.1 *Clinical and technological evidence selection*

The EAG aimed to identify evidence that demonstrated clinical effectiveness of the devices in the scope of this assessment. The overarching aim of this LSA is to demonstrate whether there is evidence of superior clinical effectiveness for any of the devices that justify a higher cost. Clinical evidence was therefore prioritised based on its suitability for providing appropriate inputs for the economic model developed for this LSA.

The EAG explored using registry data as real-world evidence to inform this assessment, alongside the searching and selection of relevant published literature.

4.1.1 Real-world evidence and registry data

The EAG considered the use of data from the National Audit of Percutaneous Coronary Interventions (NAPCI), hosted by the National Institute for Cardiovascular Outcomes Research (NICOR) for the purposes of providing real-world evidence for this assessment. The proposed approach for using this data in this assessment is further described in the published EAG protocol.

NICOR NAPCI data is published annually and contains information about all PCI procedures undertaken in NHS hospitals in the UK, in addition to a selection of private hospitals. The audit does not collect data beyond the point of hospital discharge.

The EAG and NICE met with representatives from NICOR, including the clinical lead, to discuss the practicalities and usefulness of audit data in answering the decision problem of this LSA. Additionally, the EAG explored the possibility of accessing NICOR data that had been linked with Hospital Episodes Statistics (HES) and Office for National Statistics (ONS) data, to allow for outcomes beyond hospital discharge,

including mortality, to be analysed. Clinical experts were also consulted on the usage of NICOR data for this assessment during the scoping workshop.

The EAG recognises the value of registry data in decision-making, particularly audit data from the UK, as it is reflective of the 'real-world' data and provides insight into the usage of technologies in the NHS. However, a number of limitations of using the NICOR data were identified by the EAG following the scoping phase, including:

- Presence of confounding in registry data factors e.g. disease severity or lesion complexity are not consistently recorded, making it difficult to attribute outcomes captured directly to stent choice.
- A limited number of the technologies in scope being recorded in NICOR database.
- Where multiple stents are implanted in one individual, not all stents used are recorded in the database and outcomes cannot be attributed to individual stents.
- Length of follow-up limited by the time the technology has been available in the NHS.
- Long-term/mortality outcomes sourced from HES/ONS cannot reasonably be attributed to stent choice.

A decision was made in conjunction with NICE to not pursue using NICOR registry data for the purposes of this LSA, due the aforementioned limitations.

4.1.2 Assessment of clinical equivalence

The EAG noted the existence of predecessors of several devices in the scope of this assessment. The EAG attempted to clarify whether evidence for previous generations of devices could be used to support the use of current generations of devices in scope, particularly where evidence for current generations was not available. Some companies provided statements of clinical equivalence between devices in their RFIs. Where clinical equivalence or generalisability of evidence

between device generations was not clearly stated, the EAG sought further clarification from companies via NICE. This information is summarised in Table 3.

Table 3: Summary of device generations and clinical equivalence.

Company	Device name	Launch date	Relationship to previous generations and technical differences, as described in information submitted by company to NICE or established via additional correspondence with companies.	EAG comment on clinical equivalence or acceptance of evidence for predecessor devices.
Abbott Medical	**Xience Pro 48 (Xpedition)**	2012	**Earlier generations**: Xience V, Xience Prime. Reference also made to Xience Alpine which sits between Xience Pro 48 (Xpedition) and Xience Pro S (Sierra) in terms of launch dates, but is not included in the scope of this assessment. All key components remain the same across Xience family: cobalt chromium scaffold, everolimus drug, and durable PVDF-HFP polymer. Instructions for use for the Pro 48, Pro S and Skypoint devices claim that performance of these devices can be predicted to be similar to the performance of Xience V and Xience Prime.	The EAG accepts that evidence for Xience V and Xience Prime is generalisable to all Xience devices in the scope of this assessment.
	Xience Pro S (Sierra)	2017		
	Xience Skypoint	2021		
	Xience Skypoint 48			
	Xience Skypoint LV			
B.Braun Medical	**Coroflex ISAR Neo**	2016	**Earlier generations**: Coroflex ISAR. In comparison to Coroflex ISAR, Coroflex ISAR Neo has a slightly modified stent architecture which enhances radiopacity and increases radial stability. All key components remain the same between the two generations: cobalt chromium scaffold, sirolimus drug, and polymer-free. The company have stated that evidence for Coroflex ISAR can be used to support the use of Coroflex ISAR Neo.	The EAG accepts that evidence for Coroflex ISAR is generalisable to Coroflex ISAR Neo.
Biosensors International	**BioFreedom**	2013	**Earlier generations**: BioFreedom is a precursor to BioFreedom Ultra. BioFreedom has a stainless steel scaffold while BioFreedom Ultra has a cobalt chromium scaffold. Both technologies have the Biolimus A9™ drug. The company have stated that clinical evidence for BioFreedom can be used to support the use of BioFreedom Ultra.	The EAG accepts that evidence for BioFreedom is generalisable to BioFreedom Ultra.
	BioFreedom Ultra	2010		
	BioMatrix Alpha	2016	**Earlier generations**: BioMatrix Flex/NeoFlex. BioMatrix Flex/NeoFlex have a stainless steel scaffold while BioMatrix Alpha has a cobalt chromium scaffold. All technologies have the Biolimus A9™ drug.	The EAG accepts that evidence for BioMatrix Flex/NeoFlex is generalisable to BioMatrix Alpha.

Company	Device name	Launch date	Relationship to previous generations and technical differences, as described in information submitted by company to NICE or established via additional correspondence with companies.	EAG comment on clinical equivalence or acceptance of evidence for predecessor devices.
			The company have stated that evidence for BioMatrix Flex/NeoFlex can be used to support the use of BioMatrix Alpha.	
Biotronik	**Orsiro Mission**	2020	**Earlier generations**: Orsiro. Compared to Orsiro, Orsiro Mission incorporates an updated delivery system to further improve deliverability. The company have stated that data for the previous generation (Orsiro) is applicable to Orsiro Mission, and this has been confirmed by the responsible notified body, BSI. Further correspondence between NICE and the company clarified that there is no clinical or technical difference between Synsiro Pro and Orsiro Mission, and that evidence identified for one device is applicable to both devices.	The EAG accepts that evidence for Orsiro is generalisable to both Orsiro Mission and Synsiro Pro.
	Synsiro Pro	2021		
Boston Scientific	**Promus Elite**	2018	**Earlier generations**: Promus Element, Promus Element Plus, Promus Premier, Promus Premier Select. The company stated that demonstrated equivalence means that previously collected clinical data for the Promus Element/Premier/Premier Select can be leveraged to support the safety and performance of Promus Elite.	The EAG accepts that evidence for Promus Element/Premier/Premier Select is generalisable to Promus Elite.
	Synergy XD	2019	**Earlier generations**: Synergy. The company stated that clinical equivalence between Synergy and Synergy XD has been demonstrated, and differences do not impact on safety and performance.	The EAG accepts that evidence for Synergy is generalisable to Synergy XD.
	Synergy Megatron	2023	**Earlier generations**: as above (Synergy). The company stated that Synergy Megatron is an extension to the Synergy family of technologies, sharing the same scaffold, drug and polymer components (platinum chromium, everolimus and biodegradable PLGA). However, due to the	The EAG will assess Synergy XD and Synergy Megatron as standalone devices.

Company	Device name	Launch date	Relationship to previous generations and technical differences, as described in information submitted by company to NICE or established via additional correspondence with companies.	EAG comment on clinical equivalence or acceptance of evidence for predecessor devices.
			specific lesion type Synergy Megatron is designed for (large proximal vessels), it cannot reasonably be stated that clinical outcomes are generalisable between the two.	
Cardionovum	**XLIMUS**	Unknown. Evidence suggests ~2014.	**Earlier generations:** Unknown, no RFI received from company. The EAG have not identified any obvious precursors in the literature.	N/A.
IHT	**ihtDEStiny BD**	Unknown. Evidence suggests ~2021.	**Earlier generations:** Unknown, no RFI received from company. The EAG have not identified any obvious precursors in the literature.	N/A.
iVascular	**Angiolite**	2014 (2024 in the UK)	**Earlier generations**: None. The company confirmed that Angiolite is the first and only generation of this technology.	N/A.
Medtronic	**Onyx Frontier**	2022	**Earlier generations**: Endeavor Resolute, Resolute Integrity, Resolute Onyx. The company have stated that from a clinical evaluation and indications for use perspective, Onyx Frontier is considered the same as Resolute Onyx as these products use an identical stent. Resolute Onyx is a newer generation of Resolute Integrity and Endeavor Resolute, but the company stated that evidence is no longer used for these devices to support the clinical efficacy and safety of Onyx Frontier, due to the availability of evidence for the Resolute Onyx device.	The EAG accepts that evidence for Resolute Onyx is generalisable to Onyx Frontier. Evidence for generations prior to Resolute Onyx will not be considered unless there is no evidence available for Resolute Onyx or Onyx Frontier.
Meril	**BioMime**	Unknown. Evidence suggests ~2011.	**Earlier generations:** Unknown, no RFI received from company. The EAG have not identified any obvious precursors in the literature.	The EAG will consider these to be standalone devices, as the relationship between devices has not been confirmed.
	BioMime Branch	Unknown. Website suggests technology is modified	**Earlier generations:** Unknown, no RFI received from company. The EAG believe BioMime Branch to be a modified iteration of BioMime.	

Company	Device name	Launch date	Relationship to previous generations and technical differences, as described in information submitted by company to NICE or established via additional correspondence with companies.	EAG comment on clinical equivalence or acceptance of evidence for predecessor devices.
		iteration of BioMime.	The company website states that BioMime Branch uses the same platform as BioMime and refers to evidence for BioMime as applicable to BioMime Branch.	
	BioMime Morph	Unknown. Website suggests technology is modified iteration of BioMime.	**Earlier generations:** Unknown, no RFI received from company. The EAG believe BioMime Morph to be a modified iteration of BioMime. BioMime Morph appears to have the same components as BioMime and BioMime Branch. However, there is no explicit statement on the company website stating that evidence for BioMime is applicable to BioMime Morph.	
	EverMine 50	Unknown. Company website suggests ~2016.	**Earlier generations:** Unknown, no RFI received from company. EverMine 50 elutes a different drug (everolimus) to other technologies in scope from the same company (sirolimus). The EAG therefore does not believe that EverMine 50 is related to the BioMime family of technologies, and evidence for the BioMime technology will not be considered applicable to the EverMine 50 technology.	
Microport	**Firehawk**	Unknown. Evidence suggests ~2013.	**Earlier generations:** Unknown, no RFI received from company. The EAG believe Firehawk Liberty to be a newer generation of Firehawk. The company website described Firehawk Liberty as 'the next generation' of Firehawk, and all key components of Firehawk are the same as Firehawk Liberty (scaffold, drug and polymer).	The EAG will consider these to be standalone devices, as the relationship between devices has not been confirmed.
	Firehawk Liberty	Unknown.		
QualiMed	**MAGMA**	Unknown.	**Earlier generations:** Unknown, no RFI received from company. The EAG have not identified any literature relating to this device, or any potential precursors.	N/A.
	Supraflex Cruz	Unknown.		

Company	Device name	Launch date	Relationship to previous generations and technical differences, as described in information submitted by company to NICE or established via additional correspondence with companies.	EAG comment on clinical equivalence or acceptance of evidence for predecessor devices.
Sahajanand Medical Technologies	**Supraflex Cruz Nevo**	Unknown.	**Earlier generations:** Supraflex and Supraflex Cruz are previous generations of the Supraflex Cruz Nevo device. No RFI was received from this company, but the company did provide clarification to state that data for Supraflex can be used to support the use of Supraflex Cruz and Supraflex Cruz Nevo.	The EAG accept that evidence for Supraflex is generalisable to Supraflex Cruz and Supraflex Nevo.
Terumo	**Ultimaster Tansei**	2018	**Earlier generations:** Ultimaster. Ultimaster is an earlier generation to both Ultimaster Tansei and Ultimaster Nagomi. The company RFI and correspondence between NICE and the company indicates that there are only minor technological differences between these generations, and that evidence for Ultimaster can be used to support the use of Ultimaster Tansei and Ultimaster Nagomi.	The EAG accept that evidence for Ultimaster is generalisable to both Ultimaster Nagomi and Ultimaster Tansei.
	Ultimaster Nagomi	2023		

Abbreviations: *BSI: British Standards Institution; EAG: External Assessment Group; N/A: Not Applicable; NICE: National Institute of Health and Care Excellence; PLGA: Poly(lactic-co-glycolic acid); RFI: Request For Information.*

4.1.3 Published evidence search strategies and study selection

The EAG conducted targeted literature searches to identify relevant clinical evidence. A search of bibliographic and clinical trial databases identified 1220 records. Additionally, 148 records were identified from company websites and a further 329 records were included in company RFIs. In total, 1697 records were identified. Details of the EAG searches are provided in Appendix B.

The 1368 records independently identified from bibliographic databases and company websites included both published evidence and records of ongoing trials. These 1368 records were sifted at title/abstract (where applicable) by one reviewer, with a random 20% of excluded records checked by a second reviewer. Records selected for screening at full-text were screened by one reviewer, with all excluded records being checked by a second reviewer. Records of conference proceedings/abstracts and ongoing trials were separated from the full-text publications at the full-text stage of screening, of which there were 130 and 197 respectively. The additional 329 records identified from company RFIs were screened by a single reviewer at both title/abstract and full-text stage.

Records were screened at full-text stage against the published scope and in accordance with the inclusion and exclusion criteria outlined in the EAG protocol. Due to the volume of evidence identified, the EAG then made pragmatic decisions for prioritising studies to be included in this assessment, in accordance with the NICE LSA interim process and methods statement, by setting criteria outlined and justified in Table 4.

A list of studies which were included at full-text stage and then excluded at the pragmatic screening stage is available in a supplementary file (S1).

Where multiple publications associated with the same study were identified, the most recent publication with the longest follow-up period was selected for inclusion. When a relevant RCT comparing two devices in scope was identified, the EAG searched for the most recent associated publication to ensure inclusion of the longest follow-up data available.

Table 4: EAG criteria for study inclusion.

Study type	Criteria for inclusion
RCTs (also applies to primary studies of any SRMA/NMAs identified).	• Both intervention and comparator devices in scope (or accepted predecessor)[α] • Designed and powered to assess clinically meaningful endpoints at a minimum follow-up period of 1 year[β] (underpowered studies accepted where no better quality evidence is available) • Full-text publication available[γ] • English language[γ]
Non-randomised/observational comparative studies.	• Both intervention and comparator devices in scope (or accepted predecessor)[α] • Assessed clinically meaningful endpoints at a minimum follow-up of 1 year[β] • Full-text publication available[γ] • English language[γ]
Prospective and retrospective single-arm studies and registry studies.	• Intervention device in scope (or accepted predecessor)[α] • Assessed clinically meaningful endpoints at a minimum follow-up of 1 year[β] • Full-text publication available[γ] • English language[γ]
Key: **α**: based on the scope and information relating to clinical equivalence of devices. **β**: based on guidance from clinical experts who indicated that clinically meaningful endpoints should be prioritised during this assessment (e.g. mortality, myocardial infarction (MI), target lesion revascularisation (TLR) and stent thrombosis (ST)) over outcomes measured via angiographic follow-up such as late lumen loss, minimal luminal diameter and neointimal healing. **γ**: based on volume and availability of evidence.	

Abbreviations: *NMA: network meta-analysis; SRMA: systematic review and meta-analysis.*

Overall, the following clinical evidence was identified as relevant to the decision problem:

- 22 key RCTs
- 15 non-randomised/observational comparative studies
- 34 prospective single-arm studies
- 20 retrospective single-arm studies

Additionally, 10 RCTs comparing DAPT regimens using a stent in scope were identified.

17 studies were identified as indirectly relevant to the topic. These studies are summarised in Appendix C, with reasons for their exclusion from the main assessment. One of these studies was a network meta-analysis (NMA) that is discussed briefly alongside the results of the EAG NMA in Section 5.2.4.

Seven studies were identified from information submitted by the companies that were deemed relevant to the economic evaluation only and are discussed in Section 7.2.

Conference proceedings/abstracts and ongoing trial records identified as relevant to the topic at the title/abstract screening stage were also screened against set criteria, which were defined after assessing the availability of evidence from full-text publications. No conference proceedings/abstracts met these criteria. There were four ongoing trial records identified as relevant, which are tabulated in Appendix D, alongside the criteria used for screening.

4.2 *Quality appraisal of clinical studies*

Key RCTs feeding into the planned network meta-analysis were evaluated in accordance with the NICE health technology evaluations manual. Critical appraisal of each study was carried out by using the Joanna Briggs Institute (JBI) critical appraisal tools and checked by a second reviewer. A summary of these appraisals can be found in Section 5.2.3. Comments on quality of other RCTs are included narratively alongside the results reported in Section 5.1.1.

The quality of non-randomised comparative studies, RCTs comparing DAPT regimens and non-comparative studies was not assessed; these studies did not feed into the network meta-analysis and subsequent economic modelling, and are therefore not considered to be key studies.

4.3 *Evidence synthesis*

The EAG considered network meta-analysis (NMA) to synthesise evidence from RCTs. This allows the comparison of multiple interventions by combining direct and indirect evidence across a network of studies. Direct evidence is obtained from head-to-head intervention comparison in RCTs, while in the absence of direct evidence, indirect evidence is estimated using RCTs comparing interventions through a common comparator. A valid NMA relies on the assumption of transitivity, where covariates that act as effect modifiers across trials must be similar. When the assumption of transitivity is satisfied, this indicates randomisation in each trial is preserved, thus allowing interventions within the network to be compared in a single analysis.

Study selection

To be included in the NMA, studies must be RCTs with at least one year follow-up comparing two or more stents within the scope. Trials that were powered for short-term angiographic outcomes (e.g., in-stent late lumen loss) and trials which included only high-risk participants (e.g. high-bleeding risk, STEMI, left main lesions only) were excluded. This is because these groups are associated with poorer clinical outcomes in comparison to the general population, and this would introduce possible bias in the indirect comparisons drawn in the NMA.

Data extraction

Relevant data were extracted using a standardised data extraction form by one reviewer, and cross-checked by another reviewer independently. Data extracted include study design (interventions, study duration and setting), study participants (country, study population and number of participants), baseline characteristics (age, comorbidities and lesion characteristics) and outcomes (number of events at each time point). Authors were contacted for additional information on the study results when necessary.

Clinical characteristics of the study population were compared to ensure similar and balanced distribution of potential effect modifiers across trials. Any sources of clinical heterogeneity were identified and, the impact of clinical heterogeneity on the results is discussed in Section 5.2.4

Measure of treatment effect

Binomial data were considered in the NMA and the relative treatment effect, hazard ratio (HR) and 95% credible interval (CrI) were estimated by fitting the Poisson rate model with complimentary log-log (cloglog) link (Dias et al, 2014a). This takes account of the different length of follow-up time in each trial. The risk of clinical events is reported to be higher in the first 6 months following a PCI (Wisloff et al., 2013), however granular data are often lacking to enable such calculation to be performed. Given the variation in study duration and outcome data were reported at multiple time points, the EAG estimated HRs for the first year (Y1) and long-term follow-up (post-Y1 follow-up), respectively. In the Y1 analysis, the number of events in Y1 and the total number of participants using the intention-to-treat principal were used. For the long-term follow-up analysis, the EAG assumed no censoring and constant hazards over the entire follow-up duration after Y1. The number of events during the long-term follow-up was the total number of events at the longest follow-up period excluding the events in Y1, whereas the denominator was denoted by the at-risk number of participants after Y1. The hazard of each device in the trials are calculated as follows:

$$Hazard_{t=1} = \frac{r_{t=1}}{n_{t=k}}$$

$$Hazard_{\,t=k-1} = \frac{r_{t=k} - r_{t=1}}{n_{t=k} - r_{t=1}}$$

where *r* is the cumulative number of events, *n* is the number of participants, *t* is time in year and *k* is the longest follow-up time in year.

The EAG had explored several different approaches to generate the relative treatment effects: (i) estimating a set of yearly odds ratio using repeated trial data at multiple time points within a study, and (ii) assuming constant odds over the whole study duration using the data at the longest follow-up period. However, because of

data sparsity, the analyses had a number of problems such as non-convergence of the model, low effective sample size and uncertainty with prior distributions. In addition, one of the recommended approaches is to fit a piecewise hazard model where time-varying rates are generated (Dias et al. 2014a). However, the EAG believe this approach would not yield more reliable estimates given that the underlying data sparsity issue would lead to similar problems of not providing sufficient information to the piecewise model.

Statistical analysis

An NMA in Bayesian framework using the R package multinma was performed for each outcome (Philippo 2004). The model is estimated using the Stan programme by simulating 4 Markov chains with 2,000 iterations per chain including 1,000 burn-in iterations during each chain. Considering the variation in study population across RCTs, a random-effects (RE) model was used. The RE model assumes the true treatment effect could vary across studies, by accounting for both within- and between-study heterogeneity. Nevertheless, the model fit was assessed to determine if there are any significant differences between fixed-effects (FE) and random-effects (RE) models by comparing the goodness-of-fit indices. The indices include residual deviance and Deviance Information Criterion (DIC). Lower values were preferred and any differences of 5 or more in these indices would be considered as meaningful.

A network plot was generated to visualize the data structure for each outcome and to visually inspect if the network was connected. The size of the node represents the number of participants in each device, and the width of the lines indicate the number of studies for each pairwise comparison.

While Dias et al (2014a) recommend specifying vague or flat prior distributions in Bayesian RE meta-analysis, the between-study heterogeneity can be difficult to estimate when only few studies (<5) are included, in turn generating unreliable results on posterior means (treatment effect) and 95% credible interval (Dias et al. 2014a; Bender et al. 2018). For meta-analysis of very few studies, Lilienthal et al (2023) suggest the use of an empirical prior heterogeneity distribution for meta-analysis, derived using meta-analyses in 134 reports by the Institute for Quality and Efficiency in Health Care (IQWiG). Following Lilienthal's recommendation, a half

normal (HN) distribution with mean 0 and standard deviation (SD) 0.1 for HR was used as prior heterogeneity distribution in the EAG NMA. However, their findings were based on health technology assessment (HTA) reports of pharmaceutical interventions, thus this may not be reflective of the between-studies heterogeneity in medical devices. Typically, RE meta-analyses of medical devices are quite rare due to the limited number of studies comparing the same device, and therefore there is limited evidence on between-studies heterogeneity. A sensitivity analysis using a HN distribution with SD 1.0 was undertaken to explore the impact of different prior heterogeneity distribution on treatment effect.

For meta-analysis of rare events where there are studies with zero events in one or more arms, a weakly informed prior treatment distribution can improve model convergence and parameter identifiability, by slightly limited the log HR prior within the plausible range between 0.004 and 250. Based on empirical observation of 37,773 meta-analyses from the Cochrane Database of Systematic Reviews, Günhan et al. (2020) suggest the use of a normal prior distribution (mean = 0, SD = 2.82) to overcome data sparsity in Bayesian RE meta-analysis of rare events with very few studies. A similar approach was employed to the log HR in the EAG NMA.

A network plot was generated to visualize the data structure in each outcome and to visually inspect if the network was connected. The size of the node is proportional to the number of participants in each device, and the width of the lines indicate the number of studies for each pairwise comparison.

Assessment of transitivity assumption

The assumption of transitivity was assessed using the global approach. The inconsistency in the network as a whole was evaluated by comparing the direct and indirect estimates of a consistency NMA model to an inconsistency “unrelated mean effects (UME)” model (Dias et al. 2014b). This model relaxes the consistency assumption by estimating separate parameters for each direct comparison for which data are available. The posterior mean residual deviance and DIC for both models were compared. A lower residual deviance, DIC or between-study heterogeneity for the inconsistency model is suggestive of inconsistency in the network. The source of inconsistency was investigated and discussed in Section 5.2.4.

5 Key clinical evidence results

5.1 *Key RCTs*

22 key RCTs were identified which compared two drug-eluting stents (DES) in scope (or accepted predecessor DES). Overall results of these RCTs are discussed narratively in Section 5.1.1 and results relating to subgroups specified as relevant in the scope are discussed narratively in Section 5.1.2. Evidence synthesis of the RCTs deemed eligible for NMA is discussed in Section 5.2. The EAG notes the majority of the 22 RCTs were designed as non-inferiority studies and are therefore only powered to demonstrate that the intervention device is 'not worse' than the comparator, and are not designed to detect superiority.

Reported results have been split according to the nature of the comparison being made in the study, for context and ease of interpretation. It should be noted that other components of the devices being compared may also differ, in addition to the key comparison being made. However, the purpose of this assessment is not to compare 'groups' or 'types' of DES, but to draw comparisons between specific devices.

RCTs were identified involving the following devices (or an accepted predecessor) being compared against each other: Angiolite, BioMime, BioFreedom, BioFreedom Ultra, BioMatrix Alpha, Firehawk, Onyx Frontier, Orsiro Mission, Synsiro Pro, Promus ELITE, Supraflex, Supraflex Crux, Synergy XD, Ultimaster Tansei, Ultimaster Nagomi, Xience Pro 48, Xience Pro S, Xience Skypoint, Xience Skypoint 48, Xience Skypoint LV and Xlimus.

No RCTs were identified that involved any of the following devices being compared against each other (or an accepted predecessor): BioMime Branch, BioMime Morph, Coroflex ISAR NEO, EverMine 50, Firehawk Liberty, ihtDEStiny BD, MAGMA and Synergy Megatron. Therefore, the EAG is unable to comment on any differences in outcomes between these devices and any comparator devices from a controlled setting.

Several of the trials report an unspecified 'Xience' device as the comparator. The EAG attempted to identify which Xience device was being used in these trials by reviewing trial protocols, trial records, publications from previous follow-up timepoints

and contact with publication authors. Where this has been established, the exact device is named in the report. However, the EAG has accepted clinical equivalence for all Xience devices as stated in Table 3.

5.1.1 Key RCTs: overall results

Of the 22 key RCTs identified, there were:

- 14 RCTs comparing durable/permanent polymer DES (DP/PP-DES) with bioabsorbable polymer DES (BP-DES)
- Two RCTs comparing polymer free DES (PF-DES) with durable or bioabsorbable polymer DES (BP-DES)
- Two RCTs comparing thin-strut DES with thick-strut DES
- Two RCTs comparing sirolimus-eluting stents (SES) with everolimus-eluting stents (EES)
- One RCT comparing everolimus-eluting stents (EES) with Biolimus-eluting stents (BES)
- One RCT comparing DES with scaffolds made of different metals

Eighteen of the 22 RCTs reported on mixed cardiac indications/populations (ANGIOLITE, BIODEGRADE, BIOFLOW IV, BIOFLOW V, BioFreedom QCA, BIONYX, BIO-RESORT, BIOSCIENCE, CASTLE, CENTURY II, EVOLVE II, meriT-V, PLATINUM, SORT-OUT IX, SORT OUT VIII, TALENT, TARGET-AC and XLIMIT). One RCT reported on a STEMI population (BIOSTEMI), one RCT reported on those with left main lesions (IDEAL-LM) and the remaining two RCTs reported on people of high bleeding risk (Bioflow-DAPT and Onyx ONE).

Key results of these RCTs are described narratively below and summarised in Table 5.

Durable/permanent polymer DES (DP/PP-DES) versus bioabsorbable polymer DES (BP-DES)

Abizaid et al. (2023) compared the BioMime BP-DES (n=170) with the Xience V DP-DES (n=86) in a non-inferiority RCT (meriT-V) of an all-comer population. A non-

significant difference between the BioMime group and the Xience group was observed with respect to the primary composite outcome of major adverse cardiovascular events (MACE), which consisted of any cardiac death, ischaemia-driven target vessel revascularisation (TVR) or any myocardial infarction (MI), at a follow-up duration of two years (7.7% versus 9.5%, p=0.62). The EAG notes this study was not powered to detect differences in clinical endpoints beyond 9 months.

De Winter et al. (2022) compared the Supraflex BP-DES (n=720) and an unspecified Xience DP-DES (n=715) in a non-inferiority RCT (TALENT) of an all-comer population. In the ITT analysis, this study demonstrated no significant difference between the Supraflex group and Xience group with respect to the device-oriented composite endpoint (DOCE), which consisted of cardiac death, target vessel MI and clinically indicated target lesion revascularisation (TLR) (8.1% versus 9.4%, p=0.406), at a follow-up duration of three years. As this is a non-inferiority RCT, these results suggest that the Supraflex device is at least as clinically effective as the unspecified Xience device. The EAG note this trial is single-blinded, but clinical events were adjudicated by an independent blinded committee.

Iglesias et al. (2023) compared the Orsiro BP-DES (n=551) with the Xience Prime/Xpedition DP-DES (n=556) in a superiority RCT (BIOSTEMI) of individuals with STEMI. This study demonstrated significantly lower rates of TLF (driven by lower risk of TLR) in the Orsiro group compared to the Xience Prime/Xpedition group at a follow-up duration of five years. Similar rates of ST, MI and bleeding events were observed between groups. The one year results demonstrated superiority of Orsiro BP-DES against Xience Prime/Xpedition DP-DES for the primary endpoint of TLF. The EAG notes that this trial was designed to detect superiority in the composite endpoint of TLF only, so results for separate component outcomes should be interpreted with caution. Additionally, outcomes at 5 years were only available for 85% of participants.

Kandzari et al. (2022) compared the Orsiro BP-DES (n=884) with an unspecified Xience DP-DES (n=450) in a non-inferiority RCT (BIOFLOW V) of a population with ischaemic heart disease (IHD), excluding those with STEMI. This study demonstrated similar rates of the primary endpoint of target lesion failure (TLF) between the Orsiro and Xience groups (12.3% versus 15.3%, p=0.108) at a follow-up

duration of five years. Target vessel-related MI was observed to be significantly lower in the Orsiro group compared with the Xience group (p=0.015). However, the EAG notes this trial was not designed to detect superiority so results demonstrating differences should be interpreted with caution.

Kereiakes et al. (2019) compared the Synergy BP-DES (n=846) with the Promus Element Plus DP-DES (n=838) in a non-inferiority RCT (EVOLVE II) of individuals with NSTEMI acute coronary syndrome (ACS) or stable angina. This study demonstrated the non-inferiority of Synergy to the Promus Element Plus device with no significant difference in the primary endpoint of TLF at a follow-up duration of one year (6.7% versus 6.5%, p for non-inferiority =0.0005), and similar event rates were demonstrated at 5 years (14.3% versus 14.2%, p=0.91). The EAG notes that this study was not powered beyond detecting non-inferiority at one year.

Lanksy et al. (2023) compared the Firehawk BP-DES (n=823) with an unspecified Xience DP-DES (n=830) in a non-inferiority RCT (TARGET-AC) of an all-comer population. This study demonstrated no significant difference in the primary endpoint of TLF between the Firehawk group and Xience group (17.1% versus 16.3%, p=0.68) at a follow-up duration of five years, suggesting the Firehawk device is at least as clinically effective as the unspecified Xience device. The EAG notes that this study was not powered beyond detecting non-inferiority at one year.

Nakamura et al. (2022) compared the Orsiro BP-DES (n=722) with the Xience Sierra (Pro S)/Xpedition (Pro 48) DP-DES (n=718) in a non-inferiority RCT (CASTLE) of an all-comer population. The study demonstrated non-inferiority of Orsiro to Xience Sierra/Xpedition with regard to the primary endpoint of TLF at a follow-up duration of one year (6.0% versus 5.7%, p=0.843, p for non-inferiority = 0.040). The EAG notes that this RCT was not blinded to treating clinicians, participants or outcome assessors, but clinical events were adjudicated by an independent committee. It is also stated by study authors that the percentage of participants with ACS enrolled was relatively low (15%), which is not considered reflective of general practice.

Pilgrim et al. (2018) compared the Orsiro BP-DES (n=1063) with the Xience Prime/Xpedition DP-DES (n=1056) in a non-inferiority RCT (BIOSCIENCE) of an all-comer population. This study demonstrated similar outcomes for the Orsiro and

Xience Prime/Xpedition devices with regard to the primary outcome of TLF (20.2% versus 18.8%, p=0.487) at a follow-up duration of five years. Pilgrim et al. (2016) reported on the outcomes of people with STEMI enrolled in the BIOSCIENCE RCT. Of the total 2119 participants randomised, 407 presented with STEMI (211 allocated to Orsiro and 407 allocated to Xience Prime/Xpedition). This subgroup analysis suggested that the Orsiro device was associated with a lower rate of TLF at a follow-up duration of one year (3.4% versus 8.8%, p=0.024). The EAG notes that the BIOSCIENCE study was not powered beyond detecting non-inferiority at one year. Additionally, the study was not powered to assess clinical outcome differences in the STEMI subgroup, so these results should be interpreted with caution.

Ploumen et al. (2022) compared the outcomes of three DES arms: Synergy, Orsiro and Resolute Integrity (out of scope) in the BIO-RESORT RCT. The primary objective of this RCT was to compare Synergy or Orsiro (BP-DES) with Resolute Integrity (DP-DES), and not to compare Synergy and Orsiro with each other (the two devices in the scope of this assessment). Overall, the results of the study suggest clinical outcomes did not significantly differ between any of the three stent groups, with the primary outcome of TVF occurring in 12.7% of the Orsiro group and 11.6% of the Synergy group at a follow-up duration of five years.

Slagboom et al. (2023) also compared the Orsiro BP-DES (n=385) and the Xience Prime/Xpedition PP-DES (n=190) in a non-inferiority RCT (BIOFLOW-IV) of people with coronary artery disease (CAD), excluding those who had MI within 72 hours prior to the PCI procedure. This study reported similar rates of the primary outcome of TVF between the Orsiro device and the Xience Prime/Xpedition device at a follow-up duration of 5 years (12.3% versus 10.8%, p=0.652). These results suggest that the Orsiro device is at least as clinically effective as the Xience Prime/Xpedition device. As this study excludes those with acute MI, the results may not be generalisable to wider population. The EAG notes that this RCT was not blinded to treating clinicians, participants or outcome assessors, but clinical events were adjudicated by an independent committee.

Valgmigli et al. (2023) compared the Orsiro Mission BP-DES (n=969) with the Resolute Onyx DP-DES (n=979) in a non-inferiority RCT (Bioflow-DAPT) in a population of acute or chronic coronary syndrome who fulfilled one or more criteria

for being classified as high-bleeding risk. Both groups received one month of dual-antiplatelet therapy (DAPT). This study demonstrated the non-inferiority of Orsiro Mission to Resolute Onyx with respect to the primary composite outcome of death from cardiac causes, myocardial infarction or stent thrombosis at a follow-up duration of one year (3.6% versus 3.4%, p for non-inferiority <0.0001). The EAG note that the decision to continue medication such as aspirin after the one month of DAPT was at the discretion of the treating clinician.

van Geuns et al. (2022) compared the Synergy BP-DES plus four months of DAPT (n=410) with the Xience DP-DES plus 12 months of DAPT (n=408) in a non-inferiority RCT (IDEAL-LM) of individuals undergoing PCI of the left main coronary artery. This study demonstrated the non-inferiority of Synergy with four months of DAPT to Xience with 12 months of DAPT with respect to the composite endpoint of MACE, consisting of all-cause death, MI or ischaemia-driven TVR, at a follow-up duration of two years (14.6% versus 11.4%, p for non-inferiority = 0.04). The EAG note that the difference in DAPT duration between the DES groups in this study may prevent the observed outcomes being attributed to the DES itself.

van Vliet et al. (2024) compared the Resolute Onyx DP-DES (n=1243) and Orsiro BP-DES (n=1245) in a non-inferiority RCT (BIONYX) of an all-comer population. This study demonstrated no significant difference between the Resolute Onyx group and the Orsiro group in the primary endpoint of TVF (12.7% versus 13.7%, $p_{log\text{-}rank}$ = 0.55). These results suggest that the Resolute Onyx device is at least as clinically effective as the Orsiro device. The EAG had no concerns over the quality of this RCT.

Wijns et al. (2018) compared the Ultimaster BP-DES (n=562) with an unspecified Xience PP-DES (n=557) in a non-inferiority RCT (CENTURY II) of an all-comer population. This study demonstrated no significant difference between the Ultimaster group and the Xience group with respect to the primary outcome of freedom from TLF at five years (90.0% versus 91.1%, p=0.54). However, the EAG notes that this study was only powered to detect non-inferiority at 9 months with respect to TLF, so results must be interpreted with caution.

Polymer-free DES (PF-DES) versus bioabsorbable polymer DES (BP-DES) or permanent polymer DES (PP-DES)

Ellert-Gregersen et al. (2022) compared the BioFreedom PF-DES (n=1572) with the BP-DES Orsiro device (n=1579) in a non-inferiority RCT (SORT OUT IX) of all-comers. This study demonstrated no significant difference between the BioFreedom group and the Orsiro group with respect to the primary endpoint of TLF (7.8% versus 6.3%, p=0.12). However, TLR alone, which contributes to the composite outcome of TLF, was observed to be significantly higher in the BioFreedom group than the Orsiro group at two years (5.1% versus 2.6%, p=0.0004), with most of these events occurring in the first year post-implantation. The EAG notes that this trial is only powered to detect non-inferiority at one year of follow-up.

Windecker et al. (2022) compared the Resolute Onyx DP-DES (n=1003) with the BioFreedom PF-DES (n=993) in a non-inferiority RCT (Onyx ONE) in a population of people of high-bleeding risk. Both treatment groups received one month of DAPT followed by one year of single antiplatelet therapy (SAPT). The primary safety endpoint, a composite of cardiac death, MI, or definite or probable ST, occurred in 21.8% of the Resolute Onyx group and 20.7% of the BioFreedom group (p-0.78) at a follow-up duration of two years. Non-inferiority was demonstrated at one year, and the EAG notes that the trial is not powered to assess outcomes beyond this timepoint.

Thin-strut DES versus thick-strut DES

Yoon et al. (2023) compared the thin-strut Orsiro device (n=1175) with the thick-strut BioMatrix device (n=1166) in a non-inferiority RCT (BIODEGRADE) of individuals with chronic stable CAD or ACS. This study reported significantly lower rates of the primary outcome of TLF in the Orsiro group compared to the BioMatrix group (3.2% vs 5.1%, p=0.023) at a follow-up duration of three years. However, the EAG notes that this trial was not designed to detect superiority and so these results cannot be interpreted as indicative of true superiority of the Orsiro device over the Xience or BioMatrix device.

Sabaté et al. (2021) compared the polymer-free stainless steel thin-strut BioFreedom Ultra device (n=97) with the polymer-free cobalt-chromium thick strut BioFreedom device (n=97) in a non-inferiority RCT (BioFreedom QCA) of an all-comer population.

This study demonstrated the non-inferiority of BioFreedom Ultra to BioFreedom with respect to late lumen loss at a follow-up duration of nine months. This study was not powered to detect differences in meaningful clinical endpoints, but observed rates of clinical events between arms appeared similar.

Sirolimus-eluting stents (SES) versus everolimus eluting stents (EES)

Moreu at al. (2019) compared the Angiolite SES (n= 110) with Xience Xpedition (Pro 48) EES (n = 113) in a non-inferiority RCT (ANGIOLITE) of an all-comer population. This study suggested that clinical efficacy of the two devices was similar at a follow-up duration of two years with respect to TLF, but the EAG note that this trial was only designed to detect effect with respect to late lumen loss at nine months (which was found to be non-inferior in the Angiolite device).

Testa et al. (2023) compared the Xlimus device (n=117) with the Synergy device (n=60) in a non-inferiority RCT (XLIMIT) of individuals with stable or unstable angina or NSTEMI. This study was not sufficiently powered to draw meaningful clinical conclusions, but suggests similar results between devices when considering short-term angiographic outcomes as measured by optical coherence tomography (OCT).

Everolimus-eluting stents (EES) versus Biolimus-eluting stents (BES)

Maeng et al. (2019) compared the Synergy EES (n=1385) with the BioMatrix NeoFlex BES (n=1379) in a non-inferiority RCT (SORT OUT VIII) of an all-comer population. This study the non-inferiority of Synergy to BioMatrix NeoFlex with respect to TLF at a follow-up duration of one year (4.0% vs 4.4%, $p<0.001$ for non-inferiority). The EAG notes that event detection utilised registry data, but an independent committee adjudicated all clinical events.

Platinum Chromium scaffold DES (PtCr-DES) versus Cobalt Chromium scaffold DES (CoCr-DES)

Kelly et al. (2017) compared the Promus Element PtCr-DES (n=768) with the Xience V CoCr-DES (n=762) in a non-inferiority RCT (PLATINUM) of individuals with de novo atherosclerotic coronary artery lesions. This study demonstrated non-inferiority of the Promus Element group to the Xience group with respect to the primary endpoint of TLF at a follow-up duration of one year (3.2% vs. 3.5%, p=0.72). Event rates were observed to be similar at five years (9.1% and 9.3%). The EAG notes that

‘high-risk’ participants were excluded from the trial, which limits applicability of these results to a wider population.

Table 5: Summary of key results from RCTs.

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Summary of key clinical outcome results
ANGIOLITE (Moreu et al. 2019), 2 years.	All comers	Angiolite (110)	Xience Xpedition (Pro 48) (113)	Trial not powered to detect differences in clinically meaningful endpoints. However, results suggest similar results between Angiolite and Xience Xpedition with respect to TLF (7.6% vs 7.1%), MACE (11.4% vs 14.1%) and ST (1.9% vs 1%).
BIODEGRADE (Yoon et al. 2023), 3 years.	All comers	Orsiro (1175)	BioMatrix (1166)	Results suggest superior results in Orsiro in comparison to BioMatrix with respect to TLF (3.2% vs 5.1%, p=0.023), driven by differences in the rate of component outcome ID-TLR (1.5% vs 2.8%, p=0.035). However, trial only powered to demonstrate non-inferiority so results suggesting superiority must be interpreted as hypothesis-generating only.
BIOFLOW-DAPT (Valgmigli et al. 2023), 1 year.	HBR patients who received 1 month DAPT.	Orsiro Mission (969)	Resolute Onyx (979)	Demonstrated non-inferiority of Orsiro Mission to Resolute Onyx with respect to a composite endpoint of death from cardiac causes, MI or ST at (3.6% vs 3.4%, p<0.0001 for non-inferiority).
BIOFLOW IV (Slagboom et al. 2023), 5 years.	CAD (excluded those with acute MI).	Orsiro (385)	Xience Prime/Xpeditio n (Pro 48) (190)	Demonstrated no significant difference between the Orsiro device and Xience devices with respect to TVF (12.3% for Orsiro group vs 10.8% for Xience group, p=0.652) at 5 years. Non-inferiority confirmed at 1 year (p<0.001).
BIOFLOW V (Kandzari et al. 2022), 5 years.	IHD (excluded those with STEMI.	Orsiro (884)	Xience (450)	Demonstrated similar rates of TLF between Orsiro and Xience devices (12.3% vs 15.3%, p=0.108). Significantly lower rates of TVMI demonstrated in Orsiro group (6.6% vs 10.3%, p=0.015). However, trial only powered to demonstrated non-inferiority so results suggesting superiority must be interpreted as hypothesis-generating only.
BioFreedom QCA (Sabaté et al. 2021), 2 years.	All comers	BioFreedom Ultra (97)	BioFreedom (97)	Trial not powered to detect differences in clinically meaningful endpoints. However, results suggest similar clinical outcomes with respect to death (2.1% vs 1.0%), MI (4.2% vs 6.3%), TLF (7.3% vs 9.3%) and ST (2.1% vs 0.0%).
BIONYX (van Vliet et al. 2024), 5 years.	All comers	Resolute Onyx (1243)	Orsiro (1245)	Demonstrated non-inferiority of the Resolute Onyx device to the Orsiro device with respect to main endpoint of TVF (12.7% vs 13.7%, plog-rank = 0.55), or any of its individual components (cardiac death, TVMI or TVR).
BIO-RESORTα (Ploumen et al. 2022), 5 years.	All comers	Synergy (1172)	Orsiro (1169)	Similar outcomes observed between all stents regarding mortality, MI and repeated revascularisation. Statistical non-inferiority only reported between Synergy or Orsiro against the Resolute Integrity device which is not in scope.
BIOSCIENCE (Pilgrim et al. 2018), 5 years.	All comers	Orsiro (1063)	Xience Prime (1056)	Demonstrated non-inferiority of the Orsiro device to the Xience Prime device with respect to TLF at one year (6.5% vs 6.6%, p<0.0004 for non-inferiority). At 5 years, TLF was observed to be similar between devices (20.2% vs 18.8%).
BIOSTEMIβ (Iglesias et al. 2023), 5 years.	STEMI only	Orsiro (649)	Xience Prime/Xpeditio n (Pro 48) (651)	Significantly lower rates of TLF in the Orsiro group compared to the Xience group at 5 years (8% vs 11%, probability for superiority >0.975). Lower TLF rates appear driven by numerically lower risk of ID-TLR.
CASTLE (Nakamura et al. 2022), 1 year.	All comers	Orsiro (722)	Xience Sierra (Pro	Demonstrated non-inferiority of Orsiro to Xience with regard to composite outcome of TLF at 1 year (6.0% vs 5.7%, p=0.040 for non-inferiority).

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Summary of key clinical outcome results
			S)/Xpedition (Pro 48) (718)	
CENTURY II (Wijns et al. 2018, Orvin et al. 2016), 5 years.	All comers	Ultimaster (562)	Xience (557)	Results suggest similar outcomes between Ultimaster and Xience devices with regard to TLF, TVF, POCE, stent thrombosis and bleeding at 5 years. However, trial was only powered to detect non-inferiority of Ultimaster to Xience at 9 months with respect to TLF (demonstrated).
EVOLVE II (Kereiakes et al. 2019), 5 years.	NSTEMI/stable angina	Synergy (846)	Promus Element Plus (838)	Demonstrated non-inferiority of Synergy to Promus Element Plus with respect to TLF at 1 year (6.7% vs 6.5%, p=0.83 for difference, p=0.0005 for non-inferiority). TLF rate appeared similar between devices at 5 years (14.3% vs 14.2%, p=0.91).
IDEAL-LM (van Geuns et al. 2022), 2 years.	Left main only.	Synergy (410)	Xience (408)	Demonstrated non-inferiority of Synergy with 4 months DAPT compared with Xience with 12 months DAPT at 2 years with respect to MACE (14.6% vs 11.4%, p=0.04 for non-inferiority).
MERIT-V (Abizaid et al. 2023), 2 years.	All comers	BioMime (170)	Xience V (86)	Trial not powered to detect differences in clinically meaningful endpoints. However, results suggest similar clinical outcomes between devices with respect to MACE (7.74% vs 9.52%).
Onyx ONE (Windecker et al. 2022), 2 years.	HBR	Resolute Onyx (1003)	BioFreedom (993)	Non-inferiority of Resolute Onyx against BioFreedom demonstrated at 1 year. Similar results for the primary safety endpoint (a composite of cardiac death, MI or ST) observed at 2 years (21.2% vs 20.7%, p=0.78).
PLATINUM (Kelly et al. 2017), 5 years.	Stable/unstable angina pectoris or silent ischemia (excluded those with acute MI).	Promus Element (768)	Xience V (762)	Non-inferiority of Promus Element against Xience V demonstrated at 1 year with regard to TLF (3.2% vs. 3.5%, p=0.72). Rates of cardiac death or MI (2.5% vs 2.0%, p=0.56), TLR (1.9% vs 1.9%, p=0.96) and definite or probably ST (0.4% vs 0.4%, p=1.00) were observed to be similar. At 5 years, TLF rates were similar between groups (9.1% vs 9.3%, p=0.87).
SORT OUT IX (Ellert-Gregersen et al. 2022, Hansen et al. 2022), 2 years.	All comers	BioFreedom (1572)	Orsiro (1579)	BioFreedom did not meet non-inferiority criteria in comparison to Orsiro with respect to MACE at 1 year, with TLR observed to be higher in the BioFreedom group (3.5%) compared to the Orsiro group (1.3%). At 2 years, TLF was observed to be similar between groups (7.8% vs 6.3%). Driven by the 1 year results, TLR was higher in BioFreedom group than in the Orsiro group. (5.1% vs 2.6%). Study only powered to detect non-inferiority at 1 year.
SORT OUT VIII (Maeng et al. 2019), 1 year.	All comers	BioMatrix (1379)	Synergy (1385)	Demonstrated non-inferiority of BioMatrix to Synergy with respect to TLF (4.0% vs 4.4%, p<0.001 for non-inferiority).
TALENT (de Winter et al. 2022), 3 years.	All comers	Supraflex (720)	Xience family (715)	Demonstrated non-inferiority of Supraflex to Xience with respect to DOCE at 1 year (4.9% vs 5.3%, p<0.0001 for non-inferiority). Results appeared similar at 3 years with respect to DOCE (8.1% vs 9.4%, p=0.406 for difference).
TARGET-AC (Lanksy et al. 2023), 5 years.	All comers	Firehawk (823)	Xience family (830)	Demonstrated non-inferiority of Firehawk with regard to TLF at 1 year (6.1% vs 5.9%, p=0.004 for non-inferiority. TLF rates similar at 5 years (17.1% vs 16.3%, p=0.68 for difference).

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Summary of key clinical outcome results
XLIMIT (Testa et al. 2023), 1 year.	CAD (excluded those with STEMI)	Xlimus (117)	Synergy (60)	Trial not powered to detect differences in clinically meaningful endpoints. Results suggest similar clinical outcomes between Xlimus and Synergy devices with respect to cardiac death, TVMI and TLR at 1 year (9% vs 6.7%, p=0.09 for difference).
Key: α third arm from RCT not extracted (Resolute Integrity) as device not in scope. β indicates superiority RCT, all other RCTs are non-inferiority in design.				

Abbreviations: *CAD: coronary artery disease; DAPT: dual anti-platelet therapy; DOCE: device-oriented composite endpoint; HBR: high bleeding risk; ID-TLR: ischaemia driven-target lesion revascularisation; IHD: ischaemic heart disease; ITT: intention-to-treat; MACE: major adverse cardiac events; MI: myocardial infarction; NSTEMI: non-ST elevated myocardial infarction; POCE: patient-oriented composite endpoint; RCT: randomised controlled trial; ST: stent thrombosis; STEMI: ST-elevated myocardial infarction; TLF: target lesion failure; TLR: target lesion revascularisation; TVF: target vessel failure; TVMI: target vessel-related myocardial infarction*.

5.1.2 Key RCTs: subgroup results

Seven publications reporting subgroup analyses of the key RCTs discussed in Section 5.1 were identified, the results of which are summarised in Table 6.

The EAG notes that these analyses were not powered for the detection of differences in these specific subgroups, or statistical power is limited for the analyses, so results should be interpreted with caution.

Where available and applicable to the subgroups identified as relevant in the scope, subgroup data was extracted from the 22 key RCTs. A summary table of this data can be found in Appendix E. Overall, no studies reported any interaction between subgroup characteristics (with respect to subgroups in the scope) and between-stent outcomes. Observed differences (or lack of differences) remained consistent between the overall populations and the subgroup populations that were reported on.

Table 6: Subgroup analyses results.

Study name (reference), follow-up duration	Subgroup population	Device 1 (n)	Device 2 (n)	Summary of key clinical outcome results
BIO-RESORT (Ploumen et al. 2021), 2 years	Diabetes	Orsiro (211)	Synergy (203)	No statistical comparison made between Orsiro and Synergy devices, raw TVF event data appear similar for people with diabetes (10.2% versus 10.0%).
BIO-RESORT (Zocca et al. 2018), 1 year	HBR	Orsiro (337)	Synergy (336)	No significant difference in clinical outcomes between Orsiro and Synergy devices in HBR population (6.9% versus 6.0%, p=0.60).
BIO-RESORT (Buiten et al. 2019), 3 years	Bifurcation lesions	Orsiro (412)	Synergy (415)	No statistical comparison made between Orsiro and Synergy devices, raw TVF event data appear similar for people with bifurcation lesions (10.3% versus 9.8%).
BIONYX (Ploumen et al. 2021), 2 years	Diabetes	Orsiro (250)	Resolute Onyx (260)	TVF rate 10.7% in Orsiro group versus 12.2% in Resolute Onyx group, no significant difference (p=0.63).
BIOSCIENCE (Iglesias et al. 2019a), 5 years	Diabetes	Orsiro (257)	Xience (229)	No interaction observed between diabetic status and between-stent outcomes. TLF rate in people with diabetes for Orsiro was 31.0% compared with 25.8% for Xience (p=0.244).
CENTURY II (Orvin et al. 2016), 2 years	Bifurcation lesions	Ultimaster (95)	Xience (99)	TLF rate did not differ between Ultimaster and Xience groups for people treated for bifurcation lesions (5.3% versus 9.1%, p=0.30).
SORT OUT IX Hansen et al. 2022), 1 year	Diabetes	BioFreedom (304)	Orsiro (303)	TLF rate did not significantly differ between BioFreedom and Orsiro in people with diabetes (8.2% versus 6.3%, p=0.6195).

Study name (reference), follow-up duration	Subgroup population	Device 1 (n)	Device 2 (n)	Summary of key clinical outcome results
SORT OUT VIII (Gyldenkerne et al. 2019), 1 year	Diabetes	Synergy (250)	BioMatrix (262)	No interaction observed between diabetic status and between-stent outcomes (p for interaction = 0.31). TLF rate did not significantly differ between Synergy group and BioMatrix group in people with diabetes (3.6% versus 5.7%). TLF rate similar between device groups in people without diabetes (4.1% versus 4.0%).

Abbreviations: *HBR: high bleeding risk; TLF: target lesion failure; TVF: target vessel failure*

5.2 *Network meta-analysis*

5.2.1 Studies included in NMA

Of the 22 RCTs identified in Section 5.1, the EAG considered 14 RCTs involving 10 drug-eluting stents (DES) to be eligible for synthesis through NMA (BIODEGRADE, BIOFLOW IV, BIOFLOW V, BIONYX, BIO-RESORT (two of three arms), BIOSCIENCE, CASTLE, CENTURY II, EVOLVE II, PLATINUM, SORT OUT VIII, SORT OUT IX, TALENT and TARGET). The other eight RCTs did not meet the eligibility criteria outlined in Section 4.3. i.e. they were underpowered for assessing clinical endpoints at a minimum of one year (ANGIOLITE, BioFreedom QCA, meriT-V and XLIMIT), or they focussed solely on 'high-risk' populations (BIOFLOW-DAPT, BIOSTEMI, IDEAL-LM and Onyx ONE). The exclusion of these eight RCTs meant the following DES could not be integrated into the NMA: Angiolite, BioFreedom Ultra and Xlimus. However, the BioFreedom Ultra device is considered clinically equivalent to the BioFreedom device, according to information received from the company, so both devices can be represented by a single node in the network.

Based on the company information on clinical equivalence between their predecessor and the device in the scope, the NMA results could be used to inform the relative treatment effect of 18 devices in the scope. The list of devices includes:

1. Xience Pro 48 (via Xience Xpedition/Xience V/Xience Prime)
2. Xience Pro S (via Xience Xpedition/Xience V/Xience Prime)
3. Xience Skypoint (via Xience Xpedition/Xience V/Xience Prime)
4. Xience Skypoint 48 (via Xience Xpedition/Xience V/Xience Prime)
5. Xience Skypoint LV (via Xience Xpedition/Xience V/Xience Prime)

6. BioFreedom
7. BioMatrix Alpha (via BioMatrix)
8. BioFreedom Ultra (via BioFreedom)
9. Orsiro Mission (via Orsiro)
10. Synsiro Pro (via Orsiro)
11. Promus Elite (via Promus Element)
12. Synergy XD (via Synergy)
13. Onyx Frontier (via Resolute Onyx)
14. Firehawk
15. Supraflex Cruz (via Supraflex)
16. Supraflex Cruz Nevo (via Supraflex)
17. Ultimaster Nagomi (via Ultimaster)
18. Ultimaster Tansei (via Ultimaster)

5.2.2 Study and participant characteristics

The 14 RCTs included in the network meta-analysis were all designed to assess the non-inferiority of one DES against another DES. The number of participants randomised across the trials ranged from 190 to 1579, with a total of 25 974 participants. The trials were conducted across four continents, with 11 of the trials including participants in Europe. Nine of the trials described the included population as “all comers”. The remaining five trials excluded ‘high risk’ participants such as people with STEMI or acute MI. Follow-up period for the trials ranged from one to five years. A summary of study characteristics can be found in Table 7.

The mean age of trial participants ranged from 63.6 to 70.4 years and the percentage of female participants ranged from 21.4% to 29.4%. Of the 10 trials which did not exclude participants with STEMI, the percentage of trial participants with STEMI ranged from 5.6% to 32%. The percentage of trial participants with

diabetes ranged from 18% to 39.3%. The percentage of trial participants with bifurcation lesions ranged from 5.6% to 39.8% and the percentage of trial participants with left main lesions ranged from 0.5% to 3.8% (where reported and where these lesion types were not in the exclusion criteria). Studies did not report a breakdown of ethnicities included in the trials, or report on the proportion of participants who may be considered of high-bleeding risk. A summary of participant characteristics can be found in Table 8, alongside characteristics from the population included in the NICOR audit of PCI procedures in 2022/23. The EAG note the characteristics of included studies are broadly in line with that of the NICOR data, with the exception of the percentage of people with STEMI which appears higher in the NICOR data in comparison with the trials.

Table 7: Study characteristics of RCTs in NMA.

Trial name	Study design	Latest follow-up available (reference)	Intervention (n)	Comparator (n)	Population description	Setting
BIODEGRADE	Non-inferiority RCT	3 years (Yoon et al. 2023)	Orsiro (1175)	BioMatrix (1166)	All comers	South Korea
BIOFLOW IV	Non-inferiority RCT	5 years (Slagboom et al. 2023)	Orsiro (385)	Xience Prime/Xpedition (Pro 48) (190)	CAD (excludes those with acute MI)	Japan, Europe, Australia, Israel
BIOFLOW V	Non-inferiority RCT	5 years (Kandzari et al. 2023)	Orsiro (884)	Xience (450)	IHD (excludes those with STEMI)	USA, Belgium, Israel
BIONYX	Non-inferiority RCT	5 years (Van Vliet et al. 2024)	Resolute Onyx (1243)	Orsiro (1245)	All comers	The Netherlands, Belgium, Israel
BIO-RESORT	Non-inferiority RCT	5 years (Ploumen et al. 2022)	Synergy (1172)	Orsiro (1169)	All comers	The Netherlands
BIOSCIENCE	Non-inferiority RCT	5 years (Pilgrim et al. 2018)	Orsiro (1063)	Xience Prime (1056)	All comers	Switzerland
CASTLE	Non-inferiority RCT	1 year (Nakamura et al. 2022)	Orsiro (722)	Xience Sierra (Pro S)/Xpedition (Pro 48) (718)	All comers	Japan
CENTURY II	Non-inferiority RCT	5 years (Wijns et al. 2018)	Ultimaster (562)	Xience (557)	All comers	Europe, Japan, Israel
EVOLVE II	Non-inferiority RCT	5 years (Kereiakes et al. 2019)	Synergy (846)	Promus Element Plus (838)	NSTEMI/stable angina	North America, Europe, Australia, New Zealand, Japan, Singapore

PLATINUM	Non-inferiority RCT	5 years (Kelly et al. 2017)	Promus Element (768)	Xience V (762)	Stable/unstable angina pectoris or silent ischemia (excludes those with acute MI)	USA, UK, Germany
SORT OUT IX	Non-inferiority RCT	2 years (Ellert-Gregersen et al. 2022)	BioFreedom (1572)	Orsiro (1579)	All comers	Denmark
SORT OUT VIII	Non-inferiority RCT	1 year (Maeng et al. 2019)	BioMatrix (1379)	Synergy (1385)	All comers	Denmark
TALENT	Non-inferiority RCT	3 years (deWinter et al. 2022)	Supraflex (720)	Xience family (715)	All comers	Europe, India
TARGET	Non-inferiority RCT	5 years (Lansky et al. 2023)	Firehawk (823)	Xience family (830)	All comers	UK, Ireland, New Zealand, China, USA

Abbreviations: *CAD: coronary artery disease; IHD: ischaemic heart disease; MI: myocardial infarction; NSTEMI: non-ST elevated myocardial infarction; NMA: network meta-analysis; RCT: randomised controlled trial; STEMI: ST-elevated myocardial infarction; UK: United Kingdom; USA: United States of America*

Table 8: Participant characteristics of RCTs in NMA.

Trial name	% female	Mean age (years)	% STEMI	% diabetes	% bifurcation lesions	% left main lesions
BIODEGRADE	28.4	63.6	10.4	33.9	15.2	3.8
BIOFLOW IV	27.3	64.8	0	31.1	5.6	0.5
BIOFLOW V	27.1	64.6	0	37	15	NR
BIONYX	23.9	64.1	27.2	20.9	39.8	2

BIO-RESORT	28	64.2	32	18	29	2
BIOSCIENCE	23	66.1	19.9	24.2	16.9	1.8
CASTLE	22.8	70.4	6.2	39.3	32	NR
CENTURY II	21.4	65.5	5.6	31.9	14.4	1.4
EVOLVE II	29.4	63.9	0	31.1	NR	0
PLATINUM	28.9	64	0	25.1	0	0
SORT OUT IX	22.7	66.4	25.1	19.3	20.6	2.5
SORT OUT VIII	23	66	21	19	17	2.5
TALENT	24.2	66	16.5	24.9	16	1.6
TARGET	23.6	65.3	8.9	24	33.4	1.8
Population characteristics of NICOR audit data 2022/23	*24.8*	*65.5*	*24.8*	*25.9*	*NR*	*4.5*

Abbreviations: *NICOR: National Institute for Cardiovascular Outcomes Research; NR: not reported; STEMI: ST-elevated myocardial infarction.*

5.2.3 Risk of bias and quality of included RCTs

The Joanna Briggs Institute (JBI) checklist for randomised controlled trials (RCT) was used to assess risk of bias and quality of trials included in the NMA. This checklist asks questions pertaining to risk of bias within the following domains:

- selection and allocation of participants
- administration of intervention/exposure
- assessment, detection and measurement of the outcome
- participant retention

The checklist also assesses the validity of statistical conclusions made in the trials which pertains to study quality, but not risk of bias.

Guidance on the use of JBI critical appraisal tools does not recommend prescribing overall 'ratings' of bias for each domain or question (Barker et al. 2023). Therefore, the results of these checklists and key concerns around risk of bias are discussed narratively in this section and summarised in Table 9. A summary of key issues identified that may impact on NMA results is provided in Section 5.2.4: 'Limitations'.

Bias relating to selection and allocation

There were no concerns over bias relating to selection and allocation in any of the 14 included trials. This included assessment of true randomisation to treatment arms, concealment of allocation to treatment arms and similarities at baseline of the two groups of participants following randomisation.

Bias relating to administration of intervention/exposure

In six of the 14 trials, participants were blinded to the treatment arm to which they had been assigned. In the remaining eight trials, participants were aware of the treatment arm to which they had been assigned. In trials where participants are not blinded to treatment assignment, there is risk of bias arising from participants potentially reacting differently (e.g. when reporting presence or severity of symptoms post-procedure) to if they were not aware of which DES they had received.

Operators delivering the treatment were not blind to treatment assignment in any of the 14 trials. If those implanting the drug-eluting stent (DES) are aware of the type of DES being implanted, it could be argued that this may influence behaviour and performance during the procedure, which consequently could affect treatment outcomes. However, many of the studies addressed this lack of blinding by stating that the packaging of the different DES used in the trials is different, so it would not have been feasible to blind operators in a safe and effective manner.

In 11 of the 14 trials, participants were treated identically other than the intervention of interest. In two trials, it was stated that participants in both arms received further treatment which was according to standard medical guidelines, but at the discretion of the treating clinician. In the remaining trial it was unclear whether participants were treated equally other than the intervention of interest.

Bias relating to assessment, detection and measurement of the outcome

In 11 of the 14 trials, it was stated that outcome assessors were blinded to treatment assignment. This reduces the risk of bias when measuring/recording outcomes that may arise from knowing the treatment that has been assigned to the participant. In the remaining three trials, outcome assessors were aware of the treatment that had been assigned to participants.

In 12 of the 14 trials, outcomes were measured in the same way for participants in each treatment arm. In the remaining two trials, it is unclear if outcomes were measured in the same way between groups. In particular, one trial gathered results from registry data, where it can be presumed there may be variation in the way outcomes were measured.

With respect to whether outcomes were measured in a reliable way, this was mixed across the 14 trials. Nine of the trials were deemed to have met this criterion. In the remaining five trials, it is unclear if outcomes were measured in a reliable way. This is primarily due to outcomes being measured via telephone, which could be viewed as subjective as participants may not report their symptoms or experience of adverse events in a consistent manner.

Bias relating to participant retention

In four of the 14 trials, there were no concerns over bias relating to participant retention. This was either due to no loss to follow-up or adequate analysis being planned/performed in cases of loss to follow-up. In four of the 14 trials, it was unclear if there was bias present as relating to participant retention. This was primarily due to a lack of information on how loss to follow-up was handled in the analysis. In the remaining six trials, there were concerns over bias introduced as a result of loss to follow-up and subsequent inadequate description or analysis.

Statistical conclusion validity

There were no concerns over the validity of statistical conclusions drawn in 12 of the 14 trials. In the remaining two trials, there were no concerns over use of appropriate statistical analysis or trial design/deviations, but it was stated that intention-to-treat analysis was only conducted at the one year follow-up timepoint only, and not at any subsequent timepoints.

Table 9: Summary of JBI Critical Appraisal checklist results for RCTs in NMA.

Trial name	Domain/question											
	Criteria related to selection and allocation.			Criteria related to administration of intervention/exposure.			Criteria related to assessment, detection and measurement of the outcome.			Criteria related to participant retention.	Statistical conclusion validity.		
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
BIODEGRADE	Y	Y	Y	N	N	Y	N	Y	Y	N	Y	Y	Y
BIOFLOW IV	Y	Y	Y	N	N	Y	N	U	Y	N	Y	Y	Y
BIOFLOW V	Y	Y	Y	N	N	Y	Y	Y	Y	N	Y	Y	Y
BIONYX	Y	Y	Y	Y	N	Y	Y	Y	Y	U	Y	Y	Y
BIO-RESORT	Y	Y	Y	Y	N	N	Y	Y	U	U	Y	Y	Y
BIOSCIENCE	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y
CASTLE	Y	Y	Y	N	N	N	N	Y	U	Y	Y	Y	Y
CENTURY II	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y
EVOLVE II	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N	Y	Y
PLATINUM	Y	Y	Y	Y	N	Y	Y	Y	Y	U	N	Y	Y
SORT OUT IX	Y	Y	Y	Y	N	U	Y	Y	Y	Y	Y	Y	Y
SORT OUT VIII	Y	Y	Y	N	N	Y	Y	U	U	Y	Y	Y	Y
TALENT	Y	Y	Y	Y	N	Y	Y	Y	U	U	Y	Y	Y
TARGET	Y	Y	Y	N	N	Y	Y	Y	U	Y	Y	Y	Y

Questions in checklist:
Question 1: Was true randomization used for assignment of participants to treatment groups?
Question 2: Was allocation to groups concealed?
Question 3: Were treatment groups similar at the baseline?

Question 4: Were participants blind to treatment assignment?
Question 5: Were those delivering the treatment blind to treatment assignment?
Question 6: Were treatment groups treated identically other than the intervention of interest?
Question 7: Were outcome assessors blind to treatment assignment?
Question 8: Were outcomes measured in the same way for treatment groups?
Question 9: Were outcomes measured in a reliable way?
Question 10: Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?
Question 11: Were participants analysed in the groups to which they were randomized?
Question 12: Was appropriate statistical analysis used?
Question 13: Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Note: Questions 7-12 were assessed per separate outcome included in NMA (TLR and TVMI). However, answers did not differ between outcomes in any study and so are reported in the table as a single answer e.g. Y, N, U or N/A.

Abbreviations: *JBI: Joanna Briggs Institute; N: no; N/A: not applicable; NMA: network meta-analysis; RCT: randomised controlled trial; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction; U: unclear; Y: yes.*

5.2.4 NMA results

Although a number of different clinical outcomes were reported in the identified RCTs, only TLR and TVMI were analysed using NMA. This is because these 2 outcomes are reported in all 14 RCTs, thus allowing the maximum possible number of devices to be evaluated in the EAG economic modelling. The TLR and TVMI event data for each study is reported in Table 10. The EAG noted that TLR was reported differently across studies (overall TLR, clinically indicated TLR or ischaemia driven TLR), thus for consistency, only clinically indicated and ischaemia-driven TLR were included in the NMA. Results for each outcome at the first year and long-term follow-up are presented as mean HRs, standard deviation (SD) and 95% credible intervals (CrIs), derived from RE NMA models. In addition, results from the sensitivity analysis using a higher prior heterogeneity distribution, i.e. HN distribution with mean 0 and SD 1.0 are presented.

Data from all 14 RCTs comparing 10 devices with 25,794 randomised participants were included in the Y1 NMA. For long-term follow-up NMA, 2 trials that only reported 1-year follow-up data were excluded (CASTLE and SORT OUT VIII), therefore data from 12 RCTs involving 21,770 randomised participants contributed to the analysis. The network plots for both Y1 and long-term follow-up NMA are presented in Figure 4, where the comparison between Xience and Orsiro with the largest number of head-to-head RCTs are represented by the thickest edge, and Orsiro is denoted by the largest node, meaning the largest number of participants were randomised to this intervention.

Table 10: TLR and TVMI events in RCTs included in NMA.

Trial name	DES	ITT population (n)	TLR events at Y1 follow-up	TVMI events at Y1 follow-up	TLR events at final follow-up	TVMI events at final follow-up
BIODEGRADE	Orsiro	1175	10	3	18	5
	BioMatrix	1166	18	0	33	2
BIOFLOW-IV	Orsiro	385	6	13	28	17
	Xience Prime/Xpedition	190	1	6	3	9
BIOFLOW-V	Orsiro	884	17	39	48	56
	Xience	450	10	35	32	45
BIONYX	Resolute Onyx	1243	31	18	69	57
	Orsiro	1245	24	18	80	52
BIO-RESORT	Synergy	1172	17	25	50	44
	Orsiro	1169	18	26	55	50
BIOSCIENCE	Orisro	1063	35	30	103	62
	Xience Prime	1056	25	31	97	69
CASTLE	Orsiro	722	6	31		
	Xience Sierra (Pro S)/Xpedition (Pro 48)	718	7	28		
CENTURY II	Ultimaster	562	19	7	36	10
	Xience	557	20	12	34	13
EVOLVE II	Synergy	846	22	45	54	84
	Promus Element Plus	838	14	40	41	71
PLATINUM	Promus Element	768	14	6	38	14
	Xience V	762	14	12	44	17
SORT OUT IX	BioFreedom	1572	55	26	80	43
	Orsiro	1579	20	26	41	43
SORT OUT VIII	BioMatrix	1379	35	26		
	Synergy	1385	32	15		
TALENT	Supraflex	720	19	18	35	23
	Xience	715	28	20	41	32
TARGET	Firehawk	823	9	34	47	82
	Xience	830	18	30	51	81

Notes:
BIODEGRADE data are only available at 18- and 36-month of follow-up. Data at 18-month are used as Y1 data in the NMA.
Only Y1 follow-up data are available for CASTLE and SORT OUT IX.
Abbreviations*: DES: drug eluting stent; ITT: intention-to-treat; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction.*

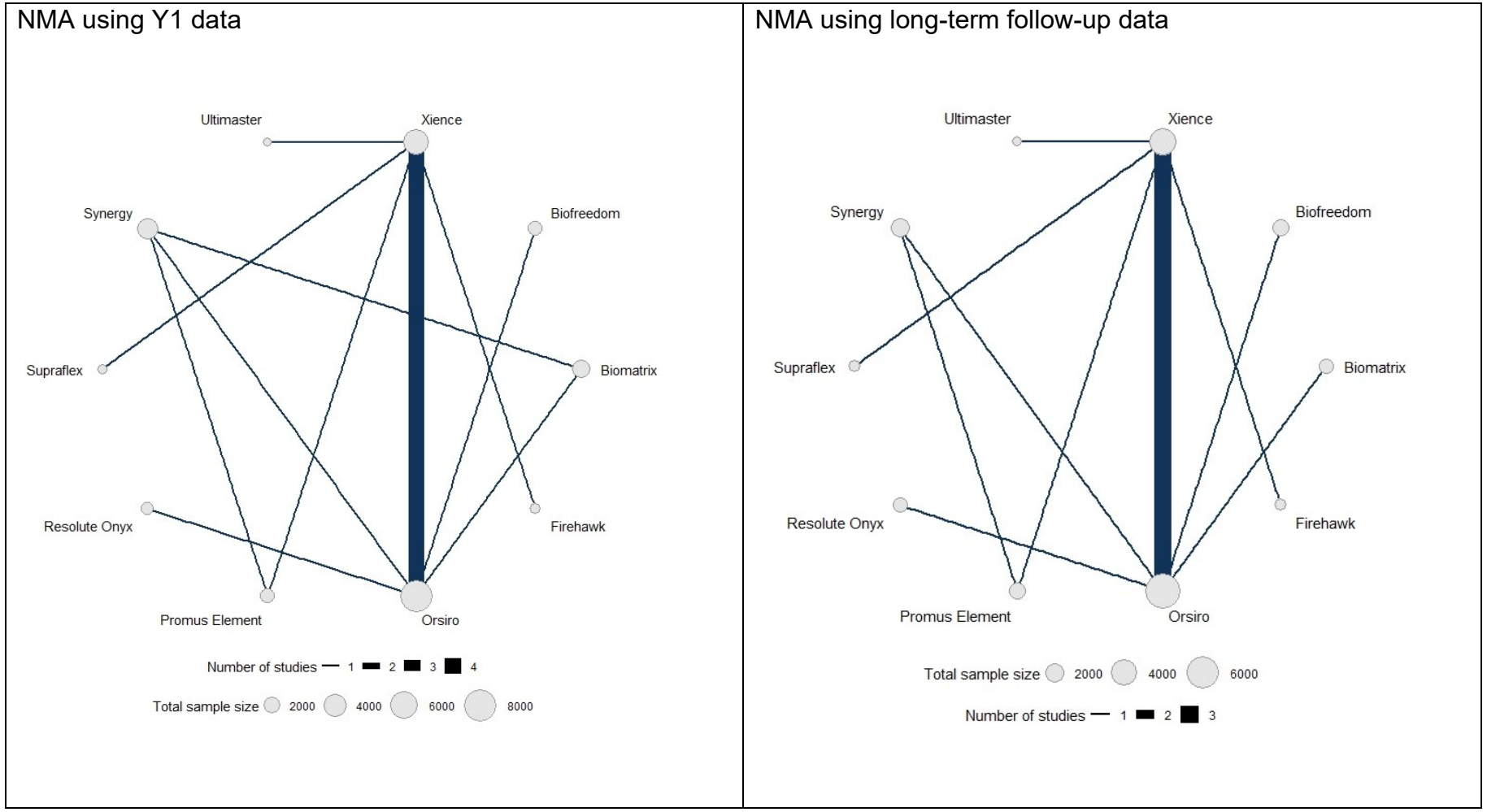


Figure 4: Network meta-analysis plot.

Outcomes at the first-year follow-up

Given that Xience is used as the comparator in the economic analysis, the relative treatment effect of each device compared to Xience is primarily discussed in this section. The strength of the evidence is categorised as “strong/clear” and “some/weak”, depending on the magnitude of effect size, 95%CrI and the margin of 95%CrI from null. If 95%CrI does not contain null and the margin from null is wide, the evidence is considered as clear/strong. Some or weak evidence is reported when 95%CrI is slightly overlapping with null. The larger the overlap with the null, the weaker the evidence becomes. There is no evidence of an effect if HR ≥1 is accompanied by an overlapping 95%CrI.

At 1 year, results from the NMA suggest there is some evidence that Promus Elite has meaningful beneficial effect on TVMI rate when compared to Xience (HR 0.59, 95%CrI 0.31 to 1.03). There is clear evidence that BioFreedom resulted in higher TLR rate than Xience (HR 3.70, 95%CrI 1.83 to 6.80).

There is weak evidence that Firehawk and Supraflex may reduce TLR rate, compared to Xience – Firehawk: HR 0.54 (95%CrI 0.20 to 1.11), Supraflex: HR 0.70 (95%CrI 0.36 to 1.22). For TVMI, there is some weak evidence that Synergy and Orsiro may lower TVMI rate compared to Xience – Synergy: HR 0.68 (95%CrI 0.37 to 1.14), Orsiro: HR 0.84 (95%CrI 0.62 to 1.10). The 95%CrIs are wide and therefore the direction of effect is uncertain.

Compared to Xience, there is no evidence that Ultimaster has an effect on TLR, similarly on TVMI, no evidence for BioFreedom, Resolute Onyx and Ultimaster. This is due to the very wide 95%CrIs. The relative effect at 1-year vs Xience is presented in Table 11 and forest plots in Figure 5.

The relative treatment effect of all pairwise comparisons is summarised in Appendix G. There is clear evidence showing BioFreedom has higher TLR rate compared to most devices. Compared to BioMatrix, there is clear evidence that Firehawk and Supraflex have a lower TLR rate. Additionally, Orsiro has a higher TLR rate than Firehawk.

Between-study posterior mean SDs for both outcomes are indicative of low heterogeneity, though these are strongly influenced by the choice of empirical prior.

– TLR 0.08 (95%CrI 0.00 to 0.21), TVMI 0.09 (95%CrI 0.00 to 0.23). The inconsistency assessment yields lower residual deviance and DIC in NMA for TLR, but higher values in TVMI (Appendix F). The dev-dev plot between NMA and UME model is presented in Appendix F. This is because of a zero cell in BIODEGRADE trial (BioMatrix arm), which therefore inflates the estimate of the direct evidence in the UME model. While this leads to a substantial difference in the residual deviance contribution for this data point between NMA and UME models, it is not considered as inconsistency. The EAG conclude that there is no evidence of inconsistency detected.

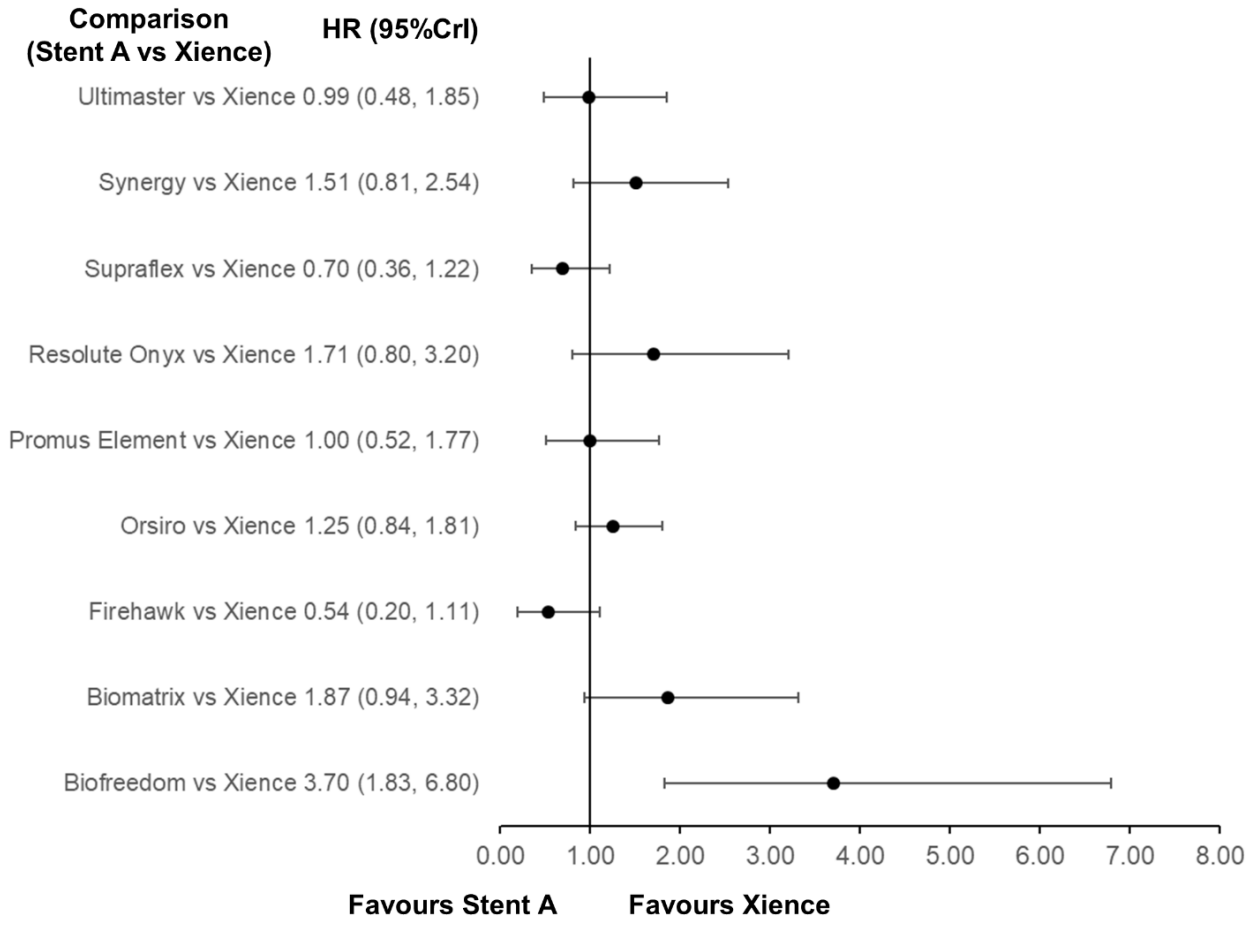
While both the uncertainty around the relative effects and between-study SD are higher with the use of a higher prior heterogeneity distribution, the overall conclusions on their relative effect remain the same.

Table 11: Results from NMA RE models using Y1 data

Device	Relative treatment effect vs Xience (HR)			
	Prior heterogeneity 0.1		Sensitivity analysis: Prior heterogeneity 1.0	
	Posterior Mean	95% CrI	Posterior Mean	95% CrI
TLR				
BioFreedom	3.70	1.83, 6.80	3.91	1.30, 9.92
BioMatrix	1.87	0.94, 3.32	1.98	0.77, 4.48
Firehawk	0.54	0.20, 1.11	0.57	0.17, 1.38
Orsiro	1.25	0.84, 1.81	1.26	0.74, 2.06
Promus Element	1.00	0.52, 1.77	1.03	0.42, 2.14
Resolute Onyx	1.71	0.80, 3.20	1.82	0.59, 4.42
Supraflex	0.70	0.36, 1.22	0.74	0.27, 1.64
Synergy	1.51	0.81, 2.54	1.57	0.67, 3.24
Ultimaster	0.99	0.48, 1.85	1.06	0.37, 2.46
Between-study SD	0.08	0.00, 0.21	0.26	0.01, 0.84
TVMI				
BioFreedom	0.88	0.43,1.61	1.17	0.27, 3.19
BioMatrix	1.05	0.43, 2.19	0.94	0.14, 2.45
Firehawk	1.19	0.67,1.94	1.40	0.39, 3.51
Orsiro	0.84	0.62, 1.10	0.90	0.52, 1.57
Promus Element	0.59	0.31, 1.03	0.60	0.17, 1.34
Resolute Onyx	0.89	0.38, 1.79	1.13	0.26, 3.38
Supraflex	0.94	0.46, 1.73	1.05	0.30, 2.76
Synergy	0.68	0.37, 1.14	0.67	0.20, 1.38
Ultimaster	0.63	0.21, 1.50	0.71	0.14, 2.10
Between-study SD	0.09	0.00, 0.23	0.38	0.03, 1.08

***Abbreviations**: CrI: credible interval; HR: hazard ratio; SD: standard deviation; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction.*

Target Lesion Revascularisation (TLR):



Target vessel-related myocardial infarction (TVMI):

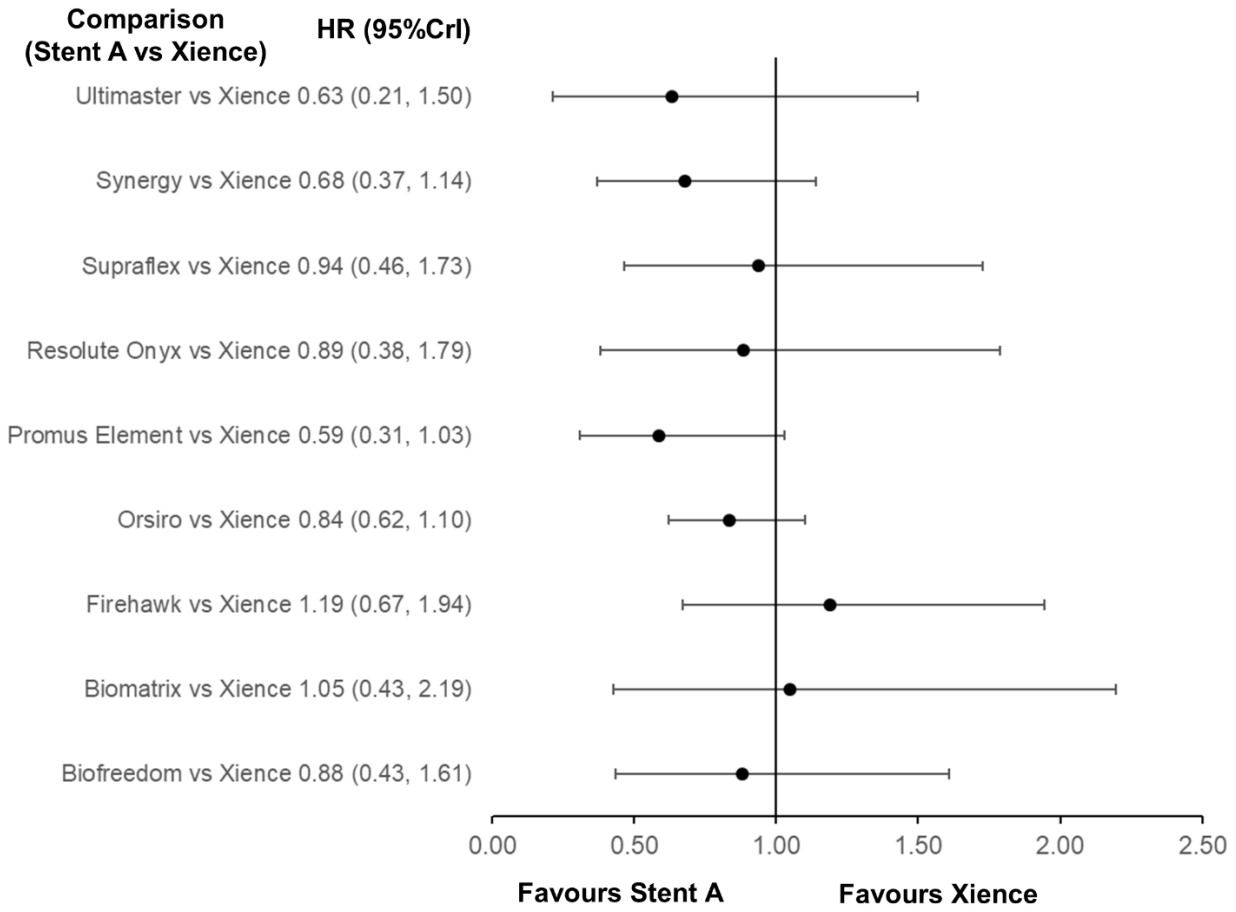


Figure 5: Forest plots: First-year follow-up (HR with CrI)

Outcomes in the long-term follow-up (>1 year)

The relative treatment effect in long-term follow-up of each device compared to Xience is primarily discussed in this section. As the long-term NMA data are very sparse and events are very rare in some studies, this increases the uncertainty significantly in the long-term NMA. In turn, unreliable long-term relative effects are generated.

In the long-term follow-up, the NMA results suggest there is no evidence for meaningful differences in TLR and TVMI rate between devices (Table 12). There is weak evidence suggesting that Resolute Onyx and Promus Element have an effect on TLR compare to Xience – Promus Element: HR 0.80 (95%CrI 0.48 to 1.25), Resolute Onyx: HR 0.72 (95%CrI 0.40 to 1.20), whereas Supraflex may result in lower TVMI (HR 0.46, 95%CrI 0.13 to 1.11). Forest plots are shown in Figure 6.

The relative treatment effect of all pairwise comparisons is summarised in Appendix G. There is clear evidence showing Resolute Onyx has meaningful beneficial effect on TLR compared to BioMatrix.

Between-study posterior mean SDs for both outcomes are indicative of low heterogeneity, though these are strongly influence by the choice of empirical prior – TLR 0.09 (95%CrI 0.00 to 0.24), TVMI 0.08 (95%CrI 0.00 to 0.22). The inconsistency assessment results in lower residual deviance and DIC in NMA for TLR, whereas in TVMI, there is no statistical evidence of inconsistency based on the model fit indices and dev-dev plot between NMA and UME model (Appendix F). Therefore, there is no evidence of inconsistency detected.

A similar trend is observed in the sensitivity analysis results where fitting a prior on heterogeneity with a higher SD leads to more uncertainty in relative effects between devices, and a higher posterior between-study SD. The long-term follow-up NMA appears to be more sensitive to the choice of prior heterogeneity than the Y1 NMA. The uncertainty surrounding treatment effects increased significantly, for example, in TLR, Ultimaster 95%CrI increased from 0.58-2.53 to 0.18-8.94, and Supraflex 95%CrI from 0.57-2.75 to 0.18-8.10. It is noted that the between-study posterior SD is almost entirely informed by the prior distribution, suggesting a more pronounced impact of data sparsity in the long-term follow-up analysis. This is because only a

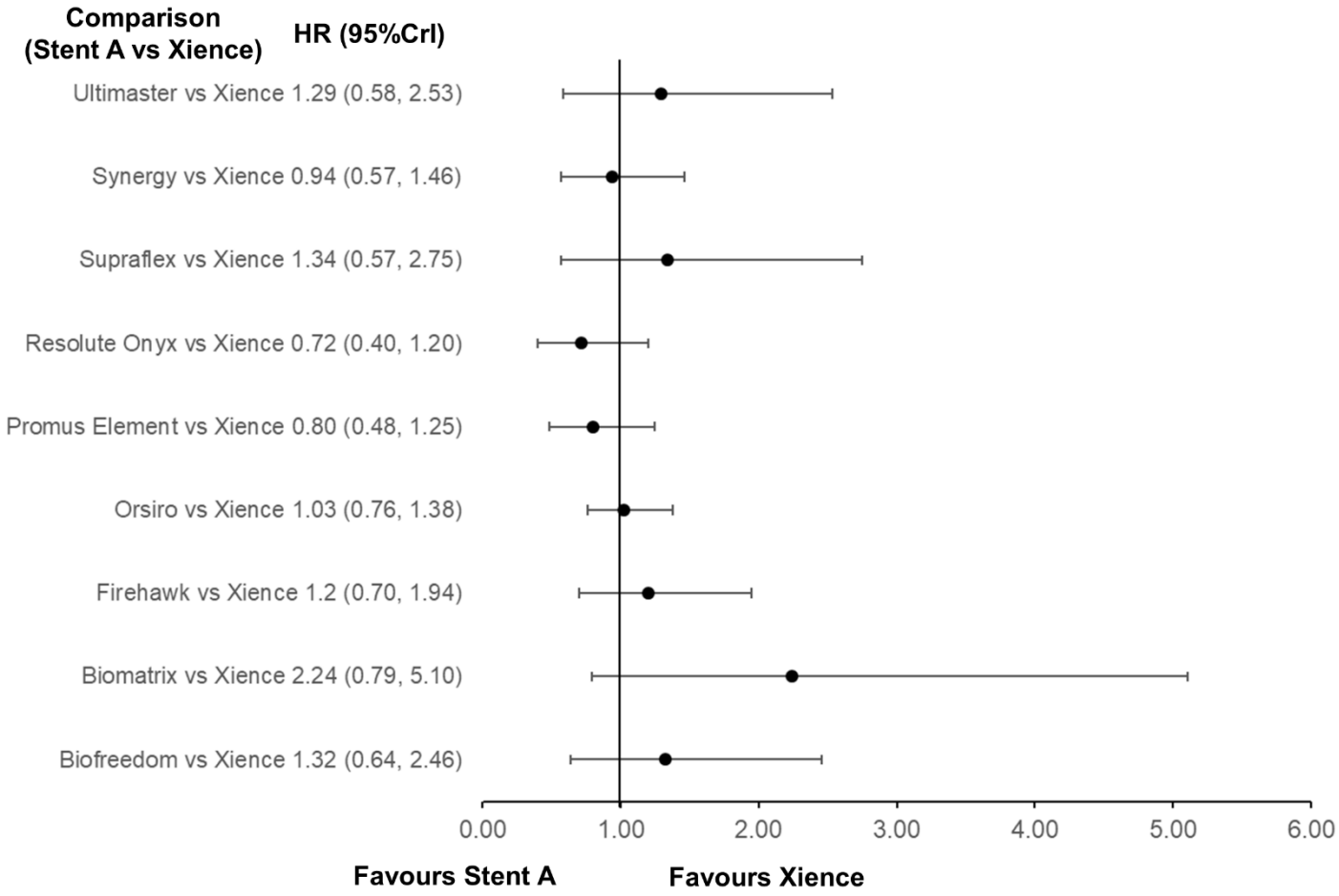
single comparison (Orsiro vs Xience) was explored in 4 studies, and one fewer trial reported outcomes at longer follow-up than in Y1. Thus, HRs from longer-term follow-up NMAs had wider CrIs than for Y1 NMA because the sparse data from very few studies were insufficient to estimate between-study posterior SD reliably.

Table 12: Results from NMA RE models using long-term follow-up data

Device	Relative treatment effect vs Xience (HR)			
	Prior heterogeneity 0.1		Sensitivity analysis: Prior heterogeneity 1.0	
	Mean	95% CrI	Mean	95% CrI
TLR				
BioFreedom	1.32	0.64, 2.46	3.57	0.21, 18.23
BioMatrix	2.24	0.79, 5.10	6.10	0.30, 26.04
Firehawk	1.20	0.70, 1.94	1.86	0.19, 7.92
Orsiro	1.03	0.76, 1.38	1.49	0.49, 4.18
Promus Element	0.80	0.48, 1.25	1.21	0.20, 4.03
Resolute Onyx	0.72	0.40, 1.20	1.85	0.11, 8.18
Supraflex	1.34	0.57, 2.75	2.50	0.18, 8.10
Synergy	0.94	0.57, 1.46	1.66	0.23, 6.28
Ultimaster	1.29	0.58, 2.53	2.63	0.18, 8.94
Between-study SD	0.09	0.00, 0.24	0.71	0.05, 1.78
TVMI				
BioFreedom	0.99	0.41, 2.04	1.14	0.28, 3.20
BioMatrix	1.58	0.12, 7.29	1.78	0.10, 8.36
Firehawk	0.97	0.62, 1.45	1.08	0.36, 2.56
Orsiro	0.92	0.62, 1.31	0.96	0.47, 1.74
Promus Element	0.86	0.40, 1.65	1.04	0.35, 2.82
Resolute Onyx	1.09	0.56, 1.92	1.25	0.32, 3.50
Supraflex	0.46	0.13, 1.11	0.52	0.10, 1.54
Synergy	0.94	0.47, 1.69	1.06	0.35, 2.66
Ultimaster	7.28	0.39, 38.93	6.63	0.36, 37.36
Between-study SD	0.08	0.00, 0.22	0.34	0.01, 1.10

***Abbreviations**: CrI: credible interval; HR: hazard ratio; SD: standard deviation; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction.*

Target Lesion Revascularisation (TLR):



Target vessel-related myocardial infarction (TVMI):

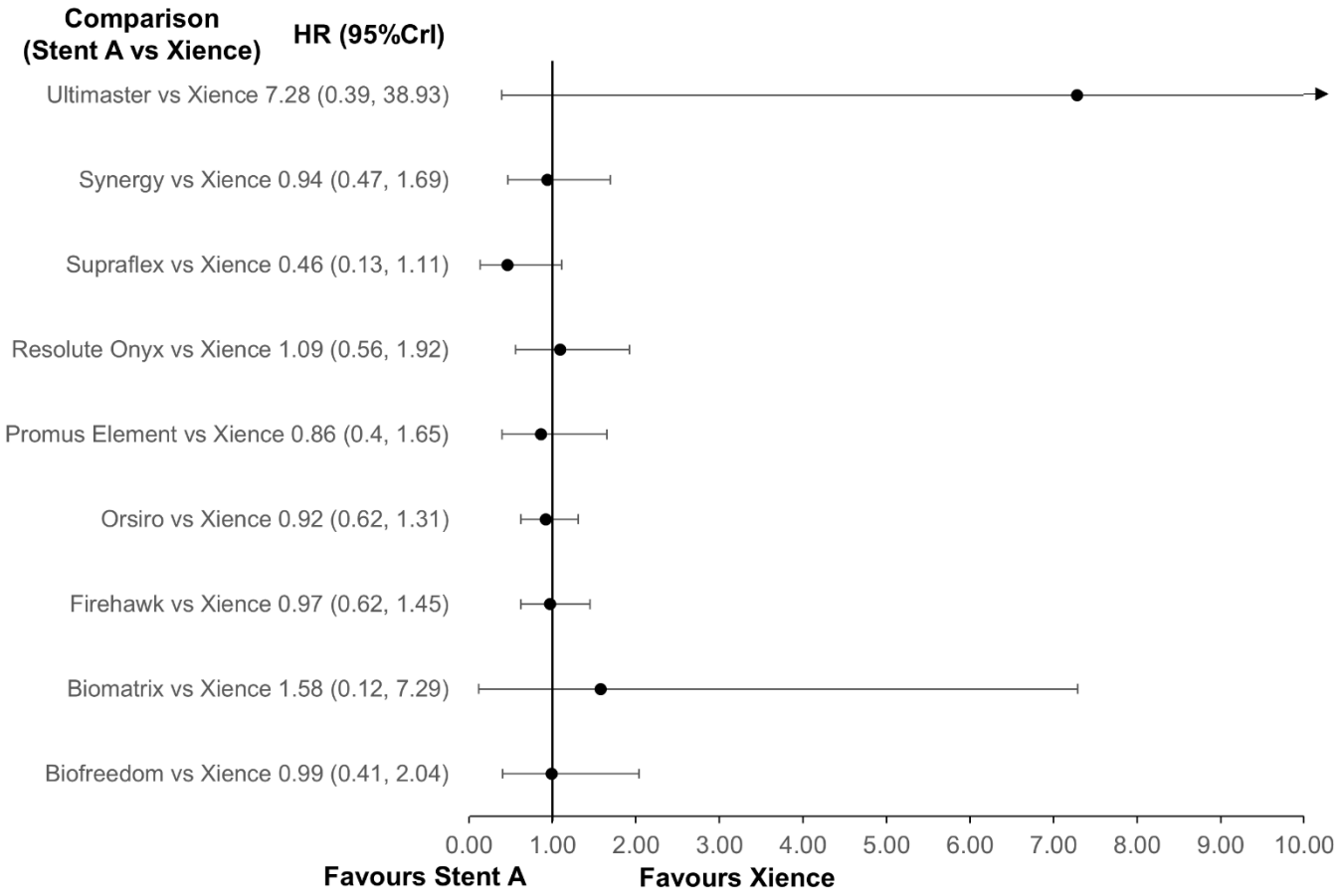


Figure 6: Forest plots: Long-term follow-up (HR with 95% CrI)

Assessment of model fitting

Model fit statistics suggest that there are no significant differences between the FE and RE model, given that the differences are less than 5-point. All model fit statistics are reported in Appendix F.

Comparison to NMA by Taglieri et al. (2020)

Taglieri et al. (2020) conducted an NMA of TLF and individual outcomes at 1 year and at long-term follow-up using 77 RCTs with 99,039 patients. A total of 10 devices were compared in this NMA, including 5 devices within the scope (BioMatrix, Orsiro, Resolute, Synergy and Xience). The EAG noted that not all of these 5 devices were compared individually in this NMA – (i) BioMatrix was combined with Nobori, a device not in the scope, as a single node, and (ii) Resolute Integrity and Resolute Onyx were combined into one "Resolute" node, however, Resolute Integrity was not considered in the EAG NMA based on the company information on clinical equivalence. As Synergy findings were not reported by Taglieri et al. (2020), the EAG were able to compare relative effect between Orsiro vs Xience reported by Taglieri et al and that of the EAG NMA.

Similar findings were noted where there were no significant differences in terms of TLR and TVMI, but narrower confidence intervals (CI) in Taglieri's results. In addition, there were some slight differences in the mean estimate for Y1 TLR – Taglieri: OR 0.94 (95%CI 0.75 to 1.17) vs EAG: HR 1.25 (95%CrI 0.84 to 1.81). As there was insufficient information on Taglieri's NMA model, it appeared that a FE model was undertaken. This will lead to a narrower CI as between-study SD is assumed to be equal to zero. The study selection undertaken by Taglieri et al. might be the key reasons on why different results were yielded – (i) papers comparing 1st generation DES and BMS were included, in order to increase the statistical power of indirect estimates, and (ii) devices that were compared in at least 3 RCTs were included in their NMA. The EAG explored the impact of Taglieri's Orsiro findings on the cost-effectiveness results in a sensitivity analysis.

Limitations

When dealing with rare events or very few studies in meta-analysis, data sparsity poses challenges in estimating between-study heterogeneity, which impacts on the precision of treatment effects in RE models (Daly et al. 2021). This means, there can

be considerable uncertainty in the resulting treatment effect when between-study heterogeneity is high or when it cannot be estimated reliably. While sparse data can be addressed in Bayesian meta-analysis through incorporating prior information, the selection of an appropriate prior distribution is important to avoid introducing bias into the analysis. Heterogeneity is not widely studied in medical devices as the current evidence base is mostly single-arm studies where it is not possible to perform meta-analysis. This is evident in the EAG NMA where data were sparse coming from 14 studies and the only available data source for most devices in the NMA was a single study. It is therefore particularly challenging to choose a suitable prior based on empirical evidence within the medical device literature.

It was noted that the posterior distribution from the between-study SD from the NMA RE model was almost entirely informed by the prior heterogeneity distribution, rather than from the trial data. This suggests that the available trial data in the NMA are not sufficient to estimate the between-study posterior mean SD. This has serious implications on the robustness of the NMA results, particularly regarding the uncertainty of treatment effects.

In addition, data used in the NMA was from non-inferiority trials and studies that were not powered for the NMA outcomes. However, given the limited evidence base, the EAG felt it was appropriate to use all available evidence that met the EAG inclusion criteria, to enable more devices to be compared in the NMA, and thus inform the economic modelling. To explore the impact of device being clinically equivalent, the EAG have perfomed a cost-comparison analysis by assuming identical clinical outcomes for all devices in the scope (Section 10). The EAG advise that the issue of data sparsity and underpowered studies leads to uncertainty in the clincal evidence and thus the economic findings. These factors should be considered in the decision-making.

The variation in study characteristics indicates that the effect modifiers are not well-balanced across trials, hence the EAG preference in fitting a RE NMA model, despite the challenges in estimating the between-study SD from the trial data. The EAG acknowledge the value of a meta-regression to investigate the impact of covariates on the pooled treatment effect. However, there are insufficient studies to explore this analysis. Given the caveats and uncertainties associated with meta analyses of

sparse data, the EAG would advise that the NMA results should be interpreted with great caution.

As with any method of quantitative evidence synthesis, the NMA will share the same limitations as the individual studies that have been included (discussed in detail in Section 5.2.3), which must be considered when interpreting results of the NMA.

Overall, none of the included studies gave rise to concern with respect to bias relating to selection and allocation of participants. Additionally, statistical conclusion validity criteria were met by all studies except two which did not conduct ITT analysis after the one year timepoint (EVOLVE II and PLATINUM). Treating clinicians being aware of the treatment assignment may introduce an aspect of performance bias, but this was present in all 14 studies included in the NMA and it could be argued that as stents are visually different, blinding is not possible. In two of the 14 studies (BIO-RESORT and CASTLE), it was stated that participants received treatment further to the PCI procedure at the clinician's discretion and in one study (SORT-OUT IX) it was not clear if participants were treated identically apart from the intervention of interest; this may have impacted on long-term clinical outcomes. In three of the 14 studies (BIODEGRADE, BIOFLOW IV and CASTLE), outcome assessors were not blinded to the treatment assignment, which could introduce measurement bias. Four of the 14 studies did not lose any participants to follow-up or sufficiently addressed loss to follow-up (CASTLE, SORT OUT IX, SORT OUT VIII and TARGET); loss to follow-up was not handled or analysed adequately in six studies (BIODEGRADE, BIOFLOW IV, BIOFLOW V, BIOSCIENCE, CENTURY II and EVOLVE II) and it was unclear if loss to follow-up was adequately addressed in the remaining four studies (BIONYX, BIO-RESORT, PLATINUM and TALENT). Loss to follow-up may reduce the robustness of results but it should be noted that studies were appraised at their most recent timepoint, and so issues with loss to follow-up may not apply at earlier timepoints.

6 Additional clinical evidence

In addition to the key RCTs discussed in Section 5, the EAG identified a large volume of other types of evidence which related to the devices in scope, but were not considered to be key studies for this assessment as they were not deemed appropriate for inclusion in the network meta-analysis or economic modelling. This evidence consisted of:

- 14 non-randomised/observational comparative studies
- 34 prospective single-arm studies
- 20 retrospective single-arm studies

Results from the non-randomised/observational comparative studies are briefly presented in Section 6.1, but are not discussed in detail.

Results were not extracted from the non-comparative studies, as this was not considered useful in answering the decision problem by the EAG and NICE. However, clinical experts indicated that the volume of clinical efficacy evidence available for specific stents, and whether there is evidence of clinical efficacy and safety in particular populations (e.g. high bleeding risk), could be useful context for decision-making. Therefore, a brief summary of these studies, including the population, intervention and setting, is included in Appendix H.

During the scoping period and user preference workshop facilitated by NICE for this LSA, the EAG noted that DAPT duration required post-procedure was of importance to clinicians involved in selecting and implanting drug-eluting stents. To address this, the EAG has summarised RCTs that were identified which compared DAPT regimens where the DES used in the procedures was one in scope (or an accepted predecessor) in section 6.2. As the duration of the DAPT regimen required post-DES implantation was not the focus of this assessment, studies presented in this section should not be viewed as a comprehensive list of studies comparing DAPT regimens post-DES implantation.

Additionally, the EAG noted in the user preference workshop held by NICE that clinical experts indicated procedural outcomes to be of interest when considering which stent to select for implantation, but not a key decision-making factor.

Therefore, the EAG has summarised any procedural outcomes that were reported in key RCTs (identified in Section 5.1) in Section 6.3. As these studies were selected pragmatically based on their relevance to the NMA and economic modelling, this is not a systematic review of procedural outcomes in relation to all of the devices in scope, and should not be interpreted as such.

6.1 *Non-randomised comparative studies*

Fifteen non-randomised comparative studies comparing devices, or groups of devices, were identified. As these trials are non-randomised and many are not comparing two named devices (and compare groups of stents instead), results from these studies are not eligible for the network meta-analysis and subsequent economic modelling. Therefore, detailed results have not been extracted from these studies and the quality of the studies has not been assessed.

The nature of the comparisons made in these studies and any notable observed differences in results are briefly summarised in Table 13 (propensity matched comparisons) and Table 14 (non-propensity matched comparisons). The EAG note that some of these studies may have overlapping populations due to data being retrieved from the same registry databases.

Table 13: Summary of non-randomised propensity matched comparative studies.

Reference	Device/group 1 (n)	Device/group 2 (n)	Overall summary of significant differences observed between groups.
Buccheri et al. 2019	Synergy, Orsiro, Ultimaster (BP-DES) (n=10,032)	Xience Prime/Xpedition, Promus Element/Element Plus/Premier, Resolute Integrity/Onyx (PP-DES) (n=47,455)	None.
Buccheri et al. 2021	Orsiro (n=4,561)	Xience Prime/Xpedition/Pro X, Promus Element/Element Plus/Premier, Resolute Integrity/Onyx, Synergy, Ultimaster (n-DES Group). (n=69,590)	TLR observed to be lower in Orsiro group (p=0.013) at 2 years. No difference in all-cause mortality or MI between groups.

Reference	Device/group 1 (n)	Device/group 2 (n)	Overall summary of significant differences observed between groups.
Buccheri et al. 2018	Synergy (n=4,889)	BioMatrix, Orsiro, Promus Element Plus, Promus Premier, Xience Xpedition, Resolute/Resolute Integrity*, Ultimaster, Resolute Onyx. ("newer-generation" DES) (n=31,403)	None.
de le Torre Hernandez et al. 2021	ihtDESTiny BD (n=350)	Durable polymer everolimus- or zotarolimus-eluting stents. (n=350)	None.
Grimfjärd et al. 2021	Any Xience (n=11,562)	Biomatrix, BioFreedom, Orsiro, Promus, Promus Element, Promus Element Plus, Promus Premier, Synergy, Endeavor*, Endeavor Resolute*, Resolute Integrity* and Resolute Onyx. (n=53,548)	None.
Han et al. 2024	Coroflex ISAR (n=559)	Orsiro (n=1449)	Orsiro associated with significantly lower TLF rate than Coroflex ISAR (1.1% versus 3.4%, p=0.01), driven by CD-TLR event rates at 1 year.
Menown et al. 2021	BioMatrix Alpha (n=400)	BioMatrix Flex (n=857)	BioMatrix Alpha associated with improved clinical outcomes compared with BioMatrix Flex at 2 years; MACE: 7.4% versus 13.4% (p=0.004).
Sarno et al. 2017	Synergy (n=4,247)	BioMatrix, Orsiro, Promus Element Plus, Promus Premier, Xience Xpedition, Resolute/Resolute Integrityα, Ultimaster, Resolute Onyx. ("newer-generation" DES) (38,110)	None.

Reference	Device/group 1 (n)	Device/group 2 (n)	Overall summary of significant differences observed between groups.
Schapiro-Dufour et al. 2019	Comparison of six 'current' DES: Xience (n=18,190), Promus (n=14,573), Resolute*(n=12,727), BioMatrix (n=4216), Nobori* (n=2634), Orsiro (n=551).		None.
Spirito et al. 2023	BioMatrix/BioMatrix Flex, Nobori* (BP-BES) (n=2321)	Other -limus eluting stents.(n=4786)	BP-BES associated with lower risk of MACE and TVF at 1 year.
Yamaji et al. 2018	Orsiro (n=1451)	Xience Prime/Xpedition (n=1451)	None.
Zanchin et al. 2019	Synergy (n=1041)	Xience Prime/Xpedition (n=1041)	None.
Key: $^{\alpha}$device out of scope.			

***Abbreviations**: BP-DES: bioabsorbable polymer drug eluting stent; CD-TLR: clinically driven-target lesion revascularisation; DES: drug eluting stent; MACE: major adverse cardiac events; PP-DES: permanent polymer drug eluting stent; TLF: target lesion failure; TLR: target lesion revascularisation; TVF: target vessel failure.*

Table 14: Summary of non-randomised non-propensity matched comparative studies.

Reference	Device/group 1 (n)	Device/group 2 (n)	Significant differences between groups.
Amirzadegan et al. 2019	Single long stents. Subgroup 1 (38mm) (n=1121): • Promus, Promus Element/ Element Plus • Resolute/Resolute Integrity$^{\alpha}$ • Xience, Xience V/Prime/Xpedition • BioMatrix/BioMatrix Flex Subgroup 2 (40mm) (n=124): • BioMime	Overlapping multiple stents (n=464).	None.
Bibi et al. 2022	Xience Prime/Xpedition (n=341).	BioMatrix NeoFlex/Alpha (n=174).	None.

Lemmert et al. 2017	Promus Premier (n=1000)	Xience Prime (n=1000)	None.
Key: [α]device out of scope.			

6.2 *RCTs comparing DAPT regimens*

The EAG identified six RCTs comparing dual antiplatelet therapy (DAPT) regimen durations post-DES implantation, where the stent(s) used in the trial are in the scope of this assessment (summarised in Table 15). These studies are presented for information only, in line with clinical expert opinion that DAPT duration given post-implantation may be considered an important factor when selecting a drug-eluting stent. In particular, the ability to shorten DAPT duration without compromising clinical outcomes is considered beneficial for patients with a high-bleeding risk. The EAG does not consider the studies discussed in this section to represent a comprehensive summary of evidence for shorter DAPT duration in conjunction with the drug-eluting stents in the scope, as this was not the focus of this assessment and a systematic review with the intention of identifying all relevant evidence has not been conducted. In five of the six RCTs, shorter DAPT regimens did not appear to worsen clinical outcomes. In one RCT (SMART-DATE), conducted in a population with ACS, the rate of MI worsened with shorter DAPT and authors concluded that the shorter DAPT regimen could not be recommended as safe.

Table 15: Summary of RCTs comparing DAPT regimens in trials using in-scope DES.

Study name (reference)	Devices	Population	DAPT Regimen 1 (n)	DAPT Regimen 2 (n)	Summary of differences observed between regimens
SMART-DATE (Hahn et al. 2018)	• Xience Prime • BioMatrix Flex • Resolute Integrity (not in scope)	ACS (including unstable angina and NSTEMI), and STEMI.	6-month DAPT (n=1357).	12-month or longer DAPT (n=1355).	• 6-month DAPT non-inferior to 12-month or longer DAPT for the primary endpoint of MACE at 18 months • Rate of MI significantly higher in the 6-month DAPT group than in the 12-month or longer group • Short-term DAPT cannot be recommended as safe
HOST-IDEA (Han et al. 2023)	• Orsiro • Coroflex ISAR	ACS (STEMI excluded).	3- to 6-month DAPT (60–150 days) (n=1002).	12-month DAPT (≥300 days) (n=1011).	• 3- to 6-month DAPT non-inferior to 12-month DAPT for primary endpoint of NACE at 12 months
MASTER DAPT (Valgimigli et al. 2021)	• Ultimaster	HBR with acute or chronic coronary syndrome.	Abbreviated DAPT (discontinue DAPT after 1 month (exact regimen dependent on OAC status)).	Standard DAPT (continue DAPT for at least 2 additional months (exact regimen dependent on OAC status)).	• Abbreviated DAPT non-inferior to standard DAPT with respect to NACE and MACCE • Abbreviated DAPT associated with significantly lower bleeding risk
ISAR-DAPT (Jin et al. 2022)	• Coroflex ISAR	Chronic SCAD or ACS (MI excluded).	3-month DAPT (n=244).	6-month DAPT (n=244).	• No observed increase in risk of primary endpoint at 12 months between two groups, but trial had limited power to detect differences.
SMART-CHOICE: Orsiro subgroup analysis (Yun et al. 2021)	• Orsiro	Mixed indications for PCI.	3-month DAPT followed by P2Y12 inhibitor monotherapy (n=481)	12-month DAPT (n=491)	• TVF rate at 1 year did not significantly differ between 3-month DAPT group (1.7%) and 12-month DAPT group (2.9%), p=0.22)
IVUS-XPL (Hong et al. 2016)	• Xience Prime	Long coronary lesions.	6=month DAPT (n=699)	12-month DAPT (n=701)	• Primary composite clinical endpoint incidence did not worsen in 6-month DAPT group (2.2%) compared to 12-month DAPT group (2.1%), p=0.854.

Abbreviations: *ACS: acute coronary syndromes; DAPT: dual anti-platelet therapy; HBR: high bleeding risk; MACCE: major adverse cardiac and cerebrovascular events; MACE: major adverse cardiac events; MI: myocardial infarction; NSTEMI: non-ST elevated myocardial infarction; NACE: net adverse clinical events; OAC: oral anti-coagulant; PCI: percutaneous coronary intervention; SCAD: stable coronary artery disease; STEMI: ST-elevated myocardial infarction; TVF: target vessel failure.*

6.3 *Procedural outcomes*

Of the 22 key RCTs identified, 16 reported technical success (or failure) rates. 11 RCTs reported clinical procedural success rates. The majority of the trials reported no difference between DES groups for either parameter (Table 16). However, technical success rates were significantly different between DES groups in the EVOLVE II, TALENT and TARGET trials. Additionally, clinical procedural success rates were significantly different between DES groups in the BIOFLOW V trial. Definitions for these outcomes varied across the evidence base, so these results should be interpreted with caution. Three of the RCTs reported fluoroscopy time and amount of contrast used. Two of these also reported procedure time. (Table 17)

Multiple factors may influence procedural outcomes such staffing, equipment and clinical facilities. Therefore, the EAG believe it would be difficult to attribute any difference in these outcomes directly to the stent itself.

Table 16: Summary of technical and clinical procedural success rates.

Trial name	*Reference*	Stents	Technical success rate	*p-value*	Clinical procedural success rate	*p-value*
ANGIOLITE	Moreu et.al., 2019	Angiolite	99.3%	0.98	99.3%	0.99
		Xience Xpedition (Pro 48)	100%		99.3%	
BIODEGRADE	Yoon et.al., 2021	BioMatrix	0.0% (failure rate)	0.319	-	-
		Orsiro	1.0% (failure rate)		-	
BIOFLOW DAPT	Valgimigli et.al., 2023	Orsiro	96.7%	NR	-	-
		Resolute Onyx	97.6%		-	-
BIOFLOW IV	Saito et.al., 2019	Orsiro	98.9%	0.67	96.1%	0.856
		Xience Prime/Xpedition (Pro 48)	99.6%		95.8%	
BIOFLOW V	Kandzari et.al., 2017	Orsiro	98%	0.415	94%	0.0191*

Trial name	*Reference*	Stents	Technical success rate	*p-value*	Clinical procedural success rate	*p-value*
		Xience	97%		90%	
BIOFREEDOM	Sabaté et.al., 2021	BioFreedom	99.3%	NR	94.4%	NR
		BioFreedom Ultra	99.4%		97.1%	
BIONYX	von Birgelen et.al. 2018	Resolute Onyx	98.4%	NR	-	-
		Orsiro	97.8%		-	
CASTLE	Nakamura et.al., 2022	Orsiro	99.6%	0.128	94.5%	0.98
		Xience Sierra (Pro S)/Xpedition (Pro 48)	99.0%		94.4%	
CENTURY II	Wijns et.al., 2018	Ultimaster	99.1%	0.23	98.0%	0.83
		Xience	99.5%		98.2%	
EVOLVE II	Kereiakes et.al., 2015	Synergy	98.3%	0.04*	94.9%	0.56
		Promus Element Plus	96.9%		94.3%	
IDEAL-LM	van Geuns et.al., 2022	Synergy	-	-	100%	1
		Xience	-		99.7%	
MERIT V	Abizaid et.al., 2018	BioMime	-	-	99.4%	0.21
		Xience V	-		98.8%	
PLATINUM	Stone et.al., 2011	Xience V	98.8%	0.14	98.2%	0.83
		Promus	99.4%		98.3%	
SORT OUT IX	Jensen et.al., 2020	BioFreedom	2.3% (failure rate)	0.48	-	-
		Orsiro	2.0% (failure rate)		-	
SORT OUT VIII	Maeng et.al., 2019	Synergy	1.8% (failure rate)	0.044	-	-

Trial name	*Reference*	Stents	Technical success rate	*p-value*	Clinical procedural success rate	*p-value*
		BioMatrix	3.0% (failure rate)		-	
TALENT	Zaman et.al., 2019	Supraflex	97.6%	0.0003*	-	-
		Xience	99.5%		-	
TARGET	Lansky et.al., 2018	Firehawk	92.4%	0.025*	-	-
		Xience	94.8%		-	
XLIMIT	Testa et.al., 2023	Synergy	100%	0.2	98%	0.1
		Xlimus	99%		97%	

Key:
* indicates statistically significant difference reported in study.

Abbreviations: *NR: not reported.*

Table 17: Summary of additional procedural outcomes.

Trial name	Reference	Stents	Procedure time	*p-value*	Fluoroscopy time	*p-value*	Amount of contrast used	*p-value*
PLATINUM	Stone et.al., 2011	Xience V	-	-	11.3±10.1 mins	0.1	184±86 (cc)	0.85
		Promus	-		12.2±11.8 mins		185±87 (cc)	
SORT OUT IX	Jensen et.al., 2020	BioFreedom	24.0 (15.0-39.0)	0.03*	7.0 (4.0-12.7)	0.08	80.0mL (50.0-120.0)	0.04*
		Orsiro	23.0(15.0-36.0)		7.0 (4.0-12.7)		80.0mL (50.0-110.0)	
SORT OUT VIII	Maeng et.al., 2019	Synergy	20 (13–33) mins	NR	6.0 (3.4–10.5) mins	NR	80 (50–110) mL	NR
		BioMatrix	21 (14–34) mins		6.0 (3.5–11.0) mins		80 (50–120) mL	

Key:
* indicates statistically significant difference reported in study.

Abbreviations: *NR: not reported.*

7 Economic evidence evaluation methods

7.1 *Evidence search strategy and study selection*

The EAG conducted literature searches to identify relevant economic literature. The EAG literature search for economic studies identified a total of 263 records. Details of the EAG searches are provided in Appendix B.

Given that the EAG economic literature aimed to identify a suitable model structure, relevant costs and utility values, the literature searches were not screened for published economic studies of technologies in the scope. The proposed inclusion criteria were slightly amended as the models in NICE guidance were found to be heterogeneous in terms of model structure and health states included. Therefore, they were been broadened to include any relevant economic models related to PCI or DES, from the original protocol which was limited to UK-based economic model papers.

The 263 records were screened at title and abstract by one reviewer, and a second reviewer checked a random 20% of the excluded records. Records were then sifted at full-text by a single reviewer. The EAG noted that 2 HTA reports and 1 peer-reviewed paper reported the same modelling approach with the same or updated model inputs as NICE guidance TA71 and TA152, hence these papers were excluded (Hill et al. 2007, Bagust et al. 2006, Hill et al. 2004).

A total of 26 studies were identified as relevant from EAG searches: 4 UK-based model papers, 1 UK-based paper on utility or quality of life, 18 non-UK model papers and 3 systematic reviews of PCI or DES-related economic evaluations. Seven additional economic papers were identified as relevant from information submitted by the companies, resulting in a total of 33 relevant studies. To ensure the comparison of relevant models and identification of UK-based model inputs, a pragmatic approach was applied to select papers for data extraction. Of the 33 relevant studies, the EAG selected 19 primary economic studies that were published after 2008 (not inclusive) as NICE guideline TA152 was first published in 2008.

Of the 19 included studies, the EAG identified a key UK-based study that reported costs and utility values that were relevant to the EAG economic model (Table 18). The UK-based economic model paper (also listed as key studies) and 18 other relevant economic model papers are summarised in Appendix I. The remaining 14 studies that did not inform the model are listed in Appendix J.

7.2 *Quality appraisal of economic studies*

Given that no existing economic models were found to be suitable, the EAG did not perform any quality appraisal.

8 Economic evidence evaluation results

8.1 *Relevant economic models*

Among the 26 studies, there were 3 NICE clinical guidelines and 19 economic evaluations that reported an economic model identified by the EAG. A total of 22 models were reviewed and summarised.

The economic models within NICE guidelines are considered to be unsuitable or insufficient to be used directly in this assessment, with the reasons listed in Table 18. Of the 19 models identified from peer-reviewed papers, only three were from a UK perspective. The remainder were from the US (n=6), Germany (n=2), Brazil (n=2), Canada, Italy, France, Mexico, Norway and Austria (Appendix I). Considerable variations in terms of modelling approach, time horizon and effectiveness outcome used are noted as follows:

- Model design: Markov model (n=13), short-term (≤ 1 year) decision-tree and lifetime Markov model (n=2), discrete simulation event (n=2), decision tree (n=1), decision analytic model (n=1)
- Markov health states: MI (n=13), revascularisation (n=12), bleeding (n=3), stent thrombosis (n=5), cardiac death (n=3), restenosis (n=2), stroke (n=2), angina (n=1)
- Markov cycle length: 1 month to 1 year
- Effectiveness outcomes used: TLR (n=8), TVR (n=5), ischemia-driven revascularization (n=1)

- Time horizon: 6 months to lifetime

There are a number of learnings related to the key issues and assumptions of the existing models. First, ST was modelled differently across models – (i) ST was explicitly excluded with authors' justification being that ST would have been captured in MI and cardiac death (Sharp et al. 2024, Turco et al. 2012), (ii) both ST and MI health states were included in the model (Ferko et al. 2016, Remak et al. 2015) or (iii) ST was considered under MACE (Baschet et al. 2016, González-Díaz et al. 2015). Similarly, for restenosis, this was not modelled separately given that it would be captured in MI and/or revascularisation (Wisloff et al. 2013). Second, TLR or TVR was used as the effectiveness measure in the existing models. However, the authors did not provide any reasons for the choice.

Table 18: Economic models in NICE guidelines.

Topic	Year	Population	Intervention(s) and comparator	Time horizon	Model structure	EAG comment
Coronary artery stent (TA71)	2003	Coronary heart disease	Stent vs coronary artery bypass and graft in 2vd Stent (BMS) vs drug-eluting stent (DES) in 1vd	5 years	The model considers survival profile of each event (AMI, stroke, adverse event following a revascularisation procedure – acute renal failure, serious bleeding)	The modelling approach using survival curves to estimate state membership can be data-intensive. Extrapolation to long term will require additional information on hazard rates beyond trial data. This increases the model uncertainty if relevant data is not available. Because of the chronic nature of coronary heart disease, the EAG thinks a Markov model is appropriate to simulate the disease progression.
Stable angina (CG126)	2011	Stable angina	CABG vs PCI (with DES or bare-metal stents or both)	10 years	Markov model with a 6-month cycle length. Health states: MI, revascularisation, death, angina, no angina	The model structure appears to be suitable to some extent, however key outcomes including bleeding, stent thrombosis, restenosis are not explicitly modelled or not included.
Drug-eluting stents (TA152)	2020	Coronary artery disease	DES vs BMS	1 year	A simple economic model of costs and outcomes, which considers TVR only	Given the short time horizon and lack of other clinical events, the total costs and outcomes is likely to be underestimated.

***Abbreviations**: AMI: acute myocardial infarction; BMS: bare metal stent; CABG: coronary artery bypass graft; DES: drug-eluting stent; EAG: External Assessment Group; MI: myocardial infarction; PCI: percutaneous coronary intervention; TA: technology appraisal; TVR: target vessel revascularisation.*

8.2 *Published economic evidence*

The EAG have identified one study reporting relevant information such as costs and utilities. The reported data are considered to be relevant to be used as model inputs in the EAG model. The paper is summarised in Table 19.

Table 19: Key studies selected for the economic model

Study name, design and location	Intervention(s) and comparator	Participants and setting length of follow-up	Relevant outcomes and key findings	EAG comments
Sharp et al. (2024) Cost-effectiveness analysis UK Published article	**Intervention:** IVUS-guided PCI **Comparator:** PCI with angiography alone	**Participants:** Patients with ACS **Setting/model structure:** 1-year decision tree and lifetime Markov model **Follow-up:** Lifetime	**Primary outcome:** • ICER per QALY gained • Incremental NMB	The model applied utility values from UK sources (NICE TA236 and NICE TA152). The authors reported IVUS costs per procedure using a microcosting approach.

***Abbreviations**: ACS: acute coronary syndrome; ICER: incremental cost-effectiveness ratio; IVUS: intravascular ultrasound; NMB: net monetary benefit; PCI: percutaneous coronary intervention; QALY: quality-adjusted life year; UK: United Kingdom.*

9 Economic modelling methods

Although the model structure in NICE guidance CG126 shares some similarities with most of the published models, a number of changes or adaptation in terms of health states, model inputs and incorporating multiple devices are needed for the context of this assessment. The EAG initially conceptualised a de novo model. Feedback from clinical experts was sought during the consultation, and incorporated into the EAG model. Given that PCI has no effect on the development of a new lesion (Hill et al. 2007), and with clinical expert feedback, the EAG think that the focus of the economic model should be on stent-related complications and outcomes. The model was further modified based on the EAG NMA where only TLR and TVMI were analysed in Section 5.2. The final EAG model was developed in Microsoft Excel® (Microsoft Corp., Redmond, WA), and it is noted that it shares some similarities with that of Sharp et al. (2024).

The economic analysis was performed in line with the NICE reference case, with an NHS and Personal Social Services perspective. Costs and quality-adjusted life years (QALYs) were discounted at 3.5% per annum. All costs were expressed in 2023 prices, and inflated using NHS Cost Inflation Index (NHSCII) where applicable.

A 1-year time horizon was used in the base case analysis, guided by the EAG NMA findings. While there is substantial uncertainty with the NMA estimates, the first-year NMA results could be estimated more reliably compared to the long-term follow-up. In the sensitivity analysis, a 5-year time horizon was evaluated as this was the longest study follow-up period among the trials included in the NMA. The risk of clinical events was assumed to be constant after the first-year follow-up in the sensitivity analysis. As the EAG is undertaking a stent-specific approach in the model, a lifetime horizon might not be appropriate. Using a lifetime horizon, patients' natural disease progression should be considered in the model, in which the risk of developing de novo lesions and other complications increases over time, leading to higher mortality risk. As such, the cost-effectiveness results may be outweighed by the impact of disease progression, rather than providing information on the economic impacts of the stents. In addition, by extrapolating final study results to a lifetime, this may not adequately reflect the true disease progression, thus the cost-effectiveness findings might be overestimated.

The comparator in the economic model was Xience Pro S, as Xience was the most studied device in the EAG NMA, and therefore the cheapest Xience device was chosen.

Compared to incremental cost-effectiveness ratio (ICER), net monetary benefit (NMB) is more straightforward to interpret for comparisons of multiple interventions in an economic evaluation. Net monetary benefit allows ranking of devices from most to least cost-effective, and eliminates the ambiguity of interpreting a positive or negative ICER. Using the willingness-to-pay (WTP) threshold of £20,000 per QALY in the base-case, the net monetary benefit of each device was calculated:

NMB = QALYs x λ – Cost, where λ is the pre-defined WTP threshold.

9.1 *Model structure*

The EAG Markov model with 1-year cycle length included 7 health states: no further event, TLR, TVMI, TVMI-repeat revascularisation, post-revascularisation, post-MI and death. A schematic of the EAG model is provided in Figure 7. This was developed based on the findings from literature in Section 8.2, feedback from clinical experts and EAG NMA output were considered.

The choice of efficacy measure (TLR or TVR) in the EAG model may have an impact on the costs and outcomes. TLR is a subset of TVR, where the restenosis occurs in the already stented lesion (TLR), rather than any place in the target vessel (TVR). Clinical experts have indicated TLR is more specific to stents, while TVR can be influenced by patient and operator factors. It is also found that disease progression contributes up to 47% of TVR (Muradi et al. 2012). In addition, disease progression might vary given the heterogeneity of patient characteristics across trials, resulting in TVR variability. This suggests that TLR is a more appropriate measure to be used in the EAG model.

To minimise double-counting, ST and in-stent restenosis (ISR) were not modelled explicitly in the EAG model. This is because of the high variability of trial data reporting – MI and TLR/TVR are often reported as aggregated values respectively without any breakdowns on MI categories or reasons for repeated revascularisation. Therefore, it is not possible for the EAG to extract relevant information from the trials to populate the model accurately such as the proportion of MI and of

revascularisation related to ST and ISR. A number of assumptions were made in the EAG model – (i) all TVMI in the model were related to in-stent restenosis or stent thrombosis, and (ii) all TLR cases had angina symptoms, although in reality patients might experience other ischaemic symptoms such as shortness of breath.

A hypothetical group of 66-year-old patients with coronary artery disease following an index PCI procedure with DES entered the Markov model through the no further event state. They may transition to another health state or remain. Those who had TVMI may survive or die, those that survived would undergo a repeated revascularisation. These patients would move to the post-MI state and remain in that state until they died. The model assumed that patients who had a TLR and survived from the repeated revascularisation would transition to the post-revascularisation state and remain there until they died. Patients would be at risk of procedural-related death during PCI. Death is an absorbing state where patients would remain once entered.

Some events (TVMI, TLR) are transient and do not last a 1-year cycle in reality, however the EAG did not adjust for the length of disutility associated with these events. This is because of the short time horizon used in the analysis, and the lack of information on the time needed to recuperate from the event to enable utility to be adjusted in the model. Therefore, the total QALYs might be underestimated

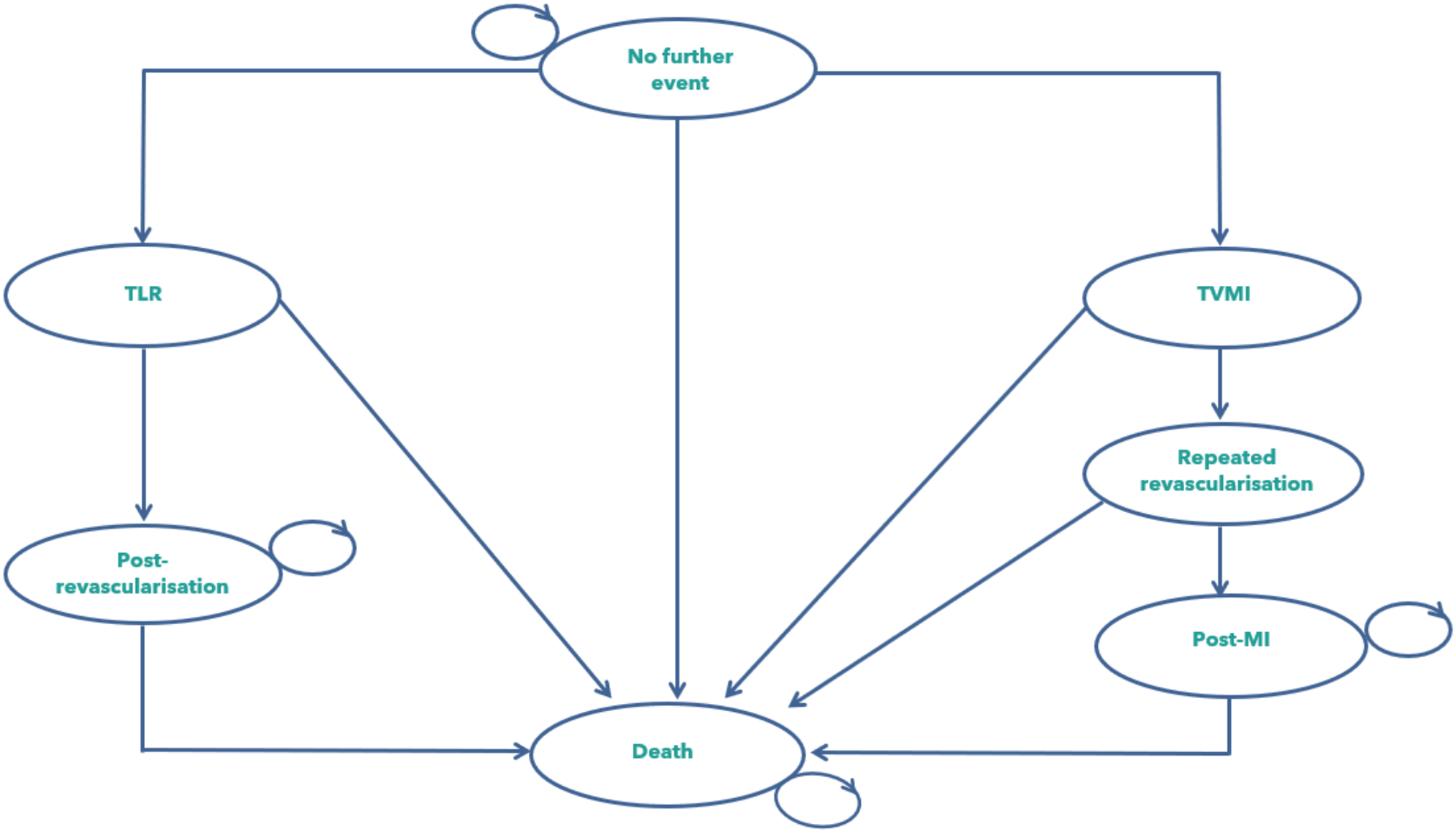


Figure 7: Schematic representation of the EAG economic model

9.2 *Model assumptions*

- The model assumes that patients receive an additional DES revascularisation with the same DES as the index procedure. In reality, patients could have several repeated revascularisations with different DES implantation. This is a simplification, however there is limited data on repeated procedure to allow further modelling.

- To simplify the clinical pathway, the model assumes that patients are treated with DES implantation in their repeated revascularisation, despite a number of alternative treatments are available in reality including drug-eluting balloons, CABG.

- The risk of TLR and TVMI is assumed to be constant after the first-year follow-up.

9.3 *Clinical parameters*

Patient characteristics:

The patient demographics used in the model is based on the NICOR PCI annual report and NICOR PCI audit in 2022.

The index procedure, and any subsequent procedures are assumed to use a mean of 1.33 stents per patient, also based on NICOR PCI audit data from 2022. Subsequent PCI procedures are assumed to use the same stent as the index procedure.

Probabilities of TLR and TVMI associated with Xience:

The baseline TLR and TVMI probabilities are taken from Xience arm of 5-year RCTs in the EAG NMA (BIOFLOW IV, BIOFLOW V, BIOSCIENCE, CENTURY II, PLATINUM). The probabilities are calculated using the formula described in Section 4.3 and converted to yearly probabilities for the model. The baseline effect should be specific to UK NHS population (Dias et al. 2012), however the EAG were not able to identify any more relevant data sources. Therefore, the approach of using the same trials to derive relative treatment effects in the NMA was undertaken.

The probabilities of TLR and TVMI for other devices were calculated by multiplying the baseline probabilities for Xience with the mean HR estimated for each device in the NMA.

Mortality risk:

The baseline mortality risk is taken from the Office of National Statistics (ONS) for the UK population, using the patient age for each year of the model. Standardised mortality rates (SMR) reported in NICE NG185, and derived from Smolina et al. (2012) were used to incorporate the additional risk of death in the states of No further event (following the index PCI), post revascularisation without TVMI, TVMI and post TVMI.

The probability of death following revascularization is taken from the 30-day mortality risk following PCI reported by NICOR in the 2024 annual report.

Table 20: Clinical parameters used in the model

Variable	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
Proportion male	75.2%	NICOR PCI annual report	PCI Audit Slide Deck, Demographics, slide 44, 2022 data
Mean age	66	NICOR PCI annual report	PCI Audit Slide Deck, Demographics, slide 44, 2022 data
Mean stents per procedure	1.33 (1.30-1.35)	NICOR PCI annual report	PCI Audit Slide Deck, weighted mean of all data on number of stents per PCI. Mean Stents by Hospital, slide 72
Mortality risk following PCI	2.655% (2.602-2.708%)	NICOR PCI annual report	PCI Audit Slide Deck, weighted mean of all data on 30 days mortality. Adverse outcomes, slide 183
General population mortality	Age and sex dependent	ONS 2024 (UK national life table)	Adjusted for the population in the model
Risk of clinical events with Xience, year 1:			
TLR	2.322% (2.320-2.323%)	EAG calculation	Pooled first year event of Xience arm in 5-year studies (BIOFLOW IV, BIOFLOW V, BIOSCIENCE, CENTURY II, PLATINUM)
TVMI	3.184% (3.182-3.186%)	EAG calculation	
Risk of clinical events with Xience, year 2-5:			

Variable	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
TLR	1.210% (1.207-1.213%)	EAG calculation	Calculated using total event at year 5 and event at year 1 of Xience arm in 5-year studies, and converted to yearly probabilities
TVMI	0.492% (0.491-0.493%)	EAG calculation	
SMR No further event	2.00 (1.99-2.01)	NICE NG185	Derived from Smolina et al. 2012, also used in Sharp et al. 2023.
SMR Reinfarction	4.50 (4.43-4.57)	NICE NG185	Derived from Smolina et al. 2012, also used in Sharp et al. 2023.
SMR Post reinfarction	3.00 (2.95-3.05)	NICE NG185	Derived from Smolina et al. 2012, also used in Sharp et al. 2023.

Abbreviations: *EAG: External Assessment Group; NICOR: National Institute for Cardiovascular Outcomes Research; ONS: Office for National Statistics; PCI: percutaneous coronary intervention; SMR: standardised mortality ratios; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction.*

9.4 *Resource use and cost parameters*

All costs are inflated to 2022/23 prices if needed, using the PSSRU indices for inflation. NHS Cost Collection data is taken from the 2021/22 tables, and inflated to 2022/23. This is due to the 2022/23 costs having been withdrawn and the updated version not yet being available.

Stent costs:

All stent costs have been provided by NHS Supply Chain, and are calculated as a weighted average of the purchase costs for all stents purchased through NHS Supply chain in 2023. For some devices the numbers are very small, leading to less certainty on the costs. Where there were no sales made via NHS Supply Chain in 2023, including where the device was not yet available on NHS Supply Chain, it was discussed and agreed by NHS Supply Chain to use NHS framework price for these devices. All costs are excluding VAT. The costs listed in Table 21 are not the same as those in the NHS Supply Chain catalogue as Trusts will negotiate their own prices based on volume of sales or other factors.

All companies were asked, by the EAG, about available training and the associated costs. Where companies responded, the training was provided to Trusts free of

charge. The provision of training varied, with some companies providing one day workshops for specialised aspects such as bifurcation, and some Trusts opting to provide training in-house as needed. Due to the relatively small amount of training required to change from one type of stent to another, the costs of staff time have not been included in the model. The EAG have listed the training offered by different suppliers in a separate table in Appendix K.

Table 21: Stent costs used in the model

BRAND	SUPPLIER	2023 Weighted Average Cost (exc. VAT)	2023 Min-Max cost (exc. VAT)	Included in NMA
Angiolite	GAP MEDICAL	[redacted]	[redacted]	
BioFreedom	BIOSENSORS	[redacted]	[redacted]	✓
BioFreedom Ultra	BIOSENSORS	[redacted]	[redacted]	✓
BioMatrix Alpha	BIOSENSORS	[redacted]	[redacted]	✓
BioMime	MERIL	[redacted]	[redacted]	
BioMime Branch	MERIL	[redacted]	[redacted]	
BioMime Morph	MERIL	[redacted]	[redacted]	
Coroflex ISAR NEO	B BRAUN	[redacted]	[redacted]	
EverMine 50	MERIL	[redacted]	[redacted]	
Firehawk	MICROPORT	[redacted]	[redacted]	✓
Firehawk Liberty		[redacted]	[redacted]	
ihtDEStiny BD	ACROSTAK	[redacted]	[redacted]	
MAGMA	LEIB MEDICAL LTD	[redacted]	[redacted]	
Onyx Frontier	MEDTRONIC	[redacted]	[redacted]	✓
Orsiro Mission	BIOTRONIK	[redacted]	[redacted]	✓
Promus ELITE	BOSTON SCIENTIFIC	[redacted]	[redacted]	✓
Supraflex Cruz	SAHAJANAND MEDICAL TECHNOLOGIES	[redacted]	[redacted]	✓
Supraflex Cruz Nevo	SAHAJANAND MEDICAL TECHNOLOGIES	[redacted]	[redacted]	✓
Synergy MEGATRON	BOSTON SCIENTIFIC	[redacted]	[redacted]	
Synergy XD	BOSTON SCIENTIFIC	[redacted]	[redacted]	✓
Synsiro Pro	BIOTRONIK	[redacted]	[redacted]	✓
Ultimaster Nagomi	TERUMO	[redacted]	[redacted]	✓
Ultimaster Tansei	TERUMO	[redacted]	[redacted]	✓
XIENCE PRO 48	ABBOTT	[redacted]	[redacted]	✓
XIENCE PRO S	ABBOTT	[redacted]	[redacted]	✓
XIENCE SKYPOINT	ABBOTT	[redacted]	[redacted]	✓
XIENCE Skypoint 48	ABBOTT	[redacted]	[redacted]	✓
XIENCE Skypoint LV	ABBOTT	[redacted]	[redacted]	✓
XLIMUS	AQUILANT	[redacted]	[redacted]	

[redacted]

Abbreviations: *NMA: network meta-analysis; VAT: value added tax.*

Procedure costs, excluding stents:

The cost of the PCI procedure is taken from a weighted average of all HRG codes [redacted], using NHS Cost Collection 20121/22, inflated to 2023. The cost of 1.33 stents was then removed from the procedure cost, based on the weighted average of all stents supplied by NHS Supply Chain in 2023. The cost of each device in the model was then added, for 1.33 stents.

Follow-up costs post-PCI:

Follow up costs after PCI include cardiac rehabilitation, one outpatient appointment and 12 months of DAPT therapy. The cost of DAPT therapy is based on the proportion of people who receive Ticagrelor or Prasugrel, as reported in NICOR audit data, with the remained assumed to receive Clopidogrel.

Other costs:

The cost of MI is calculated based on [redacted] applied to all those in the model who experience TVMI after the index PCI procedure.

Costs for those who experience no further event, and those in the post revascularisation states are taken from [redacted], and based on an analysis of a large UK data set [redacted]

Table 22: Resource use and cost parameters

Variable	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s

Cost of revascularisation:			
Total cost	[redacted]	[redacted]	[redacted]
Total cost with mean stent cost removed	[redacted]		[redacted]
Follow-up after PCI:			
Cardiac rehabilitation	[redacted]	[redacted]	[redacted]
Outpatient appointment	[redacted]	[redacted]	[redacted]
DAPT for 12 months (360 days):			Aspirin is not included, as it is received by all patients and is negligible due to the very small costs
Prasugrel 10mg	[redacted]	[redacted]	[redacted]
Ticagrelor 90mg	[redacted]	[redacted]	[redacted]
Clopidogrel 75mg	[redacted]	[redacted]	[redacted]

Proportion Ticagrelor	30.90% (24.71-37.07%)	NICOR PCI annual report	NICOR 2024 Annual Summary Report, percentage use on 2022/23. Newer P2Y12 antiplatelet drugs, Slide 23
Proportion Prasugrel	5.90% (4.70-7.06%)	NICOR PCI annual report	NICOR 2024 Annual Summary Report, percentage use on 2022/23. Newer P2Y12 antiplatelet drugs, Slide 23
Additional Markov state costs:			
Cost of no further event	[redacted]	[redacted]	[redacted]
Cost of MI	[redacted]	[redacted]	[redacted]
Cost of post-repeat revascularisation	[redacted]	[redacted]	[redacted]

***Abbreviations**: DAPT: dual antiplatelet therapy; HRG: healthcare resource group; NHS: National Health Service; PCI: percutaneous coronary intervention; PSSRU: Personal Social Services Research Unit.*

9.5 *Health state utilities*

Patients were assigned to different utility values for each health state in the model. The utility values were sourced from various NICE guidelines, or following the methods used by Sharp et al. (2024) and NICE NG185. Both of these models were based on earlier work used in NICE TA236 that used EQ-5D-3L data completed by patients with acute coronary syndrome. The quality of life data was collected across 52 participating countries, however a UK valuation tariff was applied. The Repeat PCI utility is based on the utility of no further event, with a disutility value applied of 0.0052, from NICE TA71.

Table 23: Utility values

Variable	Value	Source	EAG commentary on availability, quality, reliability and relevance of the source/s
No further event	0.842 (0.838-0.846)	Sharp et al. 2024, NICE TA236	
Repeat PCI	0.836 (0.836-0.837)	Sharp et al. 2024, NICE TA152	Disutility compared to "No further event state" due to PCI procedure, as calculated in NICE TA152. Original data includes a small proportion of CABG patients.
MI, disutility	0.240 (0.205-0.275)	NICE CG126	NICE CG126 estimated this value using a HTA report by Ward et al. (2007) obtained by Goodacre et al. (2004). The value was derived from patients who had a diagnosis of MI at a chest pain observation unit.
Angina, disutility	0.170 (0-0.374)	NICE TA152	Taken from TA152 model
Post-MI	0.821 (0.747-0.895)	Sharp et al. 2024, NICE TA236	NICE TA236 reported adjusting this value using additional information from Lacey et al. 2003. The value has been accepted by subsequent assessment work.
Post-repeat PCI	0.842 (0.838-0.846)	Sharp et al. 2024, NICE TA236	Assumes the same as no further event, an approach undertaken by Sharp et al. (2024).

***Abbreviations**: CABG: coronary artery bypass graft; HTA: health technology assessment; PCI: percutaneous coronary intervention; TA: technology appraisal.*

9.6 *Sensitivity analysis*

A probabilistic sensitivity analysis (PSA) was conducted to account for parameter uncertainty in the economic model using a second-order Monte Carlo simulation. A distribution was assigned to each parameter. Model inputs were sampled from the assigned distribution through 10,000 replicates, to give cost and QALY pairs. The assigned distribution of each model input as follows:

- Baseline event probabilities and utilities were assigned to a beta distribution,
- Disutility to a gamma distribution,
- Relative treatment effect and standardised mortality ratio to a lognormal distribution, and

- Cost input to a uniform distribution.

The reported 95%CI or standard error was used to calculate the parameters (α, β) for the probability distribution. Otherwise, an arbitrary range of ±20% was used if the range was not available from published literature. The mean costs, QALYs and NMBs of each device, alongside 95%CI were calculated using the 10,000 iterations.

A NMB plot was generated to summarise graphically the mean and 95%CI of NMB for each device. A cost-effectiveness acceptability curve (CEAC) was produced using the PSA iterations, to determine the probability of highest NMB at a range of WTP per QALY threshold.

9.7 *Scenario analysis*

A number of scenario analyses were undertaken to explore the impact of different scenarios on the cost-effectiveness findings:

- using relative treatment effect generated using a higher prior heterogeneity distribution
- a longer time horizon of 5 years using the relative treatment effect in the long-term follow-up (prior heterogeneity distribution 0.1 and 1.0)
- using the minimum and maximum stent price, as indicated by NHS Supply Chain or ±20% if no information is available
- the treatment effect for Orsiro vs Xience reported by a previous NMA by Taglieri et al. (2020): TLR OR 0.94 and TVMI OR 0.84
- Using a higher WTP threshold, £30,000 per QALY

In addition, given that the EAG NMA did not show any significant differences between devices and the primary studies are mostly non-inferiority studies, a cost-comparison analysis was performed, assuming no differences in treatment effect between devices. All 29 devices in the scope were included in this analysis to determine costs and NMB of each device.

9.8 *Model validation*

For model validation, the model was reviewed and checked by a second health economist independently. The checks include calculations used to estimate model inputs, patient movement between health states and result calculation that give total costs, QALYs and NMB. All model inputs were checked against their primary source, and model inputs were varied to check if the results were consistent with a priori expectations.

10 Economic modelling results

10.1 *Base case results*

The base case results are for a 1-year time horizon, from an NHS and personal social services perspective. The NMB is calculated using a WTP threshold of £20,000.

The base case results indicate that there is a small variation in NMB of [redacted] (NMB range: [redacted] to [redacted]) across all 18 devices, which is [redacted] of the highest NMB. A small range of [redacted] QALYs and [redacted] costs at 1 year was noted, across these devices. Although Promus Elite is found to yield the highest NMB of [redacted] at the WTP threshold, there is a modest NMB difference of [redacted] between Promus Elite and Firehawk. Promus Elite accrues the highest QALYs ([redacted]) at 1-year follow-up (Table 24). This might be driven by Promus Elite effect on TVMI reduction.

Table 24: Base case results

Device	Costs	QALYs	NMB at WTP £20,000
Promus ELITE	[redacted]	[redacted]	[redacted]
Firehawk	[redacted]	[redacted]	[redacted]
Supraflex Cruz	[redacted]	[redacted]	[redacted]
Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
Ultimaster Tansei	[redacted]	[redacted]	[redacted]
XIENCE PRO S	[redacted]	[redacted]	[redacted]
Orsiro Mission	[redacted]	[redacted]	[redacted]
Ultimaster Nagomi	[redacted]	[redacted]	[redacted]

XIENCE PRO 48	[redacted]	[redacted]	[redacted]
Synsiro Pro	[redacted]	[redacted]	[redacted]
XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
Synergy XD	[redacted]	[redacted]	[redacted]
Xience Skypoint LV	[redacted]	[redacted]	[redacted]
Skypoint	[redacted]	[redacted]	[redacted]
Onyx Frontier	[redacted]	[redacted]	[redacted]
BioMatrix Alpha	[redacted]	[redacted]	[redacted]
BioFreedom Ultra	[redacted]	[redacted]	[redacted]
BioFreedom	[redacted]	[redacted]	[redacted]

***Abbreviations**: QALY: quality-adjusted life year; NMB: net monetary benefit; WTP: willingness to pay.*

10.2 *Sensitivity analysis results*

Results from the PSA show that Promus Elite yields the highest NMB of mean [redacted] (95% CI [redacted] to [redacted]) (Table 25). When results are summarised graphically in Figure 8, it shows that 95%CI NMB for all devices are overlapping. This reflects the considerable uncertainty associated with the model inputs, which is likely due to the wide CrI in relative treatment effect of each device.

Based on the 10,000 iterations, the probability of achieving the highest NMB was less than 30% for all devices. From the CEAC, Firehawk is found to have the highest probability of yielding the greatest NMB, [redacted] at the WTP £20,000 (Figure 9). Promus Elite is associated with a [redacted] chance of having the highest NMB, despite generating the highest NMB in base case analysis. Apart from the variation in treatment effects, this might be driven by the stent price range used in the PSA where an arbitrary ±20% was used for Firehawk and the NHS Supply Chain maximum and minimum price for Promus Elite. The EAG noted that the price varied by an average of 13% to 24% from the average stent price on the NHS Supply Chain, indicating that a ±20% price variation was plausible.

Table 25: Results of probabilistic sensitivity analysis

Device	Costs (95%CI)	QALYs (95% CI)	NMB at WTP £20,000 (95%CI)	Probability of highest NMB

Promus ELITE	[redacted]	[redacted]	[redacted]	[redacted]
Firehawk	[redacted]	[redacted]	[redacted]	[redacted]
Supraflex Cruz	[redacted]	[redacted]	[redacted]	[redacted]
Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]	[redacted]
XIENCE PRO S	[redacted]	[redacted]	[redacted]	[redacted]
Ultimaster Tansei	[redacted]	[redacted]	[redacted]	[redacted]
Ultimaster Nagomi	[redacted]	[redacted]	[redacted]	[redacted]
Orsiro Mission	[redacted]	[redacted]	[redacted]	[redacted]
XIENCE PRO 48	[redacted]	[redacted]	[redacted]	[redacted]
Synsiro Pro	[redacted]	[redacted]	[redacted]	[redacted]

XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]	[redacted]
Xience Skypoint LV	[redacted]	[redacted]	[redacted]	[redacted]
Skypoint	[redacted]	[redacted]	[redacted]	[redacted]
Synergy XD	[redacted]	[redacted]	[redacted]	[redacted]
BioMatrix Alpha	[redacted]	[redacted]	[redacted]	[redacted]
Onyx Frontier	[redacted]	[redacted]	[redacted]	[redacted]
BioFreedom Ultra	[redacted]	[redacted]	[redacted]	[redacted]
BioFreedom	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations*: CI: confidence interval; QALY: quality-adjusted life year; NMB: net monetary benefit; WTP: willingness to pay.*

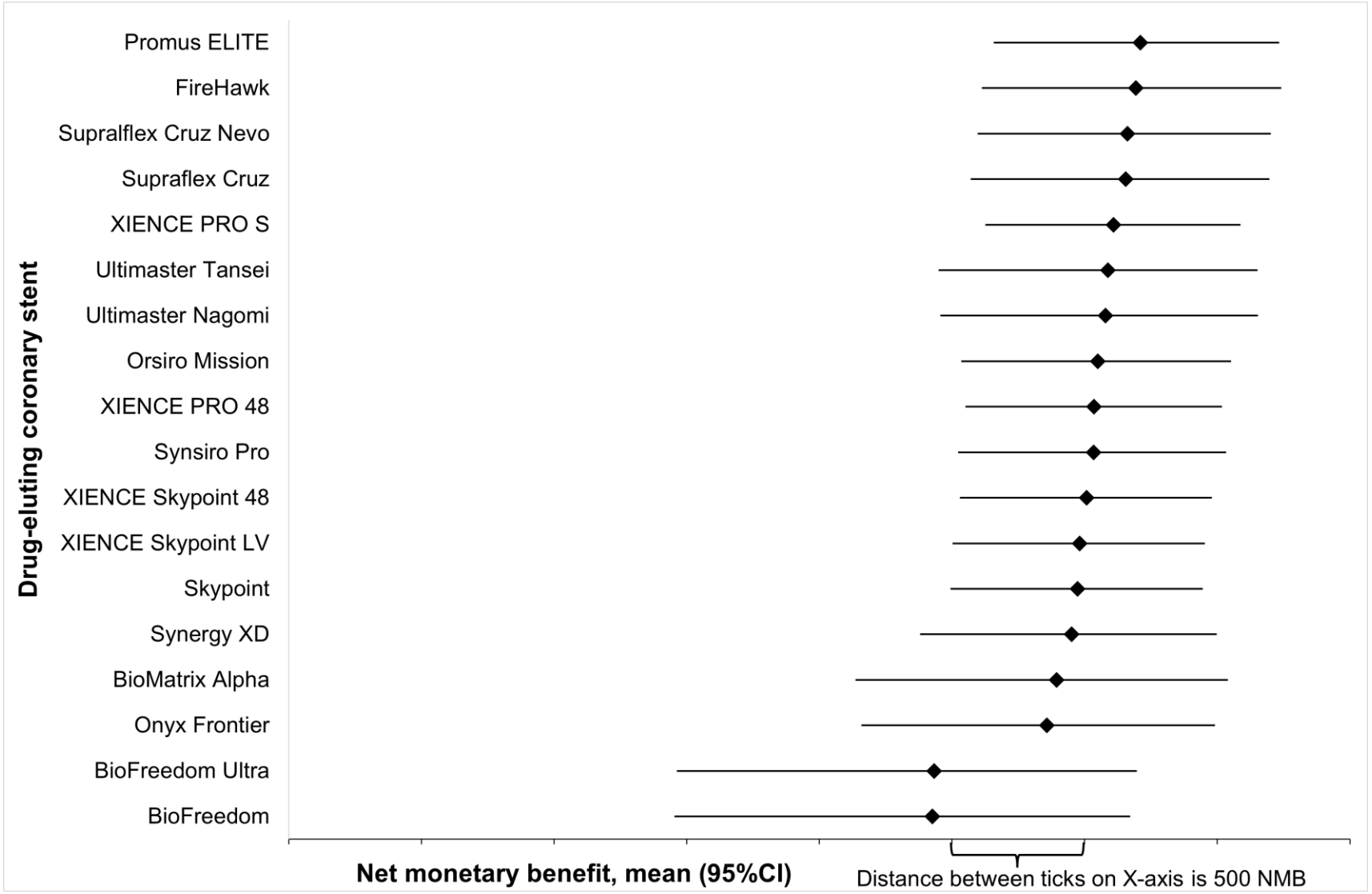


Figure 8: Net monetary benefit of each device at WTP £20,000, mean and (95%CI) [the figure has been partly redacted]

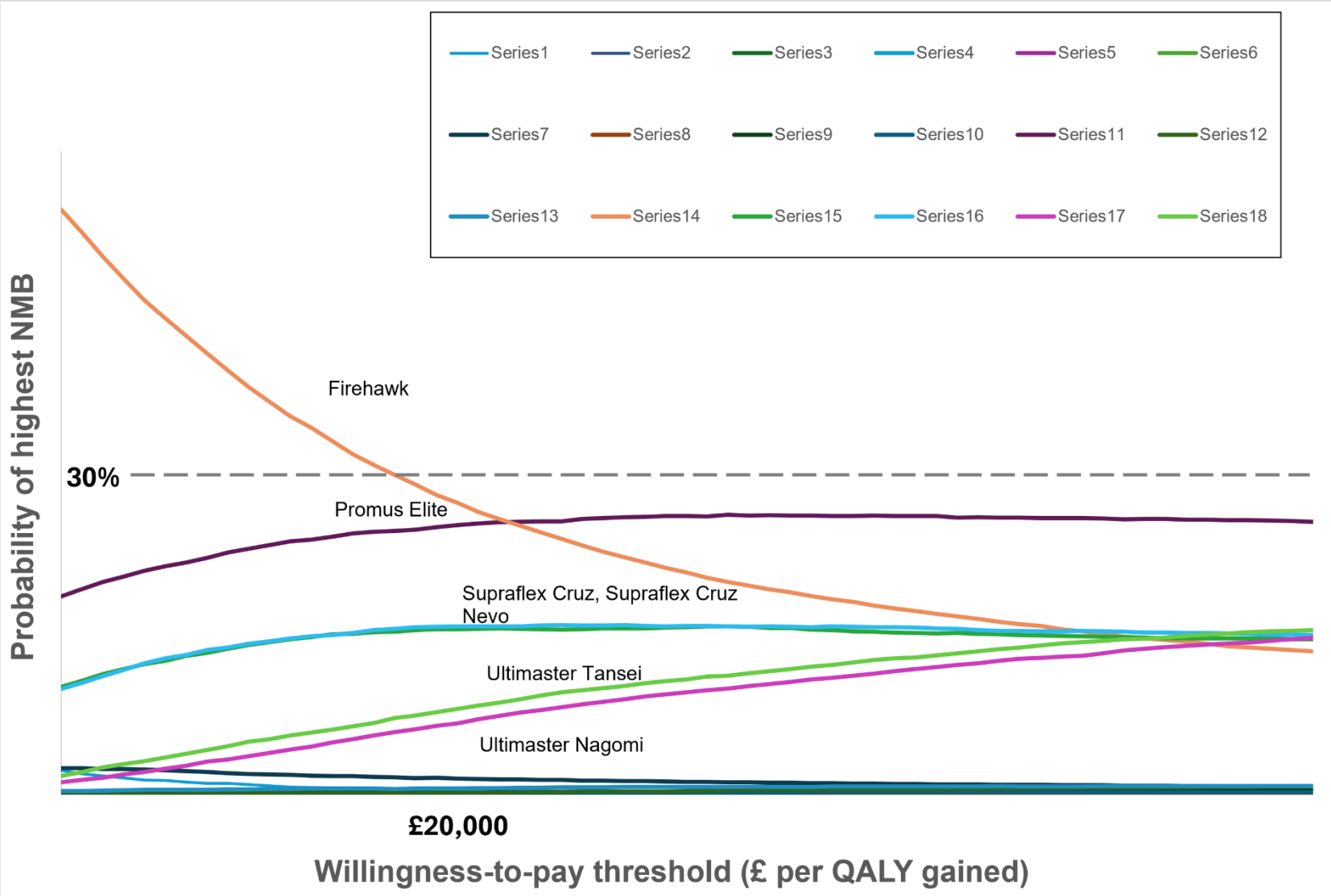


Figure 9: Cost-effectiveness acceptability curve [the figure has been partly redacted]

10.3 *Scenario analysis results*

Results from the scenario analysis are presented in Table 26. In all scenarios, there are small NMB differences across all devices, ranging between [redacted] in 1-year time horizon and between [redacted] in 5-year time horizon. However, it is noted that Promus Elite results in the highest NMB, except in the scenario using the maximum stent price.

Using the first-year relative treatment effect derived from a higher prior heterogeneity distribution, this results in slightly higher costs and lower QALYs for most devices, thus producing a relatively lower NMB. As discussed in Section 5.2.4, the NMA estimates are sensitive to the prior heterogeneity distribution. The HRs increase with the prior used. Given the small change in costs and QALYs with most devices, Promus Elite remains to generate the highest NMB. However, Firehawk NMB is found to reduce from [redacted] in the base case to [redacted] where QALYs reduce by [redacted]. This is likely driven by a relatively higher TVMI risk (HR 1.40) in the scenario analysis vs HR 1.19 in base case.

As previously discussed in Section 5.2.4, the long-term NMA estimates are unreliable because of the substantial uncertainty driven by the very sparse data and rare events. When the time horizon increases from 1 year to 5 years, the total costs and QALYs increase across all devices. Promus Elite is estimated to generate the greatest NMB when long-term treatment effect is considered. Given the unreliable long-term NMA estimates, the long-term economic findings should be interpreted with extreme caution, particularly when NMA yields high long-term HRs for some devices. In the 5-year scenario using NMA estimates from a higher prior heterogeneity distribution, there is significant change in NMB profile for most devices except Promus Elite. This is driven by the marked increase in HR for TLR and TVMI, reflecting the uncertainty in the long-term treatment estimates between devices.

In the scenario using the lowest stent price, there is relatively little difference in the costs where the EAG note that the NMB ranking for the top 5 devices remains unchanged. When the maximum stent price is used, there is slight change in the NMB ranking as Firehawk yields the highest NMB due to its low cost.

When a higher WTP £30,000 is used, there are no substantial changes in the NMB profile. The two devices that change rank are Ultimaster Tansei and Ultimaster Nagomi. These are associated with slightly higher QALYs at higher costs than some other devices, thus yield a higher NMB when the WTP threshold is increased.

The relative treatment effect finding by Taglieri et al. (2020) between Orsiro and Xience was applied to Orsiro Mission and Synsiro Pro in this scenario. Although there is no noticeable change in the NMB ranking, Orsiro Mission and Synsiro Pro accrue lower costs and higher QALYs, leading to higher NMBs (Orsiro Mission: NMB [redacted] in base case vs [redacted] in scenario analysis; Synsiro Pro: NMB [redacted] in base case vs [redacted] in scenario analysis). This is because of the more favourable relative treatment effect in TLR reported by Taglieri et al (2020).

Table 26: Results of scenario analyses

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
Base case Time horizon: 1 year NMA treatment effect: prior heterogeneity 0.1	Promus ELITE	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
Time horizon: 1 year NMA treatment effect: prior heterogeneity 1.0	Promus ELITE	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	Onyx Frontier	[redacted]	[redacted]	[redacted]
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
Time horizon: 5 year NMA treatment effect: prior heterogeneity 0.1	Promus ELITE	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
Time horizon: 5 year NMA treatment effect: prior heterogeneity 1.0	Promus ELITE	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]
Using minimum stent price	Promus ELITE	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	Synergy XD	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
Using maximum stent price	Firehawk	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Promus ELITE	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
Using WTP £30,000	Promus ELITE	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]
Taglieri et al. NMA relative treatment effect: Orsiro Mission vs Xience, Synsiro Pro vs Xience	Promus ELITE	[redacted]	[redacted]	[redacted]
	Firehawk	[redacted]	[redacted]	[redacted]
	Supraflex Cruz	[redacted]	[redacted]	[redacted]
	Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]
	Ultimaster Tansei	[redacted]	[redacted]	[redacted]
	Orsiro Mission	[redacted]	[redacted]	[redacted]
	XIENCE PRO S	[redacted]	[redacted]	[redacted]
	Synsiro Pro	[redacted]	[redacted]	[redacted]
	Ultimaster Nagomi	[redacted]	[redacted]	[redacted]

Scenario analyses	Device	Costs	QALYs	NMB at WTP £20,000
	XIENCE PRO 48	[redacted]	[redacted]	[redacted]
	XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]
	Synergy XD	[redacted]	[redacted]	[redacted]
	Xience Skypoint LV	[redacted]	[redacted]	[redacted]
	Skypoint	[redacted]	[redacted]	[redacted]
	Onyx Frontier	[redacted]	[redacted]	[redacted]
	BioMatrix Alpha	[redacted]	[redacted]	[redacted]
	BioFreedom Ultra	[redacted]	[redacted]	[redacted]
	BioFreedom	[redacted]	[redacted]	[redacted]

***Abbreviations**: QALY: quality adjusted life year; NMA: network meta-analysis; NMB: net monetary benefit; WTP: willingness to pay.*

Cost comparison analysis

In this analysis, all 29 devices in the scope are assumed to clinically equivalent, meaning the TLR and TVMI risk in the model for all devices are the same as that of Xience in the model. Therefore, the model is entirely driven by the cost of the device. It is estimated that Firehawk yields the highest NMB of [redacted] at WTP threshold of £20,000 given its low cost (Table 27). There is a noticeable increase in NMB for BioMatrix Alpha from [redacted] in base case to [redacted] when treatment effect is not considered. A similar observation is noted for Onyx Frontier, BioFreedom and BioFreedom Ultra.

Table 27: Results of cost comparison analysis

Device	Costs	QALYs	NMB at WTP £20,000	Base case NMB at WTP £20,000
Firehawk	[redacted]	[redacted]	[redacted]	[redacted]
Firehawk Liberty	[redacted]	[redacted]	[redacted]	[redacted]
BioMatrix Alpha	[redacted]	[redacted]	[redacted]	[redacted]
Promus ELITE	[redacted]	[redacted]	[redacted]	[redacted]
Supraflex Cruz Nevo	[redacted]	[redacted]	[redacted]	[redacted]
Supraflex Cruz	[redacted]	[redacted]	[redacted]	[redacted]
XIENCE PRO S	[redacted]	[redacted]	[redacted]	[redacted]
BioMime	[redacted]	[redacted]	[redacted]	[redacted]
Orsiro Mission	[redacted]	[redacted]	[redacted]	[redacted]
Onyx Frontier	[redacted]	[redacted]	[redacted]	[redacted]
Ultimaster Tansei	[redacted]	[redacted]	[redacted]	[redacted]
XIENCE PRO 48	[redacted]	[redacted]	[redacted]	[redacted]
ihtDEStiny BD	[redacted]	[redacted]	[redacted]	[redacted]
MAGMA	[redacted]	[redacted]	[redacted]	[redacted]
Synsiro Pro	[redacted]	[redacted]	[redacted]	[redacted]
BioFreedom Ultra	[redacted]	[redacted]	[redacted]	[redacted]
XIENCE Skypoint 48	[redacted]	[redacted]	[redacted]	[redacted]

Device	Costs	QALYs	NMB at WTP £20,000	Base case NMB at WTP £20,000
BioFreedom	[redacted]	[redacted]	[redacted]	[redacted]
EverMine 50	[redacted]	[redacted]	[redacted]	[redacted]
Angiolite	[redacted]	[redacted]	[redacted]	[redacted]
Xience Skypoint LV	[redacted]	[redacted]	[redacted]	[redacted]
Skypoint	[redacted]	[redacted]	[redacted]	[redacted]
Synergy XD	[redacted]	[redacted]	[redacted]	[redacted]
Ultimaster Nagomi	[redacted]	[redacted]	[redacted]	[redacted]
Coroflex ISAR NEO	[redacted]	[redacted]	[redacted]	[redacted]
BioMime Morph	[redacted]	[redacted]	[redacted]	[redacted]
BioMime Branch	[redacted]	[redacted]	[redacted]	[redacted]
XLIMUS	[redacted]	[redacted]	[redacted]	[redacted]
Synergy MEGATRON	[redacted]	[redacted]	[redacted]	[redacted]

***Abbreviations**: QALY: quality adjusted life year; NA: not applicable; NMB: net monetary benefit; WTP: willingness to pay.*

11 Combined summary and interpretation of the clinical and economic evidence

Clinical evidence

The EAG identified 22 key RCTs which compared two devices (or accepted clinically equivalent predecessors) with each other. Twenty-one of the 22 key RCTs were designed as non-inferiority studies and so were only able to demonstrate that one device was not worse than a comparator device. Non-inferiority with respect to clinically meaningful endpoints was demonstrated for the following devices against the Xience device: Orsiro Mission (demonstrated in four RCTs), Promus Elite (demonstrated in one RCT), Supraflex Cruz/Supraflex Cruz Nevo (demonstrated in one RCT), Firehawk (demonstrated in one RCT) and Ultimaster (demonstrated in one RCT). Synergy was also compared in a non-inferiority RCT against Xience, but this trial also compared differing DAPT regimens so any difference in outcomes may not be attributable to the devices. The one superiority RCT compared Orsiro versus Xience in a population of people with STEMI. The results demonstrated significantly lower rates of TLF in the Orsiro group in comparison to Xience.

Non-inferiority was also demonstrated with respect to clinically meaningful endpoints between:

- Orsiro Mission against both BioMatrix Alpha and Onyx Frontier.
- Onyx Frontier against both Orsiro Mission and BioFreedom.
- BioMatrix against Synergy
- Synergy against Promus Elite

Additionally, two RCTs suggested similar outcomes between the Angiolite and BioMime devices, respectively, against the Xience device, but neither trial was powered to assess non-inferiority of clinically meaningful endpoints. An RCT was identified between the Xlimus and Synergy device which suggested similar outcomes but again, was not powered to assess non-inferiority of clinically meaningful endpoints.

No RCTs drawing comparisons against another device in scope were identified for the following devices: BioMime Branch, BioMime Morph, Coroflex ISAR NEO, EverMine 50, Firehawk Liberty, ihtDEStiny BD, MAGMA and Synergy Megatron.

14 of the 22 key RCTs were deemed eligible for synthesis through network meta-analysis. This resulted in an NMA which drew comparisons between 10 of the 29 devices in scope. Two outcomes were analysed using the RE model at 1-year and long-term follow-up: TLR and TVMI.

At 1-year, NMA results suggest there is some evidence that Promus Elite may have beneficial effect on reducing TVMI when compared to Xience (HR 0.59, 95%CrI 0.31 to 1.03), and clear evidence that BioFreedom has a higher TLR rate than Xience (HR 3.70, 95%CrI 1.83 to 6.80). The heterogeneity is low in the NMAs, as indicated by the between-study posterior mean SDs. It is worth noting that the NMA models are highly dependent on the prior heterogeneity distribution. Although the inconsistency assessment demonstrates lower residual deviance and DIC in NMA for TLR, but higher values in TVMI, this is due to a zero cell in the BIODEGRADE trial (BioMatrix arm), which is not considered as inconsistency. The relative effect remains the same in the sensitivity analysis using a higher prior heterogeneity distribution, despite both the uncertainty around the relative effects and that of the between-study SDs are higher.

In the long-term follow-up, results suggest there is no evidence for meaningful differences between devices, in terms of TLR and TVMI. Nevertheless, some weak evidence suggests that Resolute Onyx and Promus Element have a beneficial effect on reducing TLR compared to Xience, whereas Supraflex may result in lower TVMI. The heterogeneity is low in the NMAs, as indicated by the between-study posterior mean SDs. No evidence of inconsistency was detected. In the sensitivity analyses, more uncertainty in the relative effects between devices and a higher posterior between-study SD were found. The impact of data sparsity is more obvious in the long-term follow-up where it is noted that the between-study posterior SD is almost entirely informed by the prior distribution. This indicates that the sparse data from very few studies are insufficient to estimate between-study posterior SD reliably, leading to wider CrIs for HRs in the long-term follow-up NMAs than for Y1 NMA.

Data sparsity is a fundamental issue in meta-analysis of rare events or of very few studies. It represents a significant challenge particularly when the between-study heterogeneity is not widely reported in medical devices literature as RE models are quite rare in medical devices. Therefore, it is difficult to select a suitable prior based on the limited empirical evidence from the literature. This has serious implications on the precision of treatment effects generated from RE models, leading to wide CrIs. Hence, this uncertainty is translated in the economic results when used to populate the economic model.

Economic evidence

The EAG conceptualised an economic model based on feedback from clinical experts and the EAG NMA output. It was not possible to directly adapt existing models in NICE guidelines for the comparison of multiple devices in a single analysis and to incorporate the clinical outcomes from the NMA. The model was populated using available UK data sources for cost and utility parameters. In addition, the relative treatment effects between devices in the model were informed by the EAG NMA for both short- and long-term outcomes. A number of sensitivity and scenario analyses were undertaken to explore the impact of uncertainty on the cost-effectiveness findings.

The economic evidence from both deterministic and probabilistic analyses suggest that there is substantial uncertainty with the NMB results, which outweighs the small NMB differences between devices. In the 1-year base case analysis, there was a modest NMB difference between Promus Elite and Firehawk, though Promus Elite appeared to yield the highest NMB. When the impact of parameter uncertainty was examined, the PSA results showed that 95%CI of NMB for all devices were overlapping and CEAC suggested that Firehawk and Promus Elite had the highest probability of achieving the greatest NMB. This indicates the high degree of parameter uncertainty driven by the wide treatment effect CrI. By modelling different scenarios, the NMB differences between devices were small. It was found that the device NMB ranking is sensitive to the long-term relative treatment effect and substantial uncertainty was noted in the NMA of long-term follow-up. When all devices are assumed to be clinically equivalent, Firehawk appears to be yield the highest NMB, due to its low cost. The uncertainty around the relative treatment effect

can have serious implications on the robustness of the economic findings. In addition, the use of underpowered studies in the NMA can lead to biased results due to the chance findings. Nevertheless, it is not uncommon to use underpowered studies to populate an economic model because of the difficulty in sourcing all relevant model inputs from sufficiently powered studies. Hence, all available relevant evidence is used to undertake this assessment. Although it appears that Promus Elite may yield the highest NMB, it is difficult to make any firm conclusion on the cost-effectiveness of these devices given the uncertainty in relative treatment effect.

Additional limitations include the generalisability of the findings to the UK NHS settings and the variation of stent price across trusts. Ideally, both baseline event risk and relative treatment effect should be representative of the patient population in the UK where only 2 UK-based trials were included in the EAG NMA (Table 7). However, it is a common practice to inform treatment efficacy using trial data. Given the lack of suitable data sources for this assessment, this limits the representation of the modelled population to that of the NHS setting. Additionally, the EAG recognise the different pricing levels across trusts, however the price data from NHS SC is used in the model to ensure consistency. Nevertheless, the significant uncertainty with relative effect between devices would outweigh the impact of price variation.

The EAG model structure and model inputs are guided by the trial data. It is noted that the clinical characteristics of study population vary across trials, in turn, this can have an impact on the treatment effect. However, without the availability of individual patient-level data, it was not possible for the EAG to adjust the patient characteristics to enable fair comparison. Similarly, subgroup analyses of high-risk patients in the scope were not undertaken given the lack of relevant data.

12 Discussion

In this LSA, the EAG has synthesised comparative evidence for devices in scope to inform an economic analysis which aimed to calculate net monetary benefit for each device, where possible, in order to assess whether price variation was justifiable.

The EAG and NICE chose to focus on published evidence to inform this analysis, primarily from RCTs, as it was decided that real-world evidence in the form of registry data was subject to confounding that would be difficult to mitigate. Taking results from an RCT setting, as opposed to a 'real world' setting, increases the likelihood that the incidence of clinical events observed can be directly attributed to the type of DES used. However, there are still multiple patient-specific and operator-specific factors that may influence outcomes and this should be taken into consideration when interpreting the evidence.

The majority of non-inferiority RCTs identified focussed on innovations relating to the polymer coating of the stent. At present, there is little direct evidence to suggest that DES with bioabsorbable polymers have any clinically meaningful benefit over DES with a permanent polymer. However, there is evidence to suggest that DES with a bioabsorbable polymer are at least as safe and effective as DES with a permanent polymer. Similarly, there is a lack of evidence to suggest that polymer-free DES have any clinically meaningful benefit over DES with a bioabsorbable or permanent polymer. There is limited evidence to suggest that polymer-free DES have similar outcomes to DES with a polymer.

It should be noted that the aim of this LSA is not to compare ‘types’ of DES, but to attribute outcomes to individual devices. The nature of DES development means there are various iterations of the same device, and the EAG acknowledged evidence may be lacking for more recent generations. The EAG aimed to establish where evidence for older generations could be deemed acceptable in supporting the use of the devices in scope, via contacting companies and clinical experts. There may be inconsistency in views between companies on what constitutes clinical equivalence so it is important to note that any acceptance of clinical equivalence of predecessor devices to current devices in scope may be subjective. Clinical experts had mixed views on whether evidence for older generation devices could be used to

support the use of current generation devices, with some commenting on a loss of granularity when merging evidence for several iterations of devices which were introduced with the intention of improving clinical outcomes. Some clinical experts commented that it is the nature of the change between iterations of a device that will determine whether evidence can be considered generalisable between generations, with changes to the stent design or individual components having greater impact on clinical outcomes than changes to other aspects such as the delivery platform. The acceptance of evidence for predecessor devices for the devices in scope may be considered a limitation of the EAG analysis.

The EAG conducted a network meta-analysis with a subset of the RCTs identified, which demonstrated an overall weak evidence on the relative effect between devices. As indicated by the wide 95%CrI, the NMA estimates are very uncertain. Key limitations include data sparsity and the lack of prior information. The underlying data sparsity from very few studies was not sufficient to generate reliable estimate on treatment effect and between-study heterogeneity. Despite Bayesian NMA allowing prior distribution specification to address data sparsity, the lack of prior information from the current medical device literature represents another challenge which is hard to attenuate. This leads to serious implications on the precision and robustness in NMA, which is then translated in the economic findings. In addition, the EAG recognises that the NMA does not capture all relevant clinical outcomes, a limitation which is shared by the subsequent economic analysis. Events such as stent thrombosis are associated with high morbidity and mortality, thus costs are underestimated and utilities are overestimated when this is not available for consideration in the economic analysis.

A longer time horizon was planned for the economic analysis, but there was a lack of published evidence. From an economic perspective, it would be ideal to incorporate the long-term cost and effect as a whole of this patient group in the economic analysis. Nevertheless, as shown by the longer term NMA, the data sparsity issue was more problematic, resulting in wider CrIs. Therefore, the economic results informed by the current evidence on treatment effect can have serious biases. Additionally, a key limitation is the lack of subgroup analyses, which was precluded by a lack of published data available to populate these into the economic analysis.

With respect to clinical decision making, clinical experts indicated that clinical efficacy, as measured by incidence of clinical events, are the key decision making factors when selecting a type of DES. However, other factors such as co-morbidities may also influence choice. In particular, in people who are considered of high-bleeding risk, there would be preference for a device that has evidence to demonstrate compatibility with shorter DAPT regimens. The EAG identified some evidence of shorter DAPT regimens being safe in conjunction with some of the stents in scope, but as a systematic review into this aspect of the care pathway was not conducted, definitive conclusions cannot be made with respect to safety of shorter DAPT in conjunction with any of the devices in scope.

To conclude, there is weak clinical and economic evidence to demonstrate any differences between devices to guide choice, and the results of this analysis should be interpreted with an understanding of its limitations.

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14 Appendices

Appendix A: Innovative features of included devices

Table 28 Innovative features of included devices

Company	Device name	Launch date	Company description of innovative features of technology from RFI (company website used if RFI not provided)
Abbott Medical UK Limited	**XIENCE PRO 48 (Xpedition)**	2012	The company provided a single RFI for the 'XIENCE' family of technologies in scope. One key innovative feature was described, which applies to all 'XIENCE' devices in scope: 1) The fluoropolymer in XIENCE stents interacts with proteins in the blood in a way that reduces thrombus formation, a process known as fluropassivation.
	XIENCE PRO S (Sierra)	2017	
	XIENCE Skypoint	2021	
	XIENCE Skypoint 48		
	XIENCE Skypoint LV		
B.Braun Medical	**Coroflex ISAR NEO**	2016	The company provided a list of 13 innovative features relating to this technology in the RFI: 1) Drug dose 2) Elution time 3) Polymer-free stent 4) Abluminal drug release 5) Radial strength 6) Side branch access 7) Properties of the delivery system 8) Expansion diameter 9) Increased radiopacity 10) Superior flexibility 11) Enhanced tracking properties 12) Probucol mimicking polymer 13) Short DAPT feasible

Company	Device name	Launch date	Company description of innovative features of technology from RFI (company website used if RFI not provided)
Biosensors International	**BioFreedom**	2013	The company provided a single RFI for the three technologies in scope. Three key innovative features were described, some of which are technology-specific: 1) BA9™ drug (all stents): properties that support healing and re-endothelialisation. 2) No polymer (BioFreedom and BioFreedom Ultra only): allows for an increased surface area for a uniform dose of BA9™ to be delivered to the target lesion. 3) Polymer biodegradation (BioMatrix Alpha only): drug release and PLA biodegradation are optimised to cover the entire period of arterial wound healing.
	BioMatrix Alpha	2016	
	BioFreedom Ultra	2020	
Biotronik	**Orsiro Mission**	2020	The company submitted a single RFI for the two technologies in scope. Three key innovative features were described, which apply to both technologies: 1) Combination of the biodegradable, ultra-thin strut with sirolimus and Pro-BIO coating. 2) Ultra-thin struts: faster endothelialisation, less metal/sheer stress into the lumen of the vessel, significantly lower clinical event rates to second-generation DES 3) Pro-BIO coating: reducing metal exposure which contributes towards better endothelial healing and reduced inflammatory response
	Synsiro Pro	2021	
Boston Scientific	**Promus ELITE**	2018	Information was provided from the company, although a formal RFI form was not completed for the Promus ELITE device. Key components were described, but no information with respect to innovative features was outlined in the information provided by the company.
	Synergy XD	2019	The company provided one RFI for both Synergy devices (XD and Megatron). One key innovative feature was described that applies to both technologies: 1) Delivery system: unique laser-cut hypotube.
	Synergy Megatron	2023	

Company	Device name	Launch date	Company description of innovative features of technology from RFI (company website used if RFI not provided)
			Innovative features pertaining to Synergy XD only were described as follows: 1) Strut design: increased axial strength while maintaining flexibility, increased radial strength 2) Novel laser cut peak design, 3) Stent alloy 4) Fast absorbing bioabsorbable polymer: emphasises suppression of neointimal growth while promoting healing. Innovative features pertaining to Synergy Megatron only were described as follows: 1) Strut design: increased axial strength, wider over expansion capability, increased radial strength, better vessel scaffolding.
Cardionovum	**XLIMUS**	Unknown. Evidence suggests ~2014.	No RFI received from company. The company website describes: • Homogenous vessel wall scaffolding which minimises the risk of tissue prolapse and optimises drug distribution • Innovative hydrophilic-coasted shaft and an extra-low tip profile to access tortuous lesions
IHT	**ihtDEStiny BD**	Unknown. Evidence suggests ~2021.	No RFI received from company. The company website describes: • Innovation that integrates a cobalt chromium platform with a sirolimus-releasing biostable abluminal polymer matrix
iVascular	**Angiolite**	2014 (2024 in the UK)	The company listed one innovative feature in their RFI: 1) Over-expansion capacity
Medtronic	**Onyx Frontier**	2022	The company provided a list of 7 innovative features relating to this technology in the RFI:

Company	Device name	Launch date	Company description of innovative features of technology from RFI (company website used if RFI not provided)
			1) Updated stent delivery system: a dual-flex balloon, lower crossing profile, and increased catheter flexibility. 2) Stent scaffolding construction: single-wire design 3) Round struts: allow for easier wire and balloon crossing access 4) Overexpansion capability and broad diameter range. 5) Visibility under fluoroscopy (radiopacity), the platinum-Iridium core is unique to Medtronic. 6) BioLinx™ biocompatible polymer 7) Zotarolimus drug
Meril	**BioMime**	Unknown. Evidence suggests ~2011.	No RFI received from company. The company website describes: • Ultra-thin struts • Novel hybrid design with closed cells and open cells • BioPoly-Biodegradable polymer • High flexibility and adequate side branch access • Strut width variability for radial strength
	BioMime Branch	Unknown. Website suggests technology is modified iteration of BioMime.	No RFI received from company. The company website describes the same features as BioMime above, in addition to: • Intuitive design for treating bifurcation lesions • 'Step-Up Balloon System': main branch and side branch segments deployed simultaneously

Company	Device name	Launch date	Company description of innovative features of technology from RFI (company website used if RFI not provided)
	BioMime Morph	Unknown. Website suggests technology is modified iteration of BioMime.	No RFI received from company. The company website describes the same features as BioMime above, in addition to: • Long tapered stent: avoids multiple overlapping stents
	EverMine 50	Unknown. Company website suggests ~2016.	No RFI received from company. The company website describes: • Ultra-low strut thickness: promoting early vascular healing • Variable strut width and variable crown design: ensures adequate radial strength • Hybrid cell stent design: open cells in the middle of the stent for side-branch access and closed cell design on ends for optimal scaffolding and conformability
Microport	**Firehawk**	Unknown. Evidence suggests ~2013.	No RFI received from company. The company website describes: • Innovative abluminal in-groove coating It is unclear from the company website what the key technological differences are between Firehawk and Firehawk Liberty.
	Firehawk Liberty	Unknown.	
QualiMed	**MAGMA**	Unknown.	No RFI received from company. The company website describes: • Inert carbon technology • Completely biodegradable polymer coating
Sahajanand Medical Technologies	**Supraflex Cruz**	Unknown.	No RFI received from company. The company website describes the following in relation to Supraflex Cruz: • Proprietary ‘LDZ’ link
	Supraflex Cruz Nevo	Unknown.	

Company	Device name	Launch date	Company description of innovative features of technology from RFI (company website used if RFI not provided)
			• Open-cell design • Unique blend of hydrophilic-hydrophobic biodegradable polymers
Terumo	**Ultimaster Tansei**	2018	The company provided one RFI for both Ultimaster devices (Nagomi and Tansei). The following key innovative features were described that apply to both technologies: 1) Innovative PDLLA-PCL copolymer bioresorbable coating. 2) Open cell, 2-link platform 3) Additional sizes in the range of 2.00 mm to 4.5 mm and lengths from 9 to 50 mm. 4) Optimised overexpansion capability, up to 6.25 mm (for 3.5 mm to 4.5 mm diameter stents)
	Ultimaster Nagomi	2023	

***Abbreviations**: DAPT: dual antiplatelet therapy; DES: drug-eluting stent; PCL: polycaprolactone; PDLLA: poly(d,l-lactide); PLA: polylactic acid; RFI: Request for information.*

Appendix B: Clinical technological and economic search strategies

The EAG conducted separate searches for clinical and economic evidence as directed by the scope. To identify clinical evidence, eight bibliographic databases were searched from inception to July 2024 using a range of free text terms and indexed terms. The searches were targeted and focused on device names, company names, and population terms. Two clinical registries were also searched for ongoing trials. The companies' websites were searched for additional literature and evidence provided by companies in the RFIs was also considered.

To identify economic studies, four bibliographic databases were searched from inception to July 2024 using a range of free text terms and indexed terms. To ensure relevance, filters were used for health utilities (CADTH, 2024), economic evaluations (CADTH, 2024), systematic reviews (Montori et al. 2004; Wilczynski et al. 2007), and the UK (Ayiku et al. 2017, 2019).

Clinical searches databases

Date	Database Name	Total number of records retrieved	Total number of records from database after de-duplication
12.07.24	Medline ALL	298	
12.07.24	Embase	741	
12.07.24	Cochrane Library CDSR CENTRAL	 0 331	
12.07.24	CRD DARE NHS EED	8 (5 DARE; 3 NHS EED)	
12.07.24	INAHTA	3	
12.07.24	Epistemonikos	13	
12.07.24	Clinical Trials.gov	84	
15.07.24	ICTRP	170	
Database searches total		1648	1220

Clinical searches company website

Date	Company websites	Total Number of records retrieved	Total number of records loaded into library (Duplicates not imported)	Total number of records from database after de-duplication
15.07.24	Abbott Medical Xience Pro 48/Xience Xpedition Xience Pro S/Xience Sierra Xience Skypoint, Xience Skypoint 48, Xience Skypoint LV	NA Browsed reference list of pages	38	
15.07.24	B. Braun Medical (Coroflex)	0	0	
15.07.24	Biosensors international BioMatrix Alpha Biofreedom Ultra Biofreedom	30 (Listed in ref list)	5	
15.07.24	Biotronik Orsiro mission Synsiro Pro	NA – browsed pages	12	
17.07.24	Boston Scientific Promus ELITE Synergy MEGATRON Synergy XD	12	12	
17.07.24	Cardionovum (XLIMUS)	4	4	
17.07.24	IHT (ihtDestiny BD)	15	15	
17.07.24	iVascular (Angiolite)	4	4	
22.07.24	Medtronic (Onyx Frontier)	6	5	
22.07.24	Meril BioMime BioMime Branch BioMime Morph Evermine 50	62	22	
22.07.24	Microport Firehawk Firehawk Liberty	1	0	
22.07.24	QualiMed (MAGMA)	0	0	
22.07.24	Sahajanand Medical Technologies Supraflex Supraflex Cruz	37	22	
22.07.24	Terumo Ultimaster Nagomi	NA	10	

Date	Company websites	Total Number of records retrieved	Total number of records loaded into library (Duplicates not imported)	Total number of records from database after de-duplication
	Ultimaster Tansei	Browsed clinical evidence pages		
			149	148

Clinical searches company RFI

Date	Company Name	Total Number of records retrieved	Total number of records from database after de-duplication
07.08.24	Abbott Medical	58	
30.07.24	B Braun	21	
01.08.24	Biosensors	90	
05.08.24	Biotronik	131	
05.08.24	Boston Scientific	29	
05.08.24	Boston Scientific – Promus Elite	2	
05.08.24	Gap Medical (iVascular)	4	
07.08.24	Medtronic	65	
07.08.24	Terumo	38	
Total		438	329

Economic searches databases

Date	Database Name	Total Number of records retrieved	Total number of records from database after de-duplication
29.07.24	Medline ALL	68	
29.07.24	Embase	165	
29.07.24	NHS EED	52	
29.07.24	CEA registry	8	
Total		293	263

EAG Search strategies for clinical evidence

Ovid MEDLINE(R) ALL <1946 to July 11, 2024>

1 (Xience* and pro).tw. 6

2 xpedition*.tw. 28

3 (Xience* and sierra*).tw. 9

4 skypoint*.tw. 1

5 xlimus*.tw. 4

6 cardionovum.tw. 8

7 coroflex*.tw. 34

8 (braun and "drug eluting stent*").tw. 16

9 biofreedom*.tw. 39

10 "biosensors international".tw. 12

11 ("biomatrix alpha*" or "BMX alpha*").tw. 4

12 "orsiro mission*".tw. 1

13 (biotronik* and (orsiro* or "drug eluting stent*")).tw. 55

14 synsiro*.tw. 0

15 ("boston scientific" and (synergy or promus)).tw. 55

16 "Synergy XD".tw. 0

17 "Synergy megatron*".tw. 6

18 "promus elite*".tw. 1

19 angiolite*.tw. 5

20 ivascular*.tw. 7

21 (magma* and ("drug eluting stent*" or QualiMed)).tw. 25

22 (QualiMed and "drug eluting stent*").tw. 0

23 "onyx frontier*".tw. 2

24 (medtronic and (onyx* or "drug eluting stent*")).tw. 133

25 biomime.tw. 25

26 "meril life".tw. 36

27 evermine*.tw. 4

28 firehawk*.tw. 28

29 (microport and "drug eluting stent*").tw. 6

30 supraflex*.tw. 24

31 ((smt or "Sahajanand Medical Technologies") and "drug eluting stent*").tw. 8

32 ultimaster*.tw. 70

33 (terumo and "drug eluting stent*").tw. 20

34 ihtDEStiny.tw. 2

35 (IHT and "drug eluting stent*").tw. 0

36 or/1-35 565

37 ((coronary or isch?emi*) adj3 "heart disease").tw. 95338

38 ((IHD or CAD) and Heart).tw. 13573

39 Coronary artery disease.tw. 101239

40 Coronary Disease/ 133333

41	Coronary Artery Disease/	79504
42	((Myocardial or Coronary) adj isch?emi*).tw.	38883
43	Myocardial Ischemia/	42600
44	(stemi or nstemi).tw.	17270
45	ST Elevation Myocardial Infarction/	8372
46	Non-ST Elevated Myocardial Infarction/	1852
47	((stable or unstable) adj angina).tw.	21431
48	Angina, Stable/	1684
49	exp Angina, Unstable/	11397
50	"acute coronary condition*".tw.	4
51	"heart attack*".tw.	6813
52	or/37-51	388678
53	36 and 52	304
54	exp animals/ not humans.sh.	5238679
55	53 not 54	302
56	limit 55 to english language	298

Embase <1974 to 2024 July 11>

1	(Xience* and pro).tw.	66
2	xpedition*.tw.	130
3	(Xience* and sierra*).tw.	35
4	skypoint*.tw.	10

5 xlimus*.tw. 8

6 cardionovum.tw. 19

7 coroflex*.tw. 92

8 (braun and "drug eluting stent*").tw. 45

9 biofreedom*.tw. 104

10 "biosensors international".tw. 25

11 ("biomatrix alpha*" or "BMX alpha*").tw. 12

12 "orsiro mission*".tw. 4

13 (biotronik* and (orsiro* or "drug eluting stent*")).tw. 133

14 synsiro*.tw. 0

15 ("boston scientific" and (synergy or promus)).tw. 230

16 "Synergy XD".tw. 2

17 "Synergy megatron*".tw. 20

18 "promus elite*".tw. 7

19 angiolite*.tw. 6

20 ivascular*.tw. 20

21 (magma* and ("drug eluting stent*" or QualiMed)).tw. 46

22 (QualiMed and "drug eluting stent*").tw. 0

23 "onyx frontier*".tw. 8

24 (medtronic and (onyx* or "drug eluting stent*")).tw. 398

25 biomime.tw. 69

26 "meril life".tw.74

27 evermine*.tw. 5

28 firehawk*.tw. 54

29 (microport and "drug eluting stent*").tw. 27

30 supraflex*.tw. 52

31 ((smt or "Sahajanand Medical Technologies") and "drug eluting stent*").tw. 19

32 ultimaster*.tw. 181

33 (terumo and "drug eluting stent*").tw. 97

34 ihtDEStiny.tw. 2

35 (IHT and "drug eluting stent*").tw. 1

36 or/1-35 1676

37 ((coronary or isch?emi*) adj3 "heart disease").tw. 135222

38 ((IHD or CAD) and Heart).tw. 26649

39 Coronary artery disease.tw. 164429

40 coronary artery disease/ 241991

41 ischemic heart disease/ 153195

42 ((Myocardial or Coronary) adj isch?emi*).tw. 52974

43 heart muscle ischemia/ 103947

44 (stemi or nstemi).tw. 42581

45 ST segment elevation myocardial infarction/ 55734

46 non ST segment elevation myocardial infarction/ 23271

47	((stable or unstable) adj angina).tw.	33961
48	stable angina pectoris/	13594
49	exp unstable angina pectoris/	28607
50	"acute coronary condition*".tw.	6
51	"heart attack*".tw.	10037
52	or/37-51	637939
53	36 and 52	752
54	limit 53 to english language	741

Cochrane Library

#1	(Xience* AND pro):ti,ab,kw	7
#2	(xpedition*):ti,ab,kw	24
#3	(Xience* AND sierra*):ti,ab,kw	1
#4	(skypoint*):ti,ab,kw	1
#5	(xlimus*):ti,ab,kw	5
#6	(cardionovum):ti,ab,kw	9
#7	(coroflex*):ti,ab,kw	37
#8	((braun AND ("drug eluting" NEXT stent*))):ti,ab,kw	30
#9	(biofreedom*):ti,ab,kw	52
#10	("biosensors international"):ti,ab,kw	6
#11	(("biomatrix alpha" OR "BMX alpha")):ti,ab,kw	3

#12 ("orsiro mission"):ti,ab,kw 6

#13 (biotronik* AND (orsiro* OR ("drug eluting" NEXT stent*))):ti,ab,kw 56

#14 (synsiro*):ti,ab,kw 0

#15 ("boston scientific" AND (synergy OR promus)):ti,ab,kw 61

#16 ("Synergy XD"):ti,ab,kw 0

#17 ("synergy megatron"):ti,ab,kw 0

#18 ("promus elite"):ti,ab,kw 2

#19 (angiolite*):ti,ab,kw 5

#20 (ivascular*):ti,ab,kw 8

#21 (magma* AND (QualiMed OR ("drug eluting" NEXT stent*))):ti,ab,kw 13

#22 (QualiMed AND ("drug eluting" NEXT stent*)):ti,ab,kw 0

#23 ("onyx frontier"):ti,ab,kw 0

#24 (medtronic AND (onyx* OR ("drug eluting" NEXT stent*))):ti,ab,kw 95

#25 (biomime):ti,ab,kw 16

#26 ("meril life"):ti,ab,kw 16

#27 (evermine*):ti,ab,kw 1

#28 (firehawk*):ti,ab,kw 39

#29 (microport AND ("drug eluting" NEXT stent*)):ti,ab,kw 12

#30 (supraflex*):ti,ab,kw 19

#31 ((smt OR "Sahajanand Medical Technologies") AND ("drug eluting" NEXT stent*)):ti,ab,kw 2

#32 (ultimaster*):ti,ab,kw 54

#33 (terumo AND ("drug eluting" NEXT stent*)):ti,ab,kw 30

#34 (ihtDEStiny):ti,ab,kw 0

#35 (IHT AND ("drug eluting" NEXT stent*)):ti,ab,kw0

#36 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 512

#37 ((coronary OR isch?emi*) NEAR/3 "heart disease"):ti,ab,kw 14325

#38 ((IHD OR CAD) AND Heart):ti,ab,kw 2883

#39 ("Coronary artery disease"):ti,ab,kw 21593

#40 MeSH descriptor: [Coronary Disease] this term only 9645

#41 MeSH descriptor: [Coronary Artery Disease] this term only 9370

#42 ((Myocardial OR Coronary) NEXT isch?emi*):ti,ab,kw 7587

#43 MeSH descriptor: [Myocardial Ischemia] this term only 4855

#44 (stemi OR nstemi):ti,ab,kw 4596

#45 MeSH descriptor: [ST Elevation Myocardial Infarction] this term only 1136

#46 MeSH descriptor: [Non-ST Elevated Myocardial Infarction] this term only 190

#47 ((stable OR unstable) NEXT angina):ti,ab,kw 7486

#48 MeSH descriptor: [Angina, Stable] this term only 479

#49 MeSH descriptor: [Angina, Unstable] explode all trees 1455

#50 ("acute coronary" NEXT condition*):ti,ab,kw 1

#51 (heart NEXT attack*):ti,ab,kw 1739

#52 #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 49793

#53 #36 AND #52 331

#54 #36 AND #52 in Cochrane Reviews 0

#55 #36 AND #52 in Trials 331

CRD

1 (Xience* and pro) 0

2 (xpedition*) 0

3 (Xience* and sierra*) 0

4 (skypoint*) 0

5 (xlimus*) 0

6 (cardionovum) 0

7 (coroflex*) 0

8 (braun and "drug eluting stent*") 0

9 (biofreedom*) 0

10 ("biosensors international")0

11 ("biomatrix alpha*" or "BMX alpha*") 0

12 ("orsiro mission*") 0

13 (biotronik* and (orsiro* or "drug eluting stent*")) 1

14 (synsiro*) 0

15 ("boston scientific" and (synergy or promus)) 1

16 ("Synergy XD") 0

17 ("Synergy megatron*") 0

18 ("promus elite*") 0

19 (angiolite*) 0

20 (ivascular*) 0

21 (magma* and ("drug eluting stent*" or QualiMed)) 0

22 (QualiMed and "drug eluting stent*") 0

23 ("onyx frontier*") 0

24 (medtronic and (onyx* or "drug eluting stent*")) 9

25 (biomime) 0

26 ("meril life") 0

27 (evermine*) 0

28 (firehawk*) 0

29 (microport and "drug eluting stent*") 0

30 (supraflex*) 0

31 ((smt or "Sahajanand Medical Technologies") and "drug eluting stent*") 0

32 (ultimaster*) 0

33 (terumo and "drug eluting stent*") 0

34 (ihtDEStiny) 0

35 (IHT and "drug eluting stent*") 0

36	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35	10
37	LIMIT #36 to DARE and NHS EED	8

INAHTA

(IHT AND "drug eluting stent*") OR (ihtDEStiny) OR (terumo AND "drug eluting stent*") OR (ultimaster*) OR (((smt OR "Sahajanand Medical Technologies") AND "drug eluting stent*")) OR (supraflex*) OR ((microport AND "drug eluting stent*")) OR (firehawk*) OR (evermine*) OR ("meril life") OR (biomime) OR (medtronic AND (onyx* OR "drug eluting stent*")) OR ("onyx frontier*") OR (QualiMed AND "drug eluting stent*") OR (magma* AND ("drug eluting stent*" OR QualiMed)) OR (ivascular*) OR (angiolite*) OR ("promus elite*") OR ("Synergy megatron*") OR ("Synergy XD") OR ("boston scientific" AND (synergy OR promus)) OR (synsiro*) OR (biotronik* AND (orsiro* OR "drug eluting stent*")) OR ("orsiro mission*") OR ("biomatrix alpha*" OR "BMX alpha*") OR ("biosensors international") OR (biofreedom*) OR (braun AND "drug eluting stent*") OR (coroflex*) OR (cardionovum) OR (xlimus*) OR (skypoint*) OR (sierra* AND (Xience* OR stent*)) OR (xpedition*) OR (Xience*): 3 Hits

Epistemonikos

(title:((title:(Xience* OR xpedition* OR sierra* OR skypoint* OR xlimus* OR cardionovum OR coroflex* OR biofreedom* OR "biosensors international" OR "biomatrix alpha*" OR "BMX alpha*" OR "orsiro mission*" OR synsiro* OR "Synergy XD" OR "Synergy megatron*" OR "promus elite*" OR angiolite* OR ivascular* OR "onyx frontier*" OR biomime OR "meril life" OR evermine* OR firehawk* OR supraflex* OR ultimaster* OR ihtDEStiny OR ((IHT OR braun OR biotronik OR magma* OR QualiMed OR microport OR terumo OR smt OR "Sahajanand Medical Technologies" OR medtronic) AND "drug eluting stent*") OR ("boston scientific" AND (synergy OR promus)) OR (magma* AND (QualiMed)) OR (medtronic AND (onyx*))

OR (biotronik* AND (orsiro*))) OR abstract:(Xience* OR xpedition* OR sierra* OR skypoint* OR xlimus* OR cardionovum OR coroflex* OR biofreedom* OR "biosensors international" OR "biomatrix alpha*" OR "BMX alpha*" OR "orsiro mission*" OR synsiro* OR "Synergy XD" OR "Synergy megatron*" OR "promus elite*" OR angiolite* OR ivascular* OR "onyx frontier*" OR biomime OR "meril life" OR evermine* OR firehawk* OR supraflex* OR ultimaster* OR ihtDEStiny OR ((IHT OR braun OR biotronik OR magma* OR QualiMed OR microport OR terumo OR smt OR "Sahajanand Medical Technologies" OR medtronic) AND "drug eluting stent*") OR ("boston scientific" AND (synergy OR promus)) OR (magma* AND (QualiMed)) OR (medtronic AND (onyx*)) OR (biotronik* AND (orsiro*)))) AND (title:(((Coronary OR ischemi* OR ischaemi*) AND (artery OR arteries OR heart) AND disease*) OR ((IHD OR CAD) AND Heart) OR ((Myocardial OR Coronary) AND (ischemi* OR ischaemi*)) OR stemi OR nstemi OR "ST Elevation Myocardial Infarction" OR "Non-ST Elevated Myocardial Infarction" OR "stable angina" OR "unstable angina" OR "acute coronary condition*" OR "heart attack*") OR abstract:(((Coronary OR ischemi* OR ischaemi*) AND (artery OR arteries OR heart) AND disease*) OR ((IHD OR CAD) AND Heart) OR ((Myocardial OR Coronary) AND (ischemi* OR ischaemi*)) OR stemi OR nstemi OR "ST Elevation Myocardial Infarction" OR "Non-ST Elevated Myocardial Infarction" OR "stable angina" OR "unstable angina" OR "acute coronary condition*" OR "heart attack*"))) OR abstract:((title:(Xience* OR xpedition* OR sierra* OR skypoint* OR xlimus* OR cardionovum OR coroflex* OR biofreedom* OR "biosensors international" OR "biomatrix alpha*" OR "BMX alpha*" OR "orsiro mission*" OR synsiro* OR "Synergy XD" OR "Synergy megatron*" OR "promus elite*" OR angiolite* OR ivascular* OR "onyx frontier*" OR biomime OR "meril life" OR evermine* OR firehawk* OR supraflex* OR ultimaster* OR ihtDEStiny OR ((IHT OR braun OR biotronik OR magma* OR QualiMed OR microport OR terumo OR smt OR "Sahajanand Medical Technologies" OR medtronic) AND "drug eluting stent*") OR ("boston scientific" AND (synergy OR promus)) OR (magma* AND (QualiMed)) OR (medtronic AND (onyx*)) OR (biotronik* AND (orsiro*))) OR abstract:(Xience* OR xpedition* OR sierra* OR skypoint* OR xlimus* OR cardionovum OR coroflex* OR biofreedom* OR "biosensors international" OR "biomatrix alpha*" OR "BMX alpha*" OR "orsiro mission*" OR synsiro* OR "Synergy XD" OR "Synergy megatron*" OR "promus elite*" OR angiolite* OR ivascular* OR "onyx frontier*" OR biomime OR "meril life" OR evermine* OR firehawk* OR supraflex* OR ultimaster* OR ihtDEStiny

OR ((IHT OR braun OR biotronik OR magma* OR QualiMed OR microport OR terumo OR smt OR "Sahajanand Medical Technologies" OR medtronic) AND "drug eluting stent*") OR ("boston scientific" AND (synergy OR promus)) OR (magma* AND (QualiMed)) OR (medtronic AND (onyx*)) OR (biotronik* AND (orsiro*)))) AND (title:(((Coronary OR ischemi* OR ischaemi*) AND (artery OR arteries OR heart) AND disease*) OR ((IHD OR CAD) AND Heart) OR ((Myocardial OR Coronary) AND (ischemi* OR ischaemi*)) OR stemi OR nstemi OR "ST Elevation Myocardial Infarction" OR "Non-ST Elevated Myocardial Infarction" OR "stable angina" OR "unstable angina" OR "acute coronary condition*" OR "heart attack*") OR abstract:(((Coronary OR ischemi* OR ischaemi*) AND (artery OR arteries OR heart) AND disease*) OR ((IHD OR CAD) AND Heart) OR ((Myocardial OR Coronary) AND (ischemi* OR ischaemi*)) OR stemi OR nstemi OR "ST Elevation Myocardial Infarction" OR "Non-ST Elevated Myocardial Infarction" OR "stable angina" OR "unstable angina" OR "acute coronary condition*" OR "heart attack*"))))

Filter by Systematic Reviews: 13 results

Clinicaltrails.gov

Limited to the following to filters:

- Not yet recruiting
- Recruiting
- Active, not recruiting
- Enrolling by invitation
- Unknown

Search	Hits	Additional relevant hits
“Xience pro”	1	1
Xpedition	3	3
Xience sierra	7	5

Skypoint	6	3
Xlimus	0	NA
Cardionovum	2	0
Coroflex	4	3
Biofreedom	10	8
Biomatrix alpha	2	2
Orsiro mission	3	2
Synsiro pro	0	NA
Synsiro	0	NA
Promus elite	3	2
Synergy megatron	2	1
Megatron	2	0
Synergy XD	2	0
Xlimus	0	NA
ihtDestiny	1	1
Angiolite	4	3
Onyx Frontier	4	1
Biomime	2	2
Evermine	0	NA
Firehawk	5	4
Magma; Intervention/treatment: Stent	0	NA
Magma	2	0
Supraflex	8	7
Ultimaster	14	10
Biotronik; Intervention/treatment: Stent	12	8
Biosensors international	7	1
Boston Scientific; Intervention/treatment: Stent	45	11
IHT; Intervention/treatment: Stent	0	0
IHT	8	0
iVascular	8	1
Meril; Intervention/treatment: Stent	2	0
Meril	7	0
Microport; Intervention/treatment: Stent	18	4
QualiMed	3	0
Sahajanand Medical Technologies	4	0
Terumo; Intervention/treatment: Stent	17	1
Total	**84**	

ICTRP

Search (simple search)	Hits	Additional relevant hits
“Xience pro”	0	N/A
Xpedition	12	12
Xience sierra	4	3
Skypoint	3	3
Xlimus	2	2
Coroflex	17	17
Biofreedom	30	30
Biomatrix alpha	3	3
Orsiro mission	6	6
Synsiro pro	0	N/A
Synsiro	0	N/A
Promus elite	0	N/A
Synergy megatron	2	2
Megatron	3	1
Synergy XD	1	0
ihtDestiny	1	1
Angiolite	7	7
Onyx Frontier	1	1
Biomime	13	12
Evermine	3	3
Firehawk	16	16
Magma	8	8
Supraflex	15	14
Ultimaster	34	29
Total	**170**	

EAG Search strategies for economic evidence

Ovid MEDLINE(R) ALL <1946 to July 26, 2024>

1 Drug-Eluting Stents/14020

2 ((drug adj5 (elut* or coat* or cover* or release*)) and stent*).tw. 14638

3 (stent* and DES).tw. 6052

4 Stents/ and des.tw. 1644

5 (stent* and (everolimus or sirolimus or biolimus or zotarolimus)).tw. 5144

6 Stents/ and (everolimus or sirolimus or biolimus or zotarolimus).tw. 1437

7 exp Sirolimus/ and stent*.tw. 5048

8 exp Sirolimus/ and Stents/ 1804

9 Angioplasty/ and (stent* adj5 drug).tw. 158

10 (angioplasty and (stent* adj5 drug)).tw. 1785

11 Percutaneous Coronary Intervention/ and (stent* adj5 drug).tw. 3634

12 (("percutaneous coronary intervention" or PCI or PTCA) and (stent* adj5 drug)).tw. 5276

13 or/1-12 21669

14 ((coronary or isch?emi*) adj3 "heart disease").tw. 95490

15 ((IHD or CAD) and Heart).tw. 13622

16 Coronary artery disease.tw. 101472

17 Coronary Disease/ 133356

18 Coronary Artery Disease/ 79638

19 ((Myocardial or Coronary) adj isch?emi*).tw. 38935

20 Myocardial Ischemia/ 42623

21 (stemi or nstemi).tw. 17319

22 ST Elevation Myocardial Infarction/ 8395

23 Non-ST Elevated Myocardial Infarction/ 1865

24 myocardial infarction.tw. 215161

25 "heart attack*".tw. 6838

26 Myocardial Infarction/ 183078

27 ((stable or unstable or pectoris) adj3 angina).tw. 36134

28 Angina, Stable/ 1684

29 exp Angina, Unstable/ 11401

30 Angina Pectoris/ 33263

31 "acute coronary condition*".tw. 4

32 Acute Coronary Syndrome/ 21164

33 (coronary adj3 (stenosis or restenosis)).tw. 16158

34 exp Coronary Stenosis/ 21440

35 or/14-34 609385

36 13 and 35 15550

37 exp animals/ not humans.sh. 5242324

38 36 not 37 15307

39 limit 38 to english language 14510

40 "Value of Life"/ 5828

41 Quality of Life/ 291132

42 quality of life.ti,kf. 127299

43 ((instrument or instruments) adj3 quality of life).ab. 4090

44 Quality-Adjusted Life Years/ 16612

45 quality adjusted life.ti,ab,kf. 18891

46 (qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf. 30947

47 Disability-Adjusted Life Years/ 377

48 disability adjusted life.ti,ab,kf. 6337

49 Healthy Life Expectancy/ 78

50 (daly* or disability free life expectanc* or haly* or health* life expectanc*).ti,ab,kf. 7492

51 (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf. 32270

52 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf. 2803

53 (sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kf. 655

54 (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf. 8216

55 (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf. 43

56 (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf. 468

57 (hql or hqol or h qol or hrqol or hr qol).ti,ab,kf. 26451

58 (hye or hyes).ti,ab,kf. 78

59 (health* adj2 year* adj2 equivalent*).ti,ab,kf. 48

60 (pqol or qls).ti,ab,kf. 484

61 (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf. 768

62 nottingham health profile*.ti,ab,kf. 1267

63 sickness impact profile.ti,ab,kf. 1102

64 exp health status indicators/ 349165

65 (health adj3 (utilit* or status)).ti,ab,kf. 98849

66 (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf. 17217

67 (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf. 15613

68 disutilit*.ti,ab,kf. 690

69 rosser.ti,ab,kf. 112

70 willingness to pay.ti,ab,kf. 9661

71 standard gamble*.ti,ab,kf. 926

72 (time trade off or time tradeoff).ti,ab,kf. 1733

73 tto.ti,ab,kf. 1512

74 (hui or hui1 or hui2 or hui3).ti,ab,kf. 2121

75 (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf. 25092

76 duke health profile.ti,ab,kf. 94

77 functional status questionnaire.ti,ab,kf. 134

78 dartmouth coop functional health assessment*.ti,ab,kf. 14

79 or/40-78 797531

80 Economics/ 27538

81 exp "Costs and Cost Analysis"/ 271939

82 Economics, Nursing/ 4013

83 Economics, Medical/ 9286

84 Economics, Pharmaceutical/ 3143

85 exp Economics, Hospital/ 25914

86 Economics, Dental/ 1922

87 exp "Fees and Charges"/ 31481

88 exp Budgets/ 14233

89 budget*.ti,ab,kf. 38415

90 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. 299239

91 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 413048

92 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. 229181

93 (value adj2 (money or monetary)).ti,ab,kf. 3242

94 exp models, economic/ 16427

95 economic model*.ab,kf. 4501

96 markov chains/ 16308

97 markov.ti,ab,kf. 31197

98 monte carlo method/ 33090

99 monte carlo.ti,ab,kf. 63847

100 exp Decision Theory/ 13748

101 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. 44018

102 or/80-101 959024

103 79 or 102 1656110

104 search:.tw. 710647

105 meta-analysis.mp,pt. 313181

106 review.pt. 3356973

107 di.xs. 4310362

108 associated.tw. 4980089

109 or/104-108 11282870

110 exp United Kingdom/ 396910

111 (national health service* or nhs*).ti,ab,in.295024

112 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. 130600

113 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in. 2572516

114 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in. 1856768

115 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in. 75193

116 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in. 273104

117 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in. 36345

118 or/110-117 3297784

119 (exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp australia/ or exp oceania/) not (exp United Kingdom/ or europe/) 3446605

120 118 not 119 3092186

121 39 and 103 and 109 and 120 68

Embase <1974 to 2024 July 26>

1 drug eluting stent/ 34040

2 drug eluting coronary stent/ 3306

3 ((drug adj5 (elut* or coat* or cover* or release*)) and stent*).tw. 26973

4 (stent* and DES).tw. 13839

5 stent/ and des.tw. 4445

6 (stent* and (everolimus or sirolimus or biolimus or zotarolimus)).tw. 10417

7 stent/ and (everolimus or sirolimus or biolimus or zotarolimus).tw. 3618

8 (sirolimus/ or everolimus/ or zotarolismus/) and stent*.tw. 4883

9 (sirolimus/ or everolimus/ or zotarolismus/) and stent/ 1980

10 biolimus eluting coronary stent/ 712

11 everolimus eluting coronary stent/4240

12 sirolimus eluting coronary stent/ 2606

13 zotarolimus eluting coronary stent/ 1625

14 angioplasty/ and (stent* adj5 drug).tw. 1511

15 (angioplasty and (stent* adj5 drug)).tw. 3433

16 exp percutaneous coronary intervention/ and (stent* adj5 drug).tw. 11284

17 percutaneous transluminal angioplasty/ and (stent* adj5 drug).tw. 2198

18 (("percutaneous coronary intervention" or PCI or PTCA) and (stent* adj5 drug)).tw. 11215

19 bioabsorbable stent/ 107

20 or/1-19 49407

21 ((coronary or isch?emi*) adj3 "heart disease").tw. 135735

22 ((IHD or CAD) and Heart).tw. 26780

23 Coronary artery disease.tw. 165161

24 ischemic heart disease/ 153668

25 coronary artery disease/ 243054

26 ((Myocardial or Coronary) adj isch?emi*).tw. 53137

27 heart muscle ischemia/ 104158

28 (stemi or nstemi).tw. 42817

29 ST segment elevation myocardial infarction/ 56090

30 non ST segment elevation myocardial infarction/ 23422

31 myocardial infarction.tw. 324130

32 "heart attack*".tw. 10099

33 heart infarction/ 325107

34 ((stable or unstable or pectoris) adj3 angina).tw. 50924

35 stable angina pectoris/ 13629

36 exp unstable angina pectoris/ 28685

37 "acute coronary condition*".tw. 6

38 acute coronary syndrome/ 78362

39 (coronary adj3 (stenosis or restenosis)).tw. 25257

40 exp coronary stenosis/ 2485

41 or/21-40 963704

42 20 and 41 32520

43 limit 42 to english language 31316

44 socioeconomics/ 169136

45 exp Quality of Life/ 709879

46 quality of life.ti,kf. 194409

47 ((instrument or instruments) adj3 quality of life).ab. 5677

48 Quality-Adjusted Life Year/ 38116

49 quality adjusted life.ti,ab,kf. 28871

50 (qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf. 48776

51 disability-adjusted life year/ 5779

52 disability adjusted life.ti,ab,kf. 7622

53 healthy life expectancy/ 305

54 (daly* or disability free life expectanc* or haly* or health* life expectanc*).ti,ab,kf. 9306

55 exp Short form 36/ 53382

56 (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf. 52489

57 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf. 3143

58 (sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kf. 1080

59 (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf. 13012

60 (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf. 73

61 (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf. 548

62 (hql or hqol or h qol or hrqol or hr qol).ti,ab,kf. 42566

63 (hye or hyes).ti,ab,kf. 200

64 (health* adj2 year* adj2 equivalent*).ti,ab,kf. 56

65 (pqol or qls).ti,ab,kf. 789

66 (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf. 947

67 nottingham health profile*.ti,ab,kf. 1709

68 nottingham health profile/ 689

69 sickness impact profile.ti,ab,kf. 1304

70 sickness impact profile/ 2414

71 health status indicator/ 3612

72 (health adj3 (utilit* or status)).ti,ab,kf. 129990

73 (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf. 27547

74 (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf. 20685

75 disutilit*.ti,ab,kf. 1385

76 rosser.ti,ab,kf. 147

77 Willingness To Pay/ 4555

78 willingness to pay.ti,ab,kf. 14456

79 Standard Gamble/ 100

80 standard gamble*.ti,ab,kf. 1242

81 time trade-off method/ 600

82 (time trade off or time tradeoff).ti,ab,kf. 2517

83 tto.ti,ab,kf. 2396

84 (hui or hui1 or hui2 or hui3).ti,ab,kf. 3402

85 (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf. 41859

86 duke health profile.ti,ab,kf. 121

87 functional status questionnaire.ti,ab,kf. 182

88 dartmouth coop functional health assessment*.ti,ab,kf. 14

89 or/44-88 1081612

90 Economics/ 246240

91 Cost/ 64836

92 exp Health Economics/ 1086783

93 Budget/ 35018

94 budget*.ti,ab,kf. 50799

95 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. 368601

96 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 577578

97 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. 315620

98 (value adj2 (money or monetary)).ti,ab,kf. 4375

99 Statistical Model/ 178544

100 exp economic model/ 4344

101 economic model*.ab,kf. 6759

102 Probability/ 157362

103 markov.ti,ab,kf. 41126

104 monte carlo method/ 54393

105 monte carlo.ti,ab,kf. 67642

106 Decision Theory/ 1882

107 Decision Tree/ 25368

108 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. 59044

109 or/90-108 2135163

110 89 or 109 3006198

111 exp methodology/ 8128684

112 search:.tw. 890919

113 review.pt. 3262753

114 or/111-113 10981604

115 exp United Kingdom/ 479705

116 (national health service* or nhs*).ti,ab,in,ad. 505668

117 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. 65824

118 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jx,in,ad. 3887113

119 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or

((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*"))))).ti,ab,in,ad. 3048703

120 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in,ad. 125627

121 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in,ad. 419591

122 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in,ad. 58731

123 or/115-122 4754750

124 (exp "arctic and antarctic"/ or exp oceanic regions/ or exp western hemisphere/ or exp africa/ or exp asia/) not (exp united kingdom/ or europe/) 3692903

125 123 not 124 4481061

126 43 and 110 and 114 and 125 165

NHS EED

1 MeSH DESCRIPTOR Drug-Eluting Stents 271

2 ((drug NEAR (elut* or coat* or cover* or release*)) and stent*) 438

3 (stent* and DES) 86

4 MeSH DESCRIPTOR Stents 834

5 (DES) 747

6 #4 AND #5 58

7 (stent* and (everolimus or sirolimus or biolimus or zotarolimus)) 183

8 (everolimus or sirolimus or biolimus or zotarolimus) 287

9 #4 AND #8 114

10 MeSH DESCRIPTOR Sirolimus EXPLODE ALL TREES 204

11 (stent*) 1401

12 #10 AND #11 127

13 #4 AND #10 78

14 MeSH DESCRIPTOR Angioplasty 118

15 (stent* adj5 drug) 104

16 #14 AND #15 1

17 (angioplasty and (stent* adj5 drug)) 50

18 MeSH DESCRIPTOR Percutaneous Coronary Intervention 224

19 #15 AND #18 9

20 (("percutaneous coronary intervention" or PCI or PTCA) and (stent* adj5 drug)) 47

21 #1 OR #2 OR #3 OR #6 OR #7 OR #9 OR #12 OR #13 OR #16 OR #17 OR #19 OR #20 469

22 ((coronary or isch?emi*) adj3 "heart disease") 875

23 ((IHD or CAD) and Heart) 133

24 (Coronary artery disease) 1103

25 MeSH DESCRIPTOR Coronary Disease 689

26 MeSH DESCRIPTOR Coronary Artery Disease 587

27 ((Myocardial or Coronary) adj isch?emi*) 357

28 MeSH DESCRIPTOR Myocardial Ischemia 173

29 (stemi or nstemi) 105

30 MeSH DESCRIPTOR ST Elevation Myocardial Infarction 0

31 MeSH DESCRIPTOR Non-ST Elevated Myocardial Infarction 0

32 (myocardial infarction) 2503

33 ("heart attack*") 91

34 ((stable or unstable or pectoris) adj3 angina) 421

35 MeSH DESCRIPTOR Myocardial Infarction 1052

36 MeSH DESCRIPTOR Angina, Stable 15

37 MeSH DESCRIPTOR Angina, Unstable EXPLODE ALL TREES 92

38 MeSH DESCRIPTOR Angina Pectoris 158

39 ("acute coronary condition*") 0

40 MeSH DESCRIPTOR Acute Coronary Syndrome 219

41 (coronary adj3 (stenosis or restenosis)) 312

42 MeSH DESCRIPTOR Coronary Stenosis EXPLODE ALL TREES 254

43 #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 4254

44 #21 AND #43 391

45 #45 in NHS EED 73

46 MeSH DESCRIPTOR United Kingdom EXPLODE ALL TREES 498

47 (national health service* or nhs*) 20694

48 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)) 31794

49 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*) 12412

50 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or

nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))) 8295

51 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's") 30

52 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's") 468

53 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's") 127

54 #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 43859

55 MeSH DESCRIPTOR africa EXPLODE ALL TREES 559

56 MeSH DESCRIPTOR americas EXPLODE ALL TREES 4408

57 MeSH DESCRIPTOR antarctic regions EXPLODE ALL TREES 0

58 MeSH DESCRIPTOR arctic regions EXPLODE ALL TREES 0

59 MeSH DESCRIPTOR asia EXPLODE ALL TREES 1436

60 MeSH DESCRIPTOR australia EXPLODE ALL TREES 425

61 MeSH DESCRIPTOR oceania EXPLODE ALL TREES 489

62 #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 6721

63	MeSH DESCRIPTOR united kingdom EXPLODE ALL TREES	498
64	MeSH DESCRIPTOR europe EXPLODE ALL TREES	3381
65	#68 OR #69	3381
66	#67 NOT #70	6529
67	#59 NOT #71	38146
68	#45 AND #72 IN NHSEED	52

CEA Registry

Basic search for Methods; Filter by Country UK

1. "drug eluting stent" 2
2. "drug eluting stents" 5
3. drug and stent 6

Total: 8

Appendix C: Indirectly relevant studies

7 RCTs were identified and considered to be indirectly relevant to this assessment Brief descriptions of comparisons made in the studies and reasons for exclusion from the main assessment are reported in this section.

One RCT was identified that compared durable polymer DES with bioabsorbable polymer DES (Kim et al. 2020). Some stents included in this study were outside of the scope of this assessment (DESyne and Nobori). This study was excluded from the main assessment as outcomes were not reported per stent and could not be attributed to individual stents of interest.

The remaining six RCTs (reported across 12 publications) compared an in-scope device with the first or second generation device of the in-scope Onyx Frontier device (Endeavor Resolute and Resolute Integrity). As mentioned in Section 4.1.1, the company indicated that evidence for these two generations is no longer used to support the clinical efficacy or safety of the Onyx Frontier device, due to availability of evidence for the third generation device Resolute Onyx. The comparisons drawn in these RCTs are summarised in Table 29.

Table 29: RCTs with out of scope previous generations of Onyx Frontier compared against another in-scope device.

Study name (associated references)	Comparison in RCT
TWENTE (Lam et al. 2015, Lowik et al. 2015, von Birgelen et al. 2012)	Endeavor Resolute vs Xience V
TWENTE II/DUTCH PEERS (Zocca et al. 2018b, Sen et al. 2015, van der Heijden et al. 2016, von Birgelen et al. 2014)	Resolute Integrity vs Promus Element
RESOLUTE All Comers (Iqbal et al. 2015, Taniwaki et al. 2014)	Endeavor Resolute vs Xience
ISAR-TEST 5 (Colleran et al. 2017)	Endeavor Resolute vs Coroflex ISAR
ORIENT (Kim et al. 2020	Resolute Integrity vs Orsiro
SORT OUT VI (Raungaard et al. 2015)	Resolute Integrity vs BioMatrix Flex

Additionally, 10 systematic reviews and meta-analyses (SRMA) or network meta-analyses (NMA) were identified which had broader scopes than that of this assessment. Brief descriptions of the review scopes and reasons for exclusion are summarised in Table 30. Results have not been extracted as all relevant primary studies included in these SRMA/NMAs have been considered for inclusion in the

EAG assessment on an individual basis. Additionally, there is overlap in the trials included in these SRMA/NMAs with each other. Results of one NMA have been briefly discussed in Section 5.2.4 (Taglieri et al. 2020).

Table 30: Indirectly relevant SRMA and NMA studies.

Reference	Description	Reasons for exclusion from main assessment
Bangalore et al. 2018	SRMA of newer-generation ultrathin strut DES versus older second generation thicker strut DES.	Included out of scope DES (MiStent).
Giacobbe et al. 2024	NMA of coronary stents (including bare metal stents) in high bleeding risk patients.	Included out of scope bare metal stents.
Hussain et al. 2022	SRMA of ultrathin versus standard thickness second generation DES.	Included out of scope DES (Resolute Integrity, MiStent, Nobori).
Iglesias Juan et al. 2021	SRMA of ultrathin versus standard thickness second generation DES.	Included out of scope DES (Resolute Integrity, MiStent, Nobori).
Kang et al. 2016	NMA of stent thrombosis with DES and bioabsorbable scaffolds.	Included out of scope bare metal stents, out of scope DES (including 1st generation DES) and out of scope DES with bioresorbable scaffolds.
Madhavan et al. 2021	SRMA of ultrathin versus 'conventional' second generation DES.	Included out of scope DES (Endeavor, Resolute, MiStent, Nobori).
Mir et al. 2021	SR and MA of BP-DES vs DP-metallic DES.	Included out of scope DES (Resolute Integrity, MiStent, Nobori, Tivoli).
Saito et al. 2022	SR and meta-regression analysis assessing the relationship between strut thickness and clinical outcomes.	Includes out of scope 1st generation DES.
Taglieri et al. 2020	NMA of TLF with DES.	Includes out of scope DES (Nobori, Yukon PF, Resolute) and uses RCTs with BMS comparators to strengthen network.
Zhu et al. 2018	SRMA of ultrathin BP-DES versus DP-DES.	Includes out of scope DES (Resolute Integrity) and RCTs which are underpowered for detecting differences in clinical endpoints at a minimum of one year follow-up, so do not meet EAG criteria for pragmatic selection for this assessment (BIOFLOW II, PRISON IV).

***Abbreviations**: BP-DES: bioabsorbable polymer-drug eluting stent; DES: drug eluting stent; DP-DES: durable polymer-drug eluting stent; EAG: External Assessment Group; NMA: network meta-analysis; RCT: randomised controlled trial; SRMA: systematic review and meta-analysis; TLF: target lesion failure.*

Appendix D: Conference proceedings/abstracts and ongoing trial records

The following screening criteria was used to identify relevant conference proceedings/abstracts and ongoing trial records for inclusion:

- RCT study design
- Both devices in scope (or an accepted predecessor)
- Not associated with an RCT that has already been included via a full-text publication
- Planned minimum follow-up duration of one year
- Primary outcome should be a key clinical endpoint (in scope), as advised by clinical experts

No conference proceedings/abstracts met the above criteria.

Four ongoing trials met the above criteria which are summarised in Table 31.

Table 31: Ongoing trials.

Trial record number (study name)	Status	Country	Device 1	Device 2		Primary outcome/endpoint and duration of follow-up
NCT04500912	Completed 01/09/2023	Netherlands	Supraflex Cruz 60 Micron	Ultimaster Tansei 80 Micron	High bleeding risk	Net Adverse Clinical Endpoints (NACE) defined as a composite of cardiovascular death, myocardial infarction, target vessel revascularization, stroke and bleeding events defined as BARC 3 or 5 at 12 months follow-up after the index PCI.
NCT05240781 **ZEVS-HBR**	Recruiting	Mexico	Resolute Onyx	Ultimaster Tansei / Ultimaster	High bleeding risk	Target lesion failure (TLF) at 12 months in high bleeding risk patients who underwent elective coronary percutaneous intervention with a zotarolimus eluting stent versus a sirolimus eluting stent and short Dual Antiplatelet Therapy (DAPT).
NCT05066789 **SMART-CHOICE4**	Recruiting	South Korea	BioFreedom Ultra	Orsiro Mission	Acute coronary syndromes	A composite of cardiac death, target vessel-myocardial infarction, or clinically indicated target-lesion revascularization by percutaneous or surgical methods at 12-months.
NCT05305482 **ONE-PASS**	Recruiting	South Korea	BioFreedom Ultra	Ultimaster	Acute coronary syndromes	Patient-Oriented Composite Endpoint (POCE): composite of all-cause death, MI, or any revascularization at 12-months post-randomisation.

Appendix E: Subgroup results from key RCTs.

Table 32 summarises results from the 22 key RCTs that are relevant to subgroups specified in the scope. Ethnicity has not been included as a subgroup in the table as no studies reported results for ethnic subgroups.

Table 32: Subgroup results from key RCTs.

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Subgroup				
				Diabetes	Left main stem lesions	Bifurcation lesions	HBR	Women
ANGIOLITE (Moreu et al. 2019), 2 years.	All comers	Angiolite (110)	Xience Xpedition (Pro 48) (113)	No breakdown of results in these subgroups or sub-analyses performed.				
BIODEGRADE (Yoon et al. 2023), 3 years.	All comers	Orsiro (1175)	BioMatrix (1166)	Fewer events are reported for BioMatrix than for Orsiro in the no-diabetes group (p=0.001). No difference in device outcomes in the diabetes group. P value for the interaction = 0.004.	Not reported.	Not reported.	Not reported.	Orsiro outcomes appear better than BioMatrix outcomes in males (p=0.004). No difference in device outcomes in females. P value not significant for interaction (p=0.067).
BIOFLOW-DAPT (Valgmigli et al. 2023), 1 year.	HBR patients who received 1 month DAPT.	Orsiro Mission (969)	Resolute Onyx (979)	No significant differences between the devices in the diabetes and in the no-diabetes groups.	Not reported.	Not reported.	N/A (total population is HBR).	No significant differences between the devices in males and in females.
BIOFLOW IV (Slagboom et al. 2023), 5 years.	CAD (excluded those with acute MI).	Orsiro (385)	Xience Prime/ Xpedition (Pro 48) (190)	No breakdown of results in these subgroups or sub-analyses performed.				

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Subgroup				
				Diabetes	Left main stem lesions	Bifurcation lesions	HBR	Women
BIOFLOW V (Kandzari et al. 2022), 5 years.	IHD (excluded those with STEMI.	Orsiro (884)	Xience (450)	No significant interaction observed between diabetic status and TLF rate between devices (p for interaction =0.552).	Not reported.	Not reported.	Not reported.	No significant interaction observed between sex and TLF rate between devices (p for interaction = 0.703).
BioFreedom QCA (Sabaté et al. 2021), 2 years.	All comers	BioFreedom Ultra (97)	BioFreedom (97)	Not reported for clinical endpoints (difference in LLL between devices at 9 months consistent between those with and without diabetes).	Not reported.	Not reported.	Not reported.	Not reported.
BIONYX (van Vliet et al. 2024), 5 years.	All comers	Resolute Onyx (1243)	Orsiro (1245)	Full sub-analysis reported in Ploumen et al. 2021.	Not reported.	No significant interaction observed between presence of at least 1 bifurcation and TVF rate between devices (p for interaction =0.89).	Not reported.	No significant interaction observed between sex and TVF rate between devices (p for interaction =0.32).
BIO-RESORT (Ploumen et al. 2022), 5 years.	All comers	Synergy (1172)	Orsiro (1169)	Full sub-analysis reported in Ploumen et al. 2021.	No analysis of Synergy vs Orsiro results.	No analysis of Synergy vs Orsiro results.	Not reported.	No analysis of Synergy vs Orsiro results.
BIOSCIENCE (Pilgrim et al. 2018), 5 years.	All comers	Orsiro (1063)	Xience Prime (1056)	Full sub-analysis reported in Iglesias et al. 2019a.	Not reported.	Not reported.	Not reported.	No significant interaction observed between sex and

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Subgroup				
				Diabetes	Left main stem lesions	Bifurcation lesions	HBR	Women
								TLF rate between devices (p for interaction = 0.808).
BIOSTEMI (Iglesias et al. 2023), 5 years.	STEMI only	Orsiro (649)	Xience Prime/Xpedition (Pro 48) (651)	No significant interaction observed between diabetes status and TLF rate between devices (BPP for interaction = 0.797).	Not reported.	Not reported.	Not reported.	No significant interaction observed between sex and TLF rate between devices (BPP for interaction = 0.577).
CASTLE (Nakamura et al. 2022), 1 year.	All comers	Orsiro (722)	Xience Sierra (Pro S)/Xpedition (Pro 48) (718)	No significant interaction observed between diabetes status and TLF rate between devices (p for interaction = 0.844).	Not reported.	No significant interaction observed between presence of bifurcation disease and TLF rate between devices (p for interaction = 0.862).	Not reported.	No significant interaction observed between sex and TLF rate between devices (p for interaction = 0.713).
CENTURY II (Wijns et al. 2018), 5 years.	All comers	Ultimaster (562)	Xience (557)	No significant interaction observed between diabetes status and TLF rate between devices (p for interaction = 0.86.	Not reported.	Full sub-analysis reported in Orvin et al. 2016.	Not reported.	Not reported.
EVOLVE II (Kereiakes et al. 2019), 5 years.	NSTEMI/stable angina	Synergy (846)	Promus Element Plus (838)	Not reported. Diabetes sub study performed on Synergy arm only.	Not reported.	Not reported.	Not reported.	Not reported.

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Subgroup				
				Diabetes	Left main stem lesions	Bifurcation lesions	HBR	Women
IDEAL-LM (van Geuns et al. 2022), 2 years.	Left main only.	Synergy (410)	Xience (408)	Not reported.	N/A (total population is left main lesions).	Not reported.	Not reported.	Not reported.
MERIT-V (Abizaid et al. 2023), 2 years.	All comers	BioMime (170)	Xience V (86)	No breakdown of results in these subgroups or sub-analyses performed.				
Onyx ONE (Windecker et al. 2022), 2 years.	HBR	Resolute Onyx (1003)	BioFreedom (993)	No significant differences between the devices in the diabetes and in the no-diabetes groups.	Not reported.	Not reported.	N/A (total population is HBR).	No significant differences between the devices in males or in females.
PLATINUM (Kelly et al. 2017), 5 years.	Stable/unstable angina pectoris or silent ischemia (excluded those with acute MI).	Promus (768)	Xience V (762)	No significant interaction observed between diabetes status and TLF rate between devices (p for interaction = 0.72).	Not reported.	Not reported.	Not reported.	No significant interaction observed between sex and TLF rate between devices (p for interaction = 0.53).
SORT OUT IX (Ellert-Gregersen et al. 2022), 2 years.	All comers	BioFreedom (1572)	Orsiro (1579)	Full sub-analysis reported in Hansen et al. 2022.	No significant interaction observed between presence of LAD lesion and TLF rate between devices (p for interaction = 0.36).	Not reported.	Not reported	No significant interaction observed between sex and TLF rate between devices (p for interaction = 0.35).
SORT OUT VIII (Maeng et al. 2019), 1 year.	All comers	BioMatrix (1379)	Synergy (1385)	Full sub-analysis reported in Gyldenkerne et al. 2019.	No significant interaction observed between presence of LAD	Not reported.	Not reported.	No significant interaction observed between sex and TLF rate

Study name (reference), follow-up duration.	Study population	Device 1 (ITT n)	Device 2 (ITT n)	Subgroup				
				Diabetes	Left main stem lesions	Bifurcation lesions	HBR	Women
					lesion and TLF rate between devices (p for interaction = 0.40).			between devices (p for interaction = 0.08).
TALENT (de Winter et al. 2022), 3 years.	All comers	Supraflex (720)	Xience family (715)	No significant interaction observed between diabetes status and DOCE rate between devices (p for interaction = 0.629).	No significant interaction observed between presence of left main lesion and DOCE rate between devices (p for interaction = 0.517).	No significant interaction observed between presence of bifurcation disease and DOCE rate between devices (p for interaction = 0.511).	Not reported.	Not reported.
TARGET-AC (Lanksy et al. 2023), 5 years.	All comers	Firehawk (823)	Xience family (830)	No significant interaction observed between diabetes status and TLF rate between devices (p for interaction = 0.999)	No significant interaction observed between the presence of left main lesion and TLF rate between devices (p for interaction = 0.814)	No significant interaction observed between the presence of any bifurcation lesion and TLF rate between devices (p for interaction = 0.525)	Not reported.	No significant interaction observed between sex and TLF rate between devices (p for interaction = 0.785)
XLIMIT (Testa et al. 2023), 1 year.	CAD (excluded those with STEMI)	Xlimus (117)	Synergy (60)	No breakdown of results in these subgroups or sub-analyses performed.				

Appendix F: Model Fit Summary

A. FE model vs RE model

Analysis	Fixed effects			Random effects		
	Residual deviance	**pD**	**DIC**	**Residual deviance**	**pD**	**DIC**
TLR Y1[a]	26.44	23.19	49.63	26.52	23.55	50.07
TVMI Y1[a]	32.97	22.84	55.81	32.46	23.63	56.09
TLR follow-up[b]	31.41	21.07	52.48	30.76	21.45	52.21
TVMI follow-up[b,c]	23.61	21.01	44.62	23.39	21.07	44.46

B. Inconsistency test: NMA vs UME model, prior het 0.1

Analysis	NMA (Consistency)			UME (Inconsistency)		
	Residual deviance	**pD**	**DIC**	**Residual deviance**	**pD**	**DIC**
TLR Y1[a]	26.52	23.55	50.07	27.29	25.23	52.51
TVMI Y1[a]	32.46	23.63	56.09	28.12	24.68	52.86
TLR follow-up[b]	30.76	21.45	52.21	31.27	22.12	53.39
TVMI follow-up[b,c]	23.39	21.07	44.46	22.23	22.11	44.35

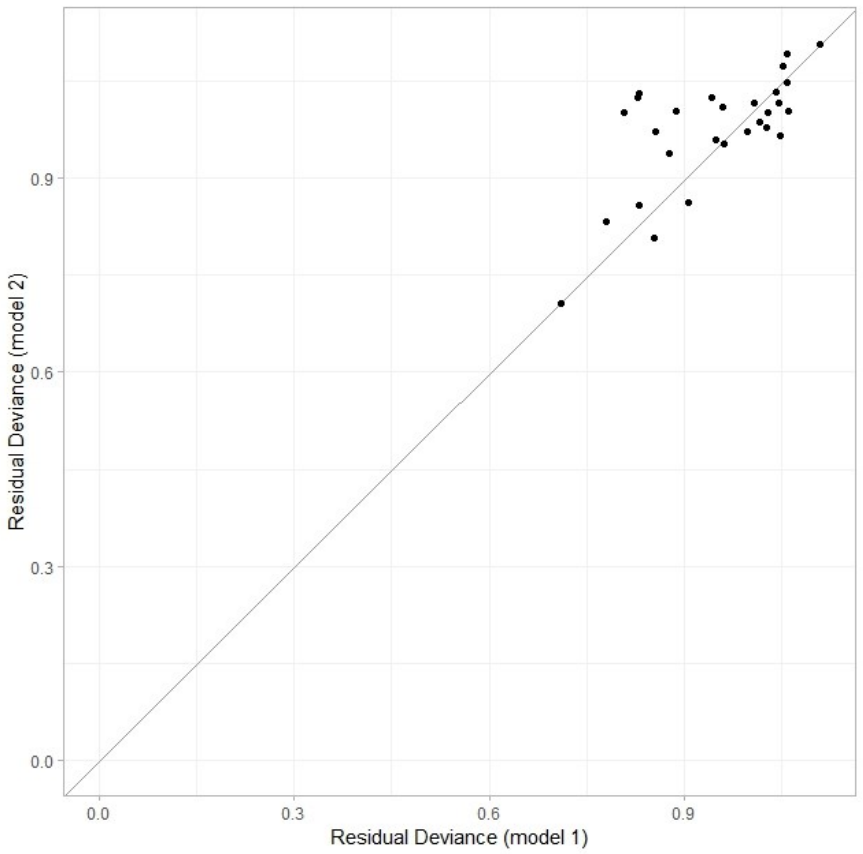
Notes:

[a] On 28 data points
[b] On 24 data points
[c] Prior treatment effect: Normal (SD 2.82)

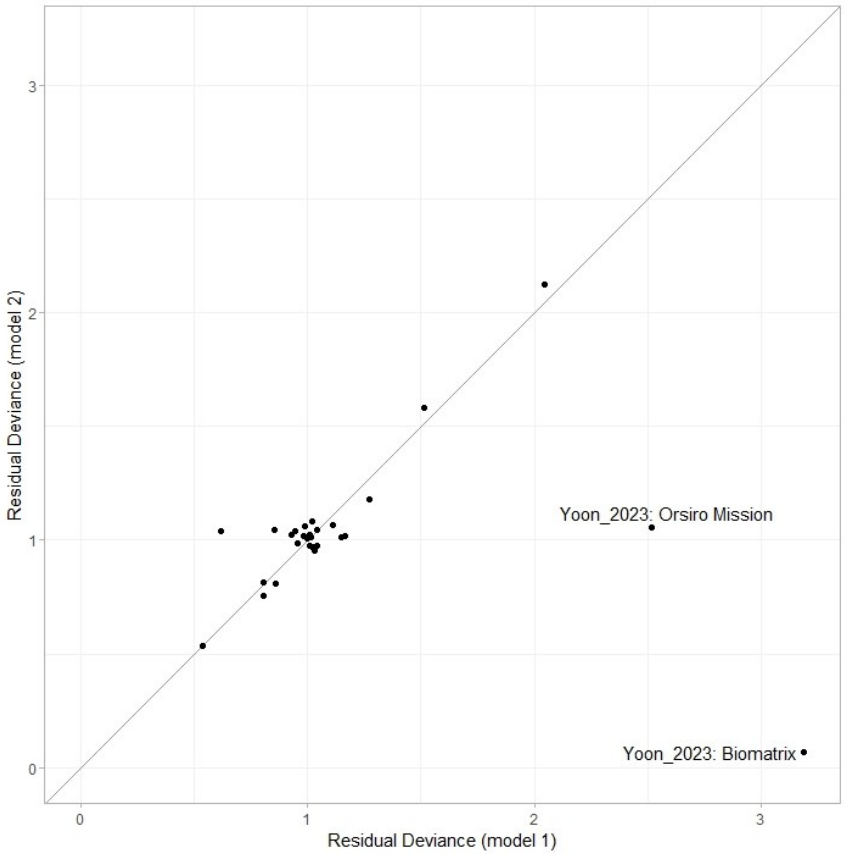
Abbreviations*: DIC: Deviance Information Criterion; FE: fixed effects; NMA: network meta-analysis; pD: effective number of parameters; RE: random effects; SD: standard deviation; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction; UME: unrelated mean effects.*

C. **Dev-dev plot between NMA vs UME model, prior het 0.1**

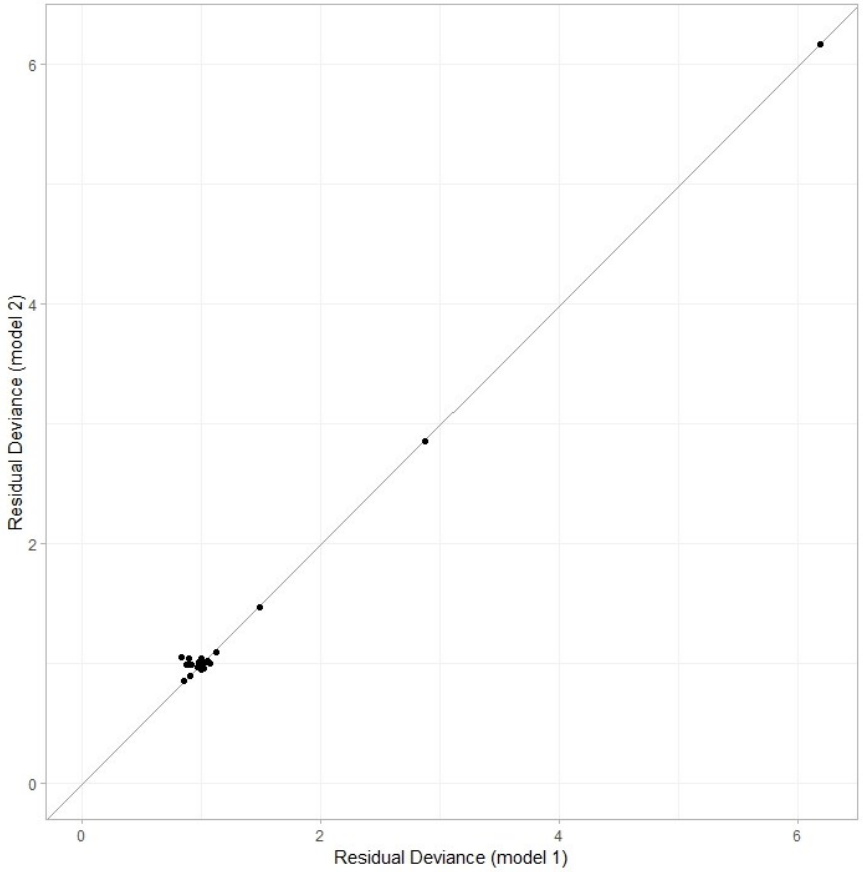
Y1 NMA: TLR



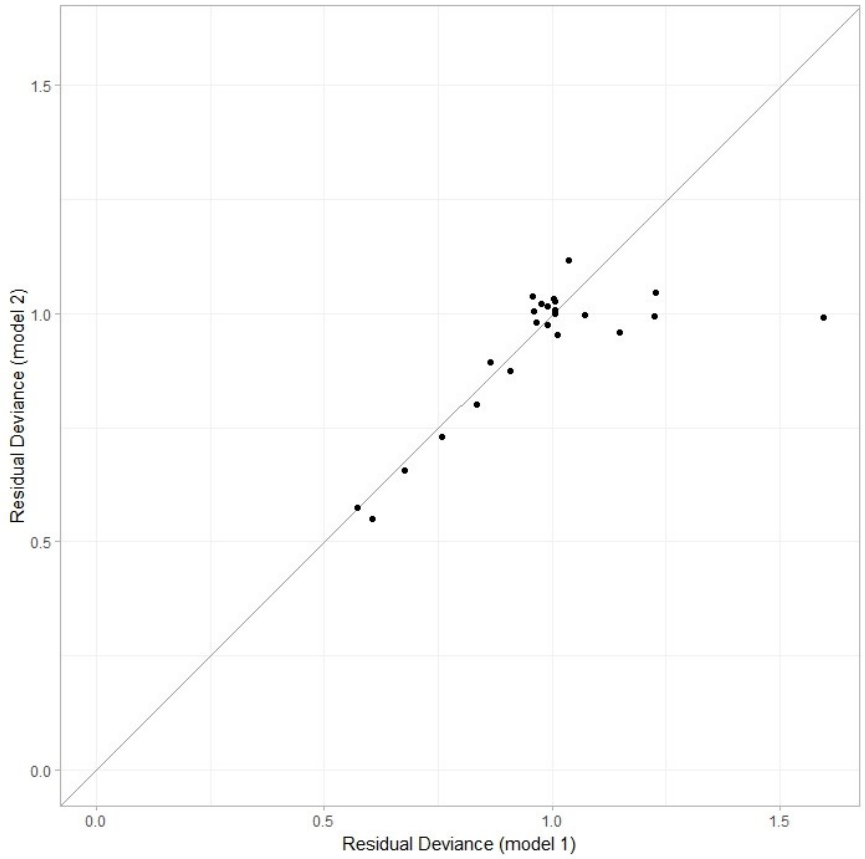
Y1 NMA: TVMI



Long-term follow-up NMA: TLR



Long-term follow-up: TVMI



Appendix G: NMA league tables.

NMA league table: Y1 TLR (HR with 95%CrI)

	Xience	BioFreedom	BioMatrix	Firehawk	Orsiro	Promus Element	Resolute Onyx	Supraflex	Synergy	Ultimaster
Xience		-	-	0.49 (0.20, 1.14)	1.21 (0.80, 1.81)	1.00 (0.45, 2.16)	-	0.67 (0.37, 1.23)	-	0.94 (0.48, 1.82)
BioFreedom	**3.70** (1.83, 6.80)		-	-	**0.35** (0.20, 0.61)	-	-	-	-	-
BioMatrix	1.87 (0.94, 3.32)	0.55 (0.23, 1.11)		-	0.54 (0.23, 1.19)	-	-	-	0.91 (0.54, 1.52)	-
Firehawk	0.54 (0.20, 1.11)	**0.16** (0.05, 0.39)	0.32 (0.09, 0.78)		-	-	-	-	-	-
Orsiro	1.25 (0.84, 1.81)	**0.36** (0.20, 0.59)	0.72 (0.39, 1.19)	2.84 (1.01, 6.75)		-	1.31 (0.74, 2.35)	-	0.94 (0.47, 1.88)	-
Promus Element	1.00 (0.52, 1.77)	**0.30** (0.12, 0.63)	0.57 (0.27, 1.07)	2.28 (0.71, 5.89)	0.82 (0.42, 1.49)		-	-	1.58 (0.79, 3.19)	-
Resolute Onyx	1.71 (0.80, 3.20)	**0.50** (0.20, 0.96)	0.98 (0.40, 2.01)	3.86 (1.11, 9.93)	1.36 (0.73, 2.33)	1.85 (0.70, 3.92)		-	-	-
Supraflex	0.70 (0.36, 1.22)	**0.21** (0.08, 0.47)	**0.41** (0.15, 0.90)	1.57 (0.48, 3.95)	0.58 (0.26, 1.10)	0.77 (0.29, 1.66)	0.46 (0.16, 1.00)		-	-
Synergy	1.51 (0.81, 2.54)	**0.45** (0.19, 0.86)	0.84 (0.51, 1.27)	3.42 (1.06, 8.67)	1.22 (0.71, 1.97)	1.58 (0.85, 2.70)	0.97 (0.41, 1.94)	2.39 (0.94, 5.08)		-
Ultimaster	0.99 (0.48, 1.85)	**0.30** (0.10, 0.68)	0.58 (0.22, 1.29)	2.23 (0.68, 5.88)	0.82 (0.35, 1.64)	1.09 (0.40, 2.41)	0.65 (0.22, 1.53)	1.57 (0.56, 3.56)	0.71 (0.27, 1.51)	

Notes:
Hazard ratios lower than 1 favour the row-defining device for the NMA results (lower triangle) and column-defining intervention for the pairwise results (upper triangle)
Estimates in bold indicate that 95%CrI does not include null.

NMA league table: Y1 TVMI (HR with 95%CrI)

	Xience	BioFreedom	BioMatrix	Firehawk	Orsiro	Promus Element	Resolute Onyx	Supraflex	Synergy	Ultimaster
Xience		-	-	1.16 (0.69, 1.98)	0.85 (0.63, 1.14)	0.48 (0.17, 1.33)	-	0.90 (0.43, 1.87)	-	0.56 (0.21, 1.42)
BioFreedom	0.88 (0.43, 1.61)		-	-	1.00 (0.57, 1.79)	-	-	-	-	-
BioMatrix	1.05 (0.43, 2.19)	1.31 (0.43, 3.22)		-	Not estimable	-	-	-	0.56 (0.28, 1.08)	-
Firehawk	1.19 (0.67, 1.94)	1.51 (0.59, 3.10)	1.36 (0.46, 3.17)		-	-	-	-	-	-
Orsiro	0.84 (0.62, 1.10)	1.04 (0.55, 1.84)	0.94 (0.39, 1.9)	0.76 (0.41, 1.33)		-	1.00 (0.50, 2.01)	-	0.97 (0.53, 1.81)	-
Promus Element	0.59 (0.31, 1.03)	0.74 (0.29, 1.53)	0.63 (0.28, 1.26)	0.53 (0.21, 1.06)	0.71 (0.37, 1.20)		-	-	1.12 (0.67, 1.80)	-
Resolute Onyx	0.89 (0.38, 1.79)	1.11 (0.40, 2.49)	1.00 (0.29, 2.53)	0.80 (0.28, 1.82)	1.06 (0.49, 2.03)	1.64 (0.58, 3.69)		-	-	-
Supraflex	0.94 (0.46, 1.73)	1.19 (0.42, 2.68)	1.07 (0.33, 2.66)	0.85 (0.34, 1.78)	1.15 (0.52, 2.19)	1.76 (0.65, 3.90)	1.23 (0.39, 2.96)		-	-
Synergy	0.68 (0.37, 1.14)	0.85 (0.36, 1.70)	0.72 (0.35, 1.29)	0.61 (0.27, 1.21)	0.81 (0.47, 1.30)	1.19 (0.76, 1.82)	0.88 (0.33, 1.87)	0.81 (0.31, 1.73)		-
Ultimaster	0.63 (0.21, 1.50)	0.81 (0.21, 2.21)	0.72 (0.16, 2.06)	0.57 (0.16, 1.48)	0.77 (0.25, 1.85)	1.18 (0.31, 3.06)	0.83 (0.20, 2.32)	0.75 (0.19, 2.01)	1.01 (0.27, 2.57)	

Notes:
Hazard ratios lower than 1 favour the row-defining device for the NMA results (lower triangle) and column-defining intervention for the pairwise results (upper triangle)
Estimates in bold indicate that 95%CrI does not include null.

NMA league table: Long-term follow-up TLR (HR with 95%CrI)

	Xience	BioFreedom	BioMatrix	Firehawk	Orsiro	Promus Element	Resolute Onyx	Supraflex	Synergy	Ultimaster
Xience		-	-	1.16 (0.70, 1.94)	1.01 (0.74, 1.40)	0.80 (0.44, 1.41)	-	1.22 (0.56, 2.67)	-	1.23 (0.57, 2.55)
BioFreedom	1.32 (0.64, 2.46)		-	-	0.81 (0.43, 1.50)	-	-	-	-	-
BioMatrix	2.24 (0.79, 5.10)	1.88 (0.55, 4.87)		-	0.51 (0.20, 1.18)	-	-	-	-	-
Firehawk	1.2 (0.70, 1.94)	1.02 (0.40, 2.11)	0.67 (0.19, 1.66)		-	-	-	-	-	-
Orsiro	1.03 (0.76, 1.38)	0.86 (0.44, 1.51)	0.56 (0.21, 1.22)	0.92 (0.49, 1.55)		-	0.68 (0.42, 1.10)	-	0.88 (0.53, 1.50)	-
Promus Element	0.80 (0.48, 1.25)	0.68 (0.28, 1.37)	0.44 (0.14, 1.07)	0.72 (0.33, 1.37)	0.79 (0.47, 1.24)		-	-	1.19 (0.68, 2.10)	-
Resolute Onyx	0.72 (0.40, 1.20)	0.60 (0.26, 1.17)	0.39 (0.12, 0.95)	0.64 (0.28, 1.23)	0.70 (0.43, 1.07)	0.94 (0.45, 1.76)		-	-	-
Supraflex	1.34 (0.57, 2.75)	1.14 (0.36, 2.78)	0.75 (0.18, 2.06)	1.19 (0.42, 2.74)	1.33 (0.52, 2.87)	1.77 (0.63, 3.98)	2.01 (0.67, 4.68)		-	-
Synergy	0.94 (0.57, 1.46)	0.79 (0.34, 1.54)	0.52 (0.17, 1.19)	0.84 (0.39, 1.59)	0.92 (0.57, 1.40)	1.20 (0.75, 1.86)	1.39 (0.71, 2.54)	0.83 (0.29, 1.84)		-
Ultimaster	1.29 (0.58, 2.53)	1.11 (0.35, 2.64)	0.73 (0.18, 2.03)	1.16 (0.43, 2.59)	1.29 (0.54, 2.70)	1.72 (0.64, 3.70	1.96 (0.69, 4.51)	1.14 (0.33, 2.84)	1.47 (0.55, 3.23)	

Notes:
Hazard ratios lower than 1 favour the row-defining device for the NMA results (lower triangle) and column-defining intervention for the pairwise results (upper triangle)
Estimates in bold indicate that 95%CrI does not include null.

NMA league table: Long-term follow-up TVMI (HR with 95%CrI)

	Xience	BioFreedom	BioMatrix	Firehawk	Orsiro	Promus Element	Resolute Onyx	Supraflex	Synergy	Ultimaster
Xience		-	-	0.96 (0.61, 1.50)	0.82 (0.54, 1.24)	1.60 (0.49, 5.35)	-	0.41 (0.14, 1.14)	-	3.15 (0.41, 46.66)
BioFreedom	0.99 (0.41, 2.04)		-	-	1.00 (0.50, 1.98)	-	-	-	-	-
BioMatrix	1.58 (0.12, 7.29)	1.79 (0.12, 8.54)		-	0.99 (0.12, 8.09)	-	-	-	-	-
Firehawk	0.97 (0.62, 1.45)	1.16 (0.44, 2.53)	1.81 (0.13, 8.15)		-	-	-	-	-	-
Orsiro	0.92 (0.62, 1.31)	1.05 (0.49, 1.95)	1.67 (0.13, 7.56)	0.99 (0.54, 1.65)		-	1.15 (0.70, 1.84)	-	0.79 (0.43, 1.48)	-
Promus Element	0.86 (0.40, 1.65)	1.01 (0.34, 2.37)	1.56 (0.11, 7.52)	0.93 (0.37, 1.88)	0.95 (0.47, 1.77)		-	-	1.27 (0.76, 2.16)	-
Resolute Onyx	1.09 (0.56, 1.92)	1.25 (0.48, 2.69)	1.97 (0.15, 8.91)	1.18 (0.51, 2.30)	1.19 (0.70, 1.92)	1.41 (0.56, 2.92)		-	-	-
Supraflex	0.46 (0.13, 1.11)	0.55 (0.12, 1.61)	0.86 (0.05, 4.14)	0.50 (0.14, 1.28)	0.52 (0.14, 1.34)	0.61 (0.14, 1.65)	0.47 (0.11, 1.29)		-	-
Synergy	0.94 (0.47, 1.69)	1.09 (0.39, 2.49)	1.71 (0.11, 8.14)	1.01 (0.44, 2.05)	1.03 (0.54, 1.75)	1.14 (0.69, 1.79)	0.92 (0.40, 1.79)	2.72 (0.68, 7.73)		-
Ultimaster	7.28 (0.39, 38.93)	8.56 (0.35, 47.86)	14.59 (0.21, 79.70)	8.00 (0.40, 42.59)	8.22 (0.42, 45.88)	9.53 (0.42, 49.97)	7.36 (0.34, 38.66)	19.96 (0.75, 113.43)	8.58 (0.40, 43.38)	

Notes:
Hazard ratios lower than 1 favour the row-defining device for the NMA results (lower triangle) and column-defining intervention for the pairwise results (upper triangle)
Estimates in bold indicate that 95%CrI does not include null.

Appendix H: Non-comparative studies

Table 33: Prospective studies (34 studies, reported across in 36 publications)

Reference(s)	Population	Sample size	Setting	Follow-up duration
Angiolite				
de Prado et al. 2021	All-comers	426	Multi-centre in Spain.	2 years
BioMatrix Alpha				
Lipecki et al. 2022	All-comers	2038	Multi-centre in France.	2 years
BioMime				
Dani et al. 2013	Non-complex coronary lesions.	30	Single-centre in India.	1 year.
Yun et al. 2022	CAD, with and without DM.	231	Single-centre in Korea.	1 year.
BioMime Morph				
Raghu et al. 2021	LM bifurcation lesions.	41	Single-centre in India.	20 months.
BioFreedom				
Garot et al. 2023	All-comers.	1497	Multi-centre in France.	1 year.
Sardella et al. 2018	All-comers	1104	Multi-centre in Italy.	1 year
BioFreedom Ultra				
Eberli et al. 2024	HBR.	404	Multi-centre in France and Switzerland.	3 years.
Coroflex ISAR Neo				
Tarantini et al. 2023a	All-comers	425	Multi-centre in Italy.	1 year
Landolff et al. 2023	All comers	1456	Multi-centre in France.	1 year
Evermine 50				
Sinha et al. 2020	Mixed cardiac indications.	711	Single-centre in India.	1 year.
Firehawk				
Li et al. 2019, Gao et al. 2015 (pooled multi-trial data) Xu et al. 2014 (TARGET II trial only, 1 year data)	Mixed cardiac indications.	1007 (pooled multi-trial data)	Multi-centre in China.	2 years.
Onyx Frontier				
Price et al. 2017	Coronary lesions with very small reference vessel diameter.	101	Multi-centre in USA and Japan.	1 year.
Tarantini et al. 2023b	Left-main lesions	450	Multi-centre in Italy and Portugal.	1 year.

Reference(s)	Population	Sample size	Setting	Follow-up duration
Orsiro Mission				
Waltenberger et al. 2020	All-comers	1356	Multi-centre in Europe and Chile.	5 years.
Bartorelli et al. 2019	All-comers	601	Multi-centre in Italy.	1.5 years.
Boukhris et al. 2020	All-comers	250	Multi-centre in Canada.	1 year.
Kornowski et al. 2017	Diabetics	120	Multi-centre in Israel.	1 year.
Giacaman et al. 2022	All-comers	520	Multi-centre in Chile.	1 year.
Suwannasom et al. 2021	All-comers	150	Multi-centre in Thailand.	1 year.
Supraflex Cruz/Cruz Nevo				
Choudhury et al. 2019	All-comers	469	Multi-centre in UK.	1 year.
Hudec et al. 2024	All-comers	413	Multi-centre in Slovakia.	1 year.
Leistner et al. 2024	Mixed non-HBR and HBR.	Non-HBR (737) and HBR (466)	Multi-centre in Switzerland, Germany and France.	1 year.
Singh et al. 2022	All-comers.	100	Single centre in India.	1 year.
Synergy XD				
Jolly et al. 2024	STEMI.	733	Multi-centre in 8 countries (unnamed).	1 year.
Pivato et al. 2022	HBR.	443	Multi-centre in Italy.	1 year.
Karmpiliotis et al. 2022	Long coronary lesions.	100	Multi-centre in USA, Europe and New Zealand.	2 years.
Ultimaster Tansei/Ultimaster Nagomi				
Barbato et al. 2015	Mixed cardiac indications.	105	Multi-centre in Belgium and Serbia.	2 years.
Park et al. 2024	All-comers.	576	Multi-centre in Korea.	1 year.
Saada et al. 2022	STEMI >80 years.	457	Multi-centre, worldwide.	1 year.
Shishido et al. 2023	Asymptomatic MI, stable or unstable angina.	70	Multi-centre in Japan.	5 years.
Xience (family)				

Reference(s)	Population	Sample size	Setting	Follow-up duration
Džavík et al. 2013	MI, stable or unstable angina, silent ischaemia.	2700 (492 with bifurcation lesions)	Multi-centre (global).	2 years.
Senguttuvan et al. 2022	All-comers.	92	Single centre in India.	2 years.
Xlimus				
Briguori et al. 2016	All-comers.	200	Single centre in Italy.	1 year.

Abbreviations*: CAD: coronary artery disease; DM: diabetes mellitus; HBR: high bleeding risk; LM: left main; STEMI: ST-elevated myocardial infarction.*

Table 34: Retrospective studies (20 studies, reported across 22 publications)

Reference(s)	Population	Sample size	Setting	Follow-up duration
BioFreedom				
Sgueglia et al. 2018	STEMI.	175	Single centre in Italy.	1 year.
BioMime				
Jain et al. 2016	All-comers.	1161	Multi-centre in India.	1 year.
Meennahalli Palleda et al. 2023	All-comers.	1188	Single centre in India.	4 years.
BioMime Morph				
Sharma et al. 2021	Long and multiple lesions.	172	Single centre in India.	1 year.
Patted et al. 2018	Long diffused lesions.	362	Multi-centre in India.	1 year.
Coroflex ISAR NEO				
Krackhardt et al. 2020 (pooled multi trial data)	All-comers.	7243	Multi-centre in Asia and Europe.	1 year.
Evermine 50				
Patted and Thakkar 2020	All-comers.	171	Single centre in India.	2 years.
Onyx Frontier				
Kandzari et al. 2020	HBR	1506	Multi-centre (global).	1 year.
Orsiro Mission				
De Marzo et al. 2020	STEMI	353	Multi-centre in Italy.	3 years.
Rigatelli et al. 2021	All-comers.	1161	Single centre in Italy.	3 years.
Supraflex Cruz/Cruz Nevo				

Reference(s)	Population	Sample size	Setting	Follow-up duration
Chandwani et al. 2019	All-comers.	237	Single centre in India.	3 years.
Lemos et al. 2016	All-comers.	995	Multi-centre in India.	1 year.
Nathani et al. 2020	All-comers	839	Multi-centre in India.	1 year.
Pamidimukkala et al. 2020	All-comers	141	Single centre in India.	1 year.
Synergy XD				
Kirtane et al. 2021	HBR	1487	Multi-centre (global)	15 months.
Noad et al. 2017	HBR	185	Single centre in UK.	1 year.
Synergy Megatron				
De Silva et al. 2023	All-comers.	575	Multi-centre in France, Ireland and UK.	1 year.
Ultimaster Tansei/Nagomi				
Godino et al. 2019 AMI subgroup: Moscarella et al. 2019 Diabetic subgroup: Beneduce et al. 2020	All-comers.	1660	Multi-centre in Italy.	1 year.
Xience Pro 48 (Xpedition)				
Tan et al. 2019	Long lesions.	123	Single centre in Singapore.	1 year.
Hsaio et al. 2022	Complex long diffuse lesions.	213	Multi-centre in Taiwan.	1 year.

***Abbreviations**: HBR: high bleeding risk; STEMI: ST-elevated myocardial infarction.*

Appendix I: Economic models evaluating the cost-effectiveness of drug-eluting stents/PCI

Table 35: Summary of economic models relating to cost-effectiveness of drug-eluting stents/PCI.

Study name, design and location	Intervention(s) and comparator	Trial/registry name/setting, population, time horizon and perspective	Relevant outcomes and key findings	EAG comments
Sharp et al. (2024) Decision tree and Markov model UK	**Intervention:** IVUS-guided PCI **Comparator:** PCI with angiography alone	**Trial:** ULTIMATE trial **Population:** ACS **Time horizon:** Lifetime (40 years) **Perspective:** UK NHS	Life years (LYs) gained, QALYs	A two-part model: a decision tree emulating clinical events in the first year after PCI (subdivided to 0-30 days and from 31 days to 1 year), followed by a lifetime Markov model. The Markov model had 6 health states – no further event, MI, repeat PCI (TLR), post-MI, post-repeat PCI, death. Cycle length: 1 year. The model assumed patients would not experience additional repeat reinfarctions and repeat PCIs as the available data on repeat events after 1 year is lacking. ST was not modelled separately as it is uncommon and captured by MI.
Magnuson et al. (2022) Markov model US	**Intervention:** PCI **Comparator:** CABG	**Trial:** EXCEL trial **Population:** Left main disease **Time horizon:** Lifetime **Perspective:** US healthcare system	LYs gained, QALYs	The model had 6 health states: no event, post-MI, post-stroke, post-MI+stroke, non-CV death and CV death. Variable cycle length: 0-30 days, 30 days through 1 year, then yearly. Ischemia-driven revascularisation was used in the model. The model extrapolated trial data to lifetime using a number of assumptions: (1) non-fatal events were reduced in a linear taper to 1.0 from 5 to 10 years, thereafter no differences between groups after 10 years and (2) similar approach for all deaths in PCI. Sensitivity analyses were performed to explore different variations of assumptions: (1) all events were assumed constant between 5 and 10 years, thereafter no benefit, (2) no benefit beyond the trial period, i.e. 5 years and (3) benefits continued until death.

Mattke et al. (2020) Markov model US	**Intervention:** Ultrathin strut, bioresorbable polymer SES **Comparator:** Thin strut, durable polymer EES	**Trial:** BIOFLOW V trial **Population:** Patients with ischaemic heart disease treated with PCI **Time horizon:** 4 years **Perspective:** US healthcare system	Excess deaths from adverse events	The model had 7 health states: peri-procedural MI, no peri-procedural MI, target vessel MI, post-target vessel MI, TLR, post-TLR and death. Cycle length 1 year, considering model inputs used are on a yearly basis. A number of clinical events were excluded in the model, including TLR within 2 days of the index PCI and within 5 days of any spontaneous MI, and peri-procedural MI that did not meet the authors' criterion (elevated CK-MB of more than 3x the upper normal limit).
Mattke et al. (2019) Markov model US	**Intervention:** Ultrathin strut, bioresorbable polymer SES **Comparator:** Thin strut, durable polymer EES	**Trial:** BIOFLOW V trial **Population:** Patients with ischaemic heart disease treated with PCI **Time horizon:** 12 months **Perspective:** US healthcare system	LYs gained, QALYs	The model had 5 health states: peri-procedural MI, no peri-procedural MI, prior peri-procedural MI, no prior peri-procedural MI and death. The model was divided to in-hospital phase and follow-up (1 year following discharge).
Poder et al. (2017) Discrete-event simulation Canada	**Intervention:** Second-generation DES **Comparator:** BMS	**Trial:** a systematic review of meta-analyses **Population:** Patients with coronary artery disease undergoing PCI **Time horizon:** 2 years **Perspective:** Quebec's public healthcare system perspective	Number of reinterventions avoided	A cost-benefit analysis was conducted. No information on the model. TVR was used in the model as it was widely documented and producing robust results.
Ferko et al. (2016) Markov model US	**Intervention:** Co-Cr EES **Comparator:** BMS	**Trial:** a meta-analysis of 5 RCTs (Valgimigli et al. 2014)	LYs gained, QALYs	The model had 5 health states: event-free, TVR, MI, definite ST and dead. Cycle length 1 year.

		Population: Patients with coronary artery disease undergoing PCI **Time horizon:** 2 years **Perspective:** US Medicare perspective		
Stella et al. (2016) Markov model Brazil	**Intervention:** DES (sirolimus, paclitaxel, everolimus, zotarolimus, or zotarolimus resolute) **Comparator:** BMS	**Trial:** A tertiary public hospital in southern Brazil **Population:** Patients with single vessel coronary artery disease **Time horizon:** 1 year, lifetime **Perspective:** Brazilian Public Health System perspective	TVR avoided (1-year analysis), QALYs gained (lifetime analysis)	The model simulated events during the 1st year post-PCI, by including stent-related outcomes (TVR and ST) and CAD natural disease progression (MI and revascularisation for worsening angina). Thereafter, only CAD progression and very late ST were modelled for a lifetime, assuming no stent-related events after the first year. Cycle length 1 year. The risk of ST was modelled for a lifetime, and tested for a shorter period in the sensitivity analysis. Patients with non-fatal MI due to ST would be treated with DES implantation. The model assumed patients received 1 stent per patient and 12-month DAPT after DES implantation. Patients with symptomatic restenosis were treated with PCI with the same type of stent in their index procedure. Patients who had restenosis for the third time would be treated with CABG.
Baschet et al. (2016) Markov model France	**Intervention:** DES **Comparator:** BMS	**Trial:** a meta-analysis of 76 RCTs (Bangalore et al. 2012) **Population:** Patients with coronary artery disease undergoing PCI **Time horizon:** 5 years **Perspective:** French National Health Insurance perspective	MACE-free survival year gained	The model had 3 health states: event-free, post-MACE (MI, ST without MI and revascularisation without ST or MI) and death. Cycle length 6 months. Effectiveness variable NR.

González-Díaz et al. (2015) Decision tree Mexico	**Intervention:** Early and new-generation DES **Comparator:** BMS	**Trial:** A Cardiology Hospital of the Mexican Social Security Institute **Population:** Patients with coronary artery disease undergoing PCI **Time horizon:** 1 year **Perspective:** Mexican health services provider	MACE episode	The model considered MACEs for 1 year following a PCI: angina, acute MI, in-stent restenosis, stent thrombosis and CV death.
Remak et al (2015) Markov model UK	**Intervention:** Endeavor ZES **Comparator:** BMS	**Trial:** Endeavor I, II, III, IV, V trial **Population:** Coronary artery disease **Time horizon:** 4 years **Perspective:** UK NHS	QALYs, MACE events (AMI, TVR, late ST and death)	The model had 5 health states – no events, AMI, TVR, late ST and death. Cycle length NR. The model assumed that patient would receive the same stent as the index procedure if a repeated procedure was needed. The authors considered TVR as a more stringent measure of efficacy, as compared to TLR.
Wisloff et al (2013) Markov model Norway	**Intervention:** SES, PES **Comparator:** BMS	**Registry:** Swedish Coronary Angiography and Angioplasty Registry (SCAAR), Western Denmark Heart Registry (WDHR) **Population:** 60-year old patients with coronary artery disease **Time horizon:** 5 years	LYs gained	The model had 4 health states: alive, AMI, revascularisation (TLR) and death. Cycle length: 6-month. The model excluded restenosis and MACE, as restenosis would have AMI and/or revascularisation, therefore it had been captured. MACE was considered to be not specific.

		Perspective: Norwegian health care perspective		
Dorenkamp et al (2013) Markov model Germany	**Intervention:** Repeat DES or plain old balloon angioplasty **Comparator:** DCB	**Trial:** ISAR-DESIRE 2 for DES trial **Population**: DES-ISR **Time horizon:** 6 months **Perspective:** German statutory health insurance perspective	LYs gained	The model had 5 health states: Initial DES-ISR revascularisation, post-DES-ISR revascularisation, post-TLR, post-CABG, dead. Each health state was further subdivided by complication: no complications, MI, stroke, bleeding, TLR, mortality. Cycle length: 1 month. The model assumed, after the initial ISR revascularisation, up to 1 TLR with DES implantation could be performed. A total of 3 DES implantations per lesion, including the index DES PCI.
Turco et al (2012) Markov model US	**Intervention:** TAXUS Liberté **Comparator:** TAXUS Express	**Trial:** TAXUS ATLAS SV and LL trial **Population**: Patients post- coronary stenting **Time horizon:** 5 years **Perspective:** US Medicare perspective	MACE events (MI, ST, cardiac death, TVR)	The model simulated clinical pathway without routine angiographic follow-up. A two-part model was used: event or no event for the first 9 months. For patients who had a clinical event, they would move to the clinical event tree. The model considered cardiac death, ST, MI, TVR. Stent thrombosis was considered as subsets of MI and cardiac death in the model. Patients who had ST and survived would move to a post-ST health state. Cycle length NR.
Bonaventura et al (2012) Markov model Germany	**Intervention:** PES **Comparator:** DCB angioplasty	**Trial:** systematic review by authors **Population:** patients with BMS-ISR **Time horizon:** 1 year **Perspective:** German statutory health insurance perspective	LYs gained	The model shared a similar structure as Dorenkamp et al. 2013 The model assumed post-discharge started 1 month after PCI. Complications included were MI, major bleeding, and TLR.

Jahn et al (2010) Discrete event simulation Austria	**Intervention:** DES **Comparator:** BMS	**Trial:** NA **Population:** Coronary artery disease **Time horizon:** NA **Perspective:** NR	NA	The model had 4 main timepoints within patient treatment pathway: stenting, after stenting, surgery/CABG, after surgery. The model examined the impact of waiting time and capacity, without including any clinical effects of the intervention.
Gupta et al (2010) Markov model US	**Intervention:** DES **Comparator:** BMS	**Trial:** pooled analysis of various RCTs **Population**: Patients with coronary artery stenosis at high risk of GI bleeding **Time horizon:** 1 year **Perspective:** NR	QALYs	The model had 4 health states: revascularisation, GI bleeding, cardiac death, GI bleeding death. Cycle length NR. The model did not include late and very late ST, thus bias towards DES.
Ferreira et al (2010) Decision tree and Markov model Brazil	**Intervention:** DES **Comparator:** BMS	**Trial:** prospective study in 3 private hospitals **Population:** Coronary artery disease **Time horizon:** Lifetime **Perspective:** Brazilian Public Health System and Supplementary Health System perspective	Restenosis	The model adopted from Polanczyk et al., 2007. A two-part model: (1) a 6-month decision tree with 3 possibilities following a PCI (event-free, restenosis/thrombosis requiring repeat revascularisation and died); and (2) lifetime Markov model with 5 health states: alive, AMI, restenosis, revascularisation (TVR), dead. Cycle length NR. In the model, TVR was performed for symptomatic restenosis cases. A maximum of 3 PCIs per patient were modelled before patients moved to CABG.

Henriksson et al. (2010) Decision analytic model UK	**Intervention:** 4 prioritisation strategies without biomarkers (no formal prioritisation, two urgency scores, and a risk score) **Comparator:** 3 strategies based on a risk score using biomarkers: a routinely assessed biomarker (estimated glomerular filtration rate), a novel biomarker (C reactive protein), or both	**Trial:** Swedish Coronary Angiography and Angioplasty Registry **Population:** Patients with stable angina on waiting list for CABG **Time horizon:** Lifetime **Perspective:** UK health service perspective	QALYs	For patients who undergone CABG, the model considered no event, procedural stroke/MI/death, post-MI, post-stroke, post-CABG death.
Tamburino et al. (2009) Decision tree Italy	**Intervention:** DES **Comparator:** BMS, CABG	**Trial:** Sicilian DES Registry **Population:** Patients with coronary artery disease and mid-term high restenosis risk **Time horizon:** 9 months **Perspective:** Servizio Sanitario Regionale, Regional Health Service perspective	Cost savings	The model had 2 branches: success and failure. Failure was estimated using TLR for stents, and PCI or a new CABG intervention for CABG.

Abbreviations: *ACS: acute coronary syndrome; AMI: acute myocardial infarction; BMS: bare metal stent; CABG: coronary artery bypass graft; CAD: coronary artery disease; CK-MB: creatine kinase-MB; Co-Cr: cobalt chromium; CV: cardiovascular; DAPT: dual antiplatelet therapy; DCB: drug-coated balloons; DES: drug eluting stent; EES: everolimus-eluting stent; GI: gastrointestinal; ISR: in-stent restenosis; IVUS: intravascular ultrasound; LY: life years;*

MACE: major adverse coronary event; MI: myocardial infarction; NR: not reported; PCI: percutaneous coronary intervention; PES: percutaneous endovascular stent; QALY: quality-adjusted life year; RCT: randomised controlled trial; SCAAR: Swedish Coronary Angiography and Angioplasty Registry; SES: sirolimus-eluting stent; ST: stent thrombosis; TLR: target lesion revascularisation; TVR: Target vessel revascularization; WDHR: Western Denmark Heart Registry; ZES: zotarolimus-eluting stent.

Appendix J: Economic papers not informing the model

Ariyaratne, T. V., Yap, C. H., Ademi, Z., Rosenfeldt, F., Duffy, S. J., Billah, B., & Reid, C. M. (2016). A systematic review of cost-effectiveness of percutaneous coronary intervention vs. surgery for the treatment of multivessel coronary artery disease in the drug-eluting stent era. *European Heart Journal - Quality of Care and Clinical Outcomes*, *2*(4), 261-270.

Carrillo Gomez, D. C., Ortiz Sierra, M. C., Cepeda Gil, M. C., & Guevara Cuellar, C. A. (2012). Cost-effectiveness of drug eluting stents versus bare metal stents in coronary heart disease. A systematic literature review. *Revista Argentina de Cardiologia*, *80*(5), 366-376.

Caruba, T., Katsahian, S., Schramm, C., Charles Nelson, A., Durieux, P., Begue, D., Juilliere, Y., Dubourg, O., Danchin, N., & Sabatier, B. (2014). Treatment for stable coronary artery disease: a network meta-analysis of cost-effectiveness studies. In (Vol. 9, pp. e98371). PLOS ONE.

Cohen, D. J., Van Hout, B., Serruys, P. W., Mohr, F. W., Macaya, C., Den Heijer, P., Vrakking, M. M., Wang, K., Mahoney, E. M., Audi, S., Leadley, K., Dawkins, K. D., & Kappetein, A. P. (2011). Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. *New England Journal of Medicine*, *364*(11), 1016-1026.

Cowper, P. A., Udayakumar, K., Sketch, M. H., & Peterson, E. D. (2005). Economic effects of prolonged clopidogrel therapy after percutaneous coronary intervention. *Journal of the American College of Cardiology*, *45*(3), 369-376.

Ekman, M., Sjogren, I., & James, S. (2006). Cost-effectiveness of the Taxus paclitaxel-eluting stent in the Swedish healthcare system. *Scandinavian Cardiovascular Journal*, *40*(1), 17-24.

Glaser, R., Glick, H. A., Herrmann, H. C., & Kimmel, S. E. (2006). The role of risk stratification in the decision to provide upstream versus selective glycoprotein IIb/IIIa inhibitors for acute coronary syndromes: a cost-effectiveness analysis. *Journal of the American College of Cardiology*, *47*(3), 529-537.

Kong, D. F., Eisenstein, E. L., Sketch, M. H., Zidar, J. P., Ryan, T. J., Harrington, R. A., Newman, M. F., Smith, P. K., Mark, D. B., & Califf, R. M. (2004). Economic impact of drug-eluting stents on hospital systems: a disease-state model. *American Heart Journal*, *147*(3), 449-456.

Kuukasjarvi, P., Rasanen, P., Malmivaara, A., Aronen, P., & Sintonen, H. (2007). Economic evaluation of drug-eluting stents: A systematic literature review and model-based cost-utility analysis. *International Journal of Technology Assessment in Health Care*, *23*(4), 473-479.

Merinopoulos, I., Gunawardena, T., Corballis, N., Tsampasian, V., Vassiliou, V., Eccleshall, S., Ryding, A., & Xydopoulos, G. (2023). Cost effectiveness analysis of drug coated balloon only angioplasty for de novo coronary artery disease. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*, *102*(6), 987-996.

Russell, S., Antonanzas, F., & Mainar, V. (2006). Economic impact of the Taxus coronary stent: implications for the Spanish healthcare system. *Revista Espanola de Cardiologia*, *59*(9), 889-896.

Shrive, F. M., Manns, B. J., Galbraith, P. D., Knudtson, M. L., & Ghali, W. A. (2005). Economic evaluation of sirolimus-eluting stents. *CMAJ: Canadian Medical Association Journal*, *172*(3), 345-351.

Tarricone, R., Marchetti, M., Lamotte, M., Annemans, L., & de Jong, P. (2004). What reimbursement for coronary revascularization with drug-eluting stents. *European Journal of Health Economics*, *4*, 309-316.

Wang, X., Rokoss, M., Dyub, A., Gafni, A., & Lamy, A. (2008). Cost comparison of four revascularisation procedures for the treatment of multivessel coronary artery disease. *Journal of Medical Economics*, *11*, 119-134.

Appendix K: Company-provided training.

Table 36: Description of company-provided training.

Company	Description of training
Abbott Medical	[redacted]
B. Braun Medical	
Biosensors International	
Biotronik	
Boston Scientific	
Cardionovum	No response
IHT	No response
iVascular	
Medtronic	
Meril	No response
Microport	No response
QualiMed	No response
Sahajanand Medical Technologies	No response
Terumo	

Abbreviations*: AHP: allied health professional; HCP: healthcare professional; PCI: percutaneous coronary intervention; SPR: specialist registrar; USA: United States of America.*

GID-HTE10039 Drug-eluting stents for treating coronary artery disease: Supplementary file 1.

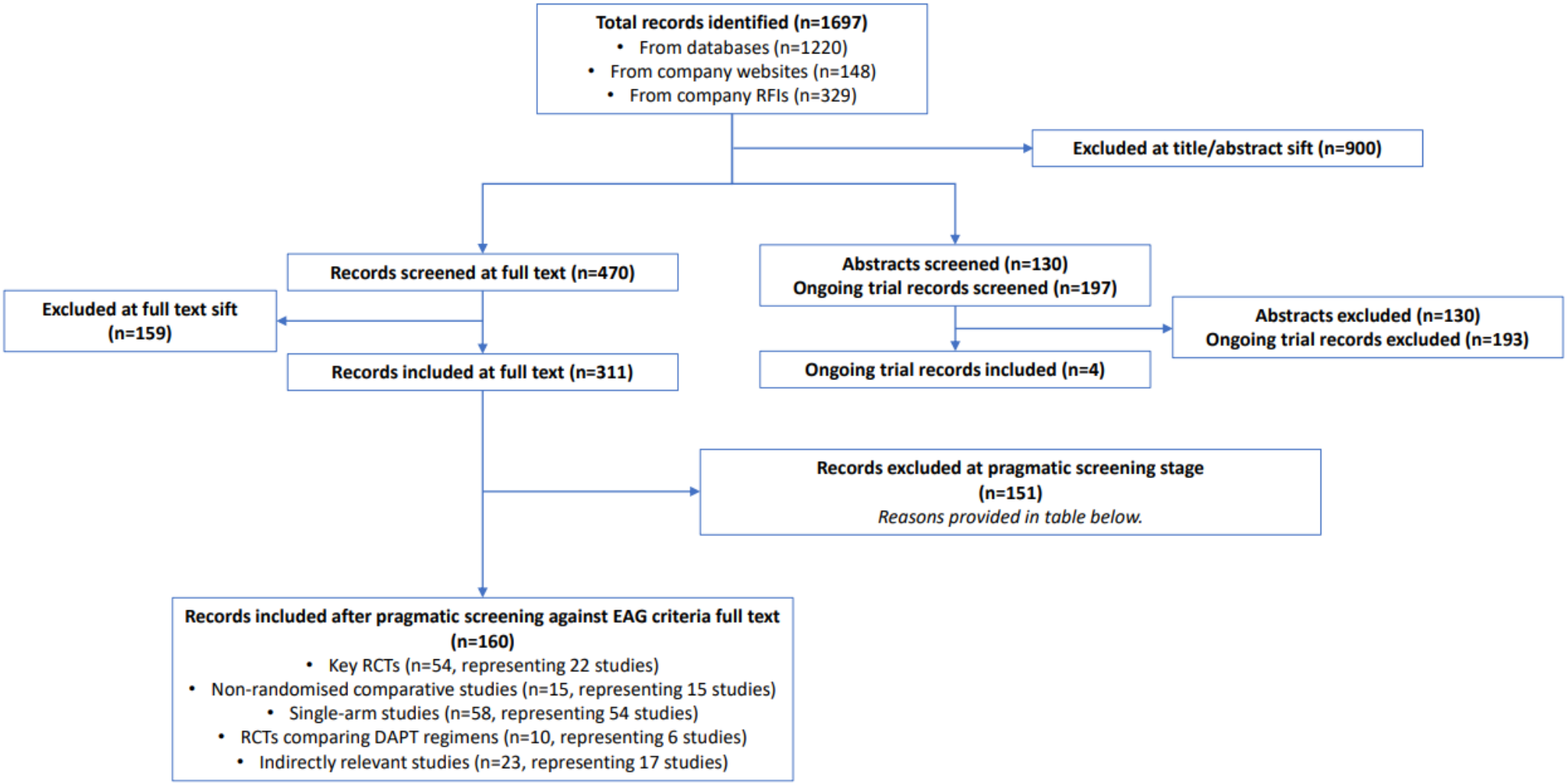


Figure 1: Study selection flowchart for clinical evidence.

Table 1: Studies excluded at pragmatic screening stage.

#	Reference	Year	Title	Reason for exclusion
1	L. N. Andreasen; I. R. Balleby; T. O. Barkholt; L. Hebsgaard; C. J. Terkelsen; E. N. Holck; L. O. Jensen; M. Maeng; J. Dijkstra; L. Antonsen; et al.	2023	Early healing after treatment of coronary lesions by thin strut everolimus, or thicker strut biolimus eluting bioabsorbable polymer stents: the SORT-OUT VIII OCT study	Less than 1 year follow-up.
2	L. N. Andreasen; I. R. Balleby; T. Ø. Barkholt; L. Hebsgaard; C. J. Terkelsen; E. N. Holck; L. O. Jensen; M. Maeng; J. Dijkstra; L. Antonsen; S. D. Kristensen; S. Tu; J. F. Lassen; E. H. Christiansen; N. R. Holm	2023	Early healing after treatment of coronary lesions by thin strut everolimus, or thicker strut biolimus eluting bioabsorbable polymer stents: The SORT-OUT VIII OCT study	Duplicate.
3	L. N. Andreasen; N. R. Holm; I. R. Balleby; L. R. Krusell; M. Maeng; L. Jakobsen; K. T. V. Veien; K. N. Hansen; S. D. Kristensen; A. Kaltoft; J. Dijkstra; J. Hjort; S. Tu; C. J. Terkelsen; J. F. Lassen; M. Madsen; H. E. Botker; L. O. Jensen; E. H. Christiansen	2016	Randomised comparison of sirolimus-eluting and biolimus-eluting bioresorbable polymer stents: The SORT-OUT VII OCT study	Comparator not in scope.
4	Anonymous	2011	BioMime - A sirolimus-eluting coronary stent system for the treatment of patients with De Novo Coronary Lesions - meriT-1 report	Duplicated data reported elsewhere.
5	U. Baber; R. Chandiramani; S. R. Mehta; S. Sartori; Z. Zhang; B. E. Claessen; C. Briguori; S. Sharma; G. Dangas; R. Mehran	2021	Safety and efficacy of the bioabsorbable polymer everolimus-eluting stent versus durable polymer drug-eluting stents in high-risk patients undergoing PCI: TWILIGHT-SYNERGY	Intervention and comparator of original RCT not in scope. Pre-specified analysis comparing DES but trial not stratified by DES type so excluded.
6	A. Baumbach; A. J. Lansky; Y. Onuma; T. Asano; T. Johnson; R. Anderson; F. Kiemeneij; M. Zheng; N. Van Royen; T. Slagboom; et al.	2018	Optical coherence tomography substudy of a prospective multicentre randomised post-market trial to assess the safety and effectiveness of the Firehawk cobalt-chromium coronary stent (rapamycin target-eluting) system for the treatment of atherosclerotic lesions: TARGET All Comers	Less than 1 year follow-up.
7	C. Bernelli; A. Chieffo; G. L. Buchanan; M. Montorfano; M. Carlino; A. Latib; F. Figini; K. Takagi; T. Naganuma; D. MacCagni; A. Colombo	2013	New-generation drug-eluting stent experience in the percutaneous treatment of unprotected left main coronary artery disease: The NEST registry	Out of scope stents included and results not reported per individual stent.
8	G. Bouras; S. Jhamnani; V. G. Ng; I. Haimi; V. Mao; R. Deible; S. Cao; K. Sudhir; A. J. Lansky	2017	Clinical outcomes after PCI treatment of very long lesions with the XIENCE V everolimus eluting stent; Pooled analysis from the SPIRIT and XIENCE V USA prospective multicenter trials	Subgroup not in scope.
9	C. Briguori; G. Visconti; M. Donahue; V. Di Palma; F. De Micco; G. Signoriello; A. Focaccio	2016	Performance of the XLIMUS Sirolimus-Eluting Coronary Stent in Very Complex Lesions	Duplicate.

#	Reference	Year	Title	Reason for exclusion
10	R. A. Buiten; E. H. Ploumen; P. Zocca; C. J. M. Doggen; L. C. van der Heijden; M. M. Kok; P. W. Danse; C. E. Schotborgh; M. Scholte; F. H. A. F. de Man; G. C. M. Linssen; C. von Birgelen	2019	Outcomes in Patients Treated With Thin-Strut, Very Thin-Strut, or Ultrathin-Strut Drug-Eluting Stents in Small Coronary Vessels: A Prespecified Analysis of the Randomized BIO-RESORT Trial	Out of scope subgroup of included RCT.
11	R. A. Buiten; E. H. Ploumen; P. Zocca; C. J. M. Doggen; K. G. van Houwelingen; P. W. Danse; C. E. Schotborgh; M. G. Stoel; M. Scholte; G. C. M. Linssen; F. H. A. F. de Man; C. von Birgelen	2020	Three contemporary thin-strut drug-eluting stents implanted in severely calcified coronary lesions of participants in a randomized all-comers trial	Out of scope subgroup of included RCT.
12	F. Burzotta; C. Aurigemma; L. Paraggio; E. Romagnoli; A. M. Leone; R. Vergallo; S. Cangemi; F. Bianchini; C. Trani	2023	Under-deployment of extra-large drug-eluting stent: an adapted provisional technique for selected patients with distal lesions in large left main	Incorrect study design.
13	P. Chandwani; P. Verma; S. Saxena; P. K. Ramachandran; A. Abhyankar; M. S. Sandhu; N. Parikh; A. Bhupali; S. Jain; J. Prajapati	2016	Comparison of Clinical Outcomes Following Single versus Multivessel Percutaneous Coronary Intervention Using Biodegradable Polymer Coated Sirolimus-Eluting Stent in an All-comers Patient Population	Comparison made not in scope (single vessel versus multivessel PCI).
14	G. Chatzantonis; G. Chatzantonis; H. Findeisen; M. Paul; A. Samol; T. Bisdas; D. Fischer	2021	Real-world analysis of a Biolimus A9 polymer-free drug-coated stent with very short dual antiplatelet therapy in patients at high bleeding risk	Less than 1 year follow-up.
15	B. Chevalier; P. C. Smits; D. Carrie; J. Mehilli; A. J. Van Boven; E. Regar; F. J. Sawaya; D. Chamie; A. O. Kraaijeveld; T. Hovasse; G. J. Vlachojannis	2017	Serial Assessment of Strut Coverage of Biodegradable Polymer Drug-Eluting Stent at 1, 2, and 3 Months After Stent Implantation by Optical Frequency Domain Imaging: The DISCOVERY 1TO3 Study (Evaluation With OFDI of Strut Coverage of Terumo New Drug Eluting Stent With Biodegradable Polymer at 1, 2, and 3 Months)	Less than 1 year follow-up.
16	M. Chiarito; M. Sturla; C. Briguori; M. Mancone; C. Tamburino; F. Fabbiocchi; D. Trabattoni; F. Tomai; A. Paggi; G. Gioffre; R. Sclafani; A. Giordano; G. G. Stefanini; G. Sardella	2022	Polymer-free biolimus-A9-eluting stent performance according to renal impairment: insights from the RUDI-FREE registry	Subgroup population not in scope.
17	S. C. Cho; M. H. Jeong; W. Kim; Y. Ahn; Y. J. Hong; Y. J. Kim; C. J. Kim; M. C. Cho; K. R. Han; H. S. Kim	2014	Clinical outcomes of everolimus- and zotarolimus-eluting stents in patients with acute myocardial infarction for small coronary artery disease	Devices out of scope.

#	Reference	Year	Title	Reason for exclusion
18	M. Cimci; J. Polad; M. Mamas; A. Iniguez-Romo; B. Chevalier; R. Abhaichand; A. Aminian; A. Roguin; G. Maluenda; M. Angioi; G. Cassel; S. Kuramitsu; L. Jacobs; R. Debrus; F. Malik; D. Hildick-Smith; P. Laanmets; M. Roffi	2022	Outcomes and regional differences in practice in a worldwide coronary stent registry	Objective/outcomes of study not relevant to decision problem.
19	C. R. F. Costantini; M. A. Denk; S. G. Tarbine; C. C. Ortiz; V. S. Ferrari; R. M. de Macedo	2024	One-year outcomes with the Firehawk sirolimus-eluting stent and biodegradable polymer guided by intravascular ultrasound	Letter.
20	K. Dan; H. M. Garcia-Garcia; P. Kolm; S. Windecker; S. Saito; D. E. Kandzari; R. Waksman	2020	Comparison of Ultrathin, Bioresorbable-Polymer Sirolimus-Eluting Stents and Thin, Durable-Polymer Everolimus-Eluting Stents in Calcified or Small Vessel Lesions	Relevant primary trials already considered for inclusion separately.
21	J. M. de la Torre Hernandez; I. Otaegui; A. Subinas; A. Gomez-Menchero; R. Moreno; J. Rondan; E. Munoz-Garcia; F. Sainz-Laso; B. Garcia del Blanco; J. R. Rumoroso; J. F. Diaz; A. Berenguer; J. Gomez-Lara; J. Zueco	2021	First-in-Man Evaluation of a Sirolimus-Eluting Stent With Abluminal Fluoropolymeric/Triflusal Coating With Ultrathin Struts by OCT at 9 Months' Follow-Up: The PROMETHEUS Study	Less than 1 year follow-up.
22	A. P. de Prado; R. Ocaranza-Sánchez; F. L. Ruiz-Poveda; J. M. Burgos; R. Á. Ramos; A. Rodrigues; L. F. González; P. Aguar; B. G. del Blanco; E. Pinar	2021	Real-world registry of the durable Angiolite fluoroacrylate polymer-based sirolimus-eluting stent: the EPIC02–RANGO study	Duplicate.
23	F. R. Eberli; H.-P. Stoll; P. Urban; M.-C. Morice; P. Brunel; L. Maillard; J. Lipiecki; S. Cook; J. Berland; T. Hovasse; D. Carrie; D. Schütte; S. S. Slama; P. Garot	2022	Polymer-free Biolimus-A9 coated thin strut stents for patients at high bleeding risk 1-year results from the LEADERS FREE III study	Longer term data available.
24	J. Fajadet; E. J. Garcia; D. Hildick-Smith; F. J. Neumann; A. S. Petronio; M. S. Spence; J. Wohrle; A. Zaman; S. Elhadad; S. Silber	2013	Results of the primary endpoint of the platinum plus trial: A prospective, randomized, multi-center trial to assess the everolimus-eluting coronary stent system (promus element) for coronary revascularization in a population of unrestricted patients	Abstract (does not meet criteria for inclusion).
25	S. Ferrarello; C. Costopoulos; A. Latib; T. Naganuma; A. Sticchi; F. Figini; S. Basavarajaiah; M. Carlino; A. Chieffo; M. Montorfano; M. Kawaguchi; C. Naim; F. Giannini; A. Colombo	2013	The role of everolimus-eluting and resolute zotarolimus-eluting stents in the treatment of coronary bifurcations	Out of scope intervention.
26	W. Fujimoto; T. Sawada; T. Toba; Y. Takahashi; T. Miyata; S. Oishi; T. Osue; T. Onishi; T. Takaya; A. Shimane; Y. Taniguchi; H. Kawai; Y. Yasaka	2018	Comparison of the 9-month intra-stent conditions and 2-year clinical outcomes after Resolute zotarolimus-eluting stent implantation between 3-month and standard dual antiplatelet therapy	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
27	R.-L. Gao; B. Xu; A. J. Lansky; Y.-J. Yang; C.-S. Ma; Y.-L. Han; S.-L. Chen; H. Li; R.-Y. Zhang; G.-S. Fu; Z.-Y. Yuan; H. Jiang; Y. Huo; W. Li; Y.-J. Zhang; M. B. Leon	2013	A randomised comparison of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent: clinical and angiographic follow-up of the TARGET I trial	Less than 1 year follow-up.
28	A. Gautier; M. Roffi; P. Laanmets; S. Munir; F. T. Malik; A. I. Romo; G. Maluenda; S. Kuramitsu; M. Angioi; W. Wijns; S. Saito; B. Chevalier	2023	Complementary evidence on the performance of coronary stents generated by a randomized controlled trial and a worldwide registry	Objective/outcomes of study not relevant to decision problem.
29	A. Gautier; M. Roffi; P. Laanmets; S. Munir; F. T.-N. Malik; A. I. Romo; G. Maluenda; S. Kuramitsu; M. Angioi; W. Wijns; S. Saito; B. Chevalier	2023	Complementary evidence on the performance of coronary stents generated by a randomized controlled trial and a worldwide registry	Duplicate.
30	J. Gomez-Lara; J. H. Heo; S. Brugaletta; S. Garg; H. M. Garcia-Garcia; R. J. van Geuns; S. Silber; S. Windecker; P. W. Serruys	2011	Risk of target lesion failure in relationship to vessel angiographic geometry and stent conformability using the second generation of drug-eluting stents	Objective/outcomes of study not relevant to decision problem.
31	J. L. Gutiérrez-Chico; R. J. van Geuns; E. Regar; W. J. van der Giessen; H. Kelbæk; K. Saunamäki; J. Escaned; N. Gonzalo; C. di Mario; F. Borgia; E. Nüesch; H. M. García-García; S. Silber; S. Windecker; P. W. Serruys	2011	Tissue coverage of a hydrophilic polymer-coated zotarolimus-eluting stent vs. a fluoropolymer-coated everolimus-eluting stent at 13-month follow-up: an optical coherence tomography substudy from the RESOLUTE All Comers trial	Does not report key clinical outcomes.
32	Y. Hamanaka; Y. Sotomi; T. Kobayashi; T. Omatsu; J. Dijkstra; Y. Sakata; A. Hirayama; A. Hirata; Y. Higuchi	2021	Comparable neointimal healing in patients with stable coronary lesions and acute coronary syndrome: 3-month optical coherence tomography analysis	Less than 1 year follow-up.
33	M. Hamon; R. Niculescu; D. Deleanu; M. Dorobantu; N. J. Weissman; R. Waksman	2013	Clinical and angiographic experience with a third-generation drug-eluting Orsiro stent in the treatment of single de novo coronary artery lesions (BIOFLOW-I): a prospective, first-in-man study	Less than 1 year follow-up.
34	J.-K. Han; D. Hwang; S. Yang; S.-H. Park; J. Kang; H.-M. Yang; K. W. Park; H.-J. Kang; B.-K. Koo; S.-H. Hur; W. Kim; S. Y. Kim; S.-H. Park; S. H. Han; S.-H. Kim; S. Shin; Y. H. Kim; K. Park; N. Lee; S. J. Lee; J. W. Kim; H.-S. Kim	2023	Comparison of 3- to 6-Month Versus 12-Month Dual Antiplatelet Therapy After Coronary Intervention Using the Contemporary Drug-Eluting Stents With Ultrathin Struts: The HOST-IDEA Randomized Clinical Trial	Duplicate.
35	K. N. Hansen; M. Maeng; L. Antonsen; A. Maehara; L. Jakobsen; J. Ellert; C. J. Terkelsen; O. Ahlehoff; T. Thim; C. O. Fallesen; M. Noori; K. T. Veien; L. O. Jensen; E. H. Christiansen	2022	Early vascular healing after implantation of the polymer-free biolimus-eluting stent or the ultrathin strut biodegradable polymer sirolimus-eluting stent in patients with ST-segment elevation myocardial infarction	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
36	Y. He; R. Wang; J. Liu; F. Li; J. Li; C. Li; J. Zhou; Z. Zhao; W. Yang; F. Mou; J. Wang; J. Kan; X. Li; Y. Li; M. Zheng; S. Chen; C. Gao; L. Tao	2022	A Randomized Comparison of the Healing Response Between the Firehawk Stent and the Xience Stent in Patients With ST-Segment Elevation Myocardial Infarction at 6 Months of Follow-Up (TARGET STEMI OCT China Trial): An Optical Coherence Tomography Study	Less than 1 year follow-up.
37	R. Hemetsberger; M. Abdelghani; R. Toelg; H. M. Garcia-Garcia; S. Farhan; N. Mankerious; K. Elbasha; A. Allali; S. Windecker; T. Lefèvre; S. Saito; D. Kandzari; R. Waksman; G. Richardt	2022	Complex vs. non-complex percutaneous coronary intervention with newer-generation drug-eluting stents: an analysis from the randomized BIOFLOW trials	Relevant primary trials already considered for inclusion separately.
38	R. Hemetsberger; N. Mankerious; R. Toelg; M. Abdelghani; S. Farhan; H. M. Garcia-Garica; A. Allali; S. Windecker; T. Lefèvre; S. Saito; D. Kandzari; R. Waksman; G. Richardt	2023	Patients with higher-atherothrombotic risk vs. lower-atherothrombotic risk undergoing coronary intervention with newer-generation drug-eluting stents: an analysis from the randomized BIOFLOW trials	Relevant primary trials already considered for inclusion separately.
39	H. Hioki; K. Kozuma; Y. Kinoshita; M. Nanasato; Y. Ito; J. Yamaguchi; N. Shiode; K. Hibi; K. Tanabe; J. Ako; Y. Morino; A. Hirohata; S. Sonoda; Y. Nakagawa; H. Okada; T. Nakagami; I. Takamisawa; K. Ando; M. Abe; Y. Ikari	2021	Ischemic/bleeding event after short dual-antiplatelet therapy in patients with high bleeding risk: Sub-analysis of the MODEL U-SES study	Objective/outcomes of study not relevant to decision problem.
40	S.-H. Hur; I.-C. Kim; K.-B. Won; Y.-K. Cho; H.-J. Yoon; C.-W. Nam; K.-B. Kim; M.-S. Kim; J. Park; S.-W. Rha; S.-C. Chae; Y.-J. Kim; C.-J. Kim; M.-C. Cho; M.-H. Jeong; Y.-K. Ahn; H.-S. Kim; T.-H. Ahn; K.-B. Seung; Y. Jang; J.-H. Yoon; I.-W. Seong; T.-J. Hong; J.-H. Bae; S.-J. Park; K. I. for the	2016	Two-Year Safety and Efficacy of Biodegradable Polymer Drug-Eluting Stent Versus Second-Generation Durable Polymer Drug-Eluting Stent in Patients With Acute Myocardial Infarction: Data from the Korea Acute Myocardial Infarction Registry (KAMIR)	Includes out of scope stents and results not reported per stent.
41	J. F. Iglesias; D. Heg; M. Roffi; S. Degrauwe; D. Tüller; O. Muller; M. Brinkert; S. Cook; D. Weilenmann; C. Kaiser; F. Cuculi; M. Valgimigli; P. Jüni; S. Windecker; T. Pilgrim	2022	Five-Year Outcomes With Biodegradable-Polymer Sirolimus-Eluting Stents Versus Durable-Polymer Everolimus-Eluting Stents in Patients With Acute Coronary Syndrome: A Subgroup Analysis of the BIOSCIENCE Trial	Out of scope subgroup of included RCT.
42	J. F. Iglesias; D. Heg; M. Roffi; D. Tüller; S. Noble; O. Muller; I. Moarof; S. Cook; D. Weilenmann; C. Kaiser; F. Cuculi; J. Häner; P. Jüni; S. Windecker; T. Pilgrim	2019	Long-Term Effect of Ultrathin-Strut Versus Thin-Strut Drug-Eluting Stents in Patients With Small Vessel Coronary Artery Disease Undergoing Percutaneous Coronary Intervention	Not a key subgroup in scope.

#	Reference	Year	Title	Reason for exclusion
43	J. F. Iglesias; O. Muller; S. Losdat; M. Roffi; D. J. Kurz; D. Weilenmann; C. Kaiser; D. Heg; M. Valgimigli; S. Windecker; T. Pilgrim	2021	Multivessel percutaneous coronary intervention with thin-strut biodegradable versus durable polymer drug-eluting stents in ST-segment elevation myocardial infarction: A subgroup analysis of the BIOSTEMI randomized trial	Out of scope subgroup of included RCT.
44	J. F. Iglesias; M. Roffi; S. Losdat; O. Muller; S. Degrauwe; D. J. Kurz; L. Haegeli; D. Weilenmann; C. Kaiser; M. Tapponnier; S. Cook; F. Cuculi; D. Heg; S. Windecker; T. Pilgrim	2023	Long-term outcomes with biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in ST-segment elevation myocardial infarction: 5-year follow-up of the BIOSTEMI randomised superiority trial	Duplicate.
45	A. Iniguez; B. Chevalier; G. Richardt; A. Neylon; V. A. Jimenez; R. Kornowski; D. Carrie; R. Moreno; E. Barbato; A. Serra-Penaranda; V. Guiducci; M. Valdes-Chavarri; J. Yajima; W. Wijns; S. Saito	2020	Comparison of long-term clinical outcomes in multivessel coronary artery disease patients treated either with bioresoarbable polymer sirolimus-eluting stent or permanent polymer everolimus-eluting stent: 5-year results of the CENTURY II randomized clinical trial	Out of scope subgroup of included RCT.
46	M. Ishida; R. Shimada; F. Takahashi; M. Niiyama; T. Ishisone; Y. Matsumoto; Y. Taguchi; T. Osaki; O. Nishiyama; H. Endo; R. Sakamoto; K. Tanaka; Y. Koeda; T. Kimura; I. Goto; R. Ninomiya; W. Sasaki; T. Itoh; Y. Morino	2024	One-Month Dual Antiplatelet Therapy Followed by P2Y12 Inhibitor Monotherapy After Biodegradable Polymer Drug-Eluting Stent Implantation - The REIWA Region-Wide Registry	Objective/outcomes of study not relevant to decision problem.
47	M. Ishida; F. Takahashi; I. Goto; M. Niiyama; H. Saitoh; T. Sakamoto; Y. Maegawa; T. Osaki; O. Nishiyama; H. Endo; R. Sakamoto; T. Kojima; Y. Koeda; T. Kimura; T. Itoh; Y. Morino	2020	Clinical outcomes of patients treated using very short duration dual antiplatelet therapy after implantation of biodegradable-polymer drug-eluting stents: rationale and design of a prospective multicenter REIWA registry	Objective/outcomes of study not relevant to decision problem.
48	T. Ishihara; T. Tsujimura; S. Okuno; O. Iida; M. Asai; M. Masuda; S. Okamoto; K. Nanto; T. Kanda; Y. Matsuda; T. Mano	2019	Early- and middle-phase arterial repair following bioresorbable- and durable-polymer drug-eluting stent implantation: An angioscopic study	Objective/outcomes of study not relevant to decision problem.
49	T. Itoh; H. Otake; T. Kimura; Y. Tsukiyama; T. Kikuchi; M. Okubo; T. Hayashi; T. Okamura; S. Kuramitsu; T. Morita; S. Sonoda; S. Ishihara; N. Kuriyama; T. Isshiki; T. Soeda; K. Hibi; T. Shinke; Y. Morino	2022	A serial optical frequency-domain imaging study of early and late vascular responses to bioresorbable-polymer sirolimus-eluting stents for the treatment of acute myocardial infarction and stable coronary artery disease patients: results of the MECHANISM-ULTIMASTER study	Objective/outcomes of study not relevant to decision problem.
50	M. Jakl; P. Cervinka; J. Kanovsky; P. Kala; M. Poloczek; M. Cervinkova; H. G. Bezerra; Z. Valenta; M. A. Costa	2023	Randomized comparison of 9-month stent strut coverage of biolimus and everolimus drug-eluting stents assessed by optical coherence tomography in patients with ST-segment elevation myocardial infarction. Long-term (5-years) clinical follow-up (ROBUST trial)	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
51	H.-L. Jen; Y.-C. Wang; T.-P. Tsao; W.-H. Yin	2021	Percutaneous Coronary Intervention for Very Small Vessels With the Use of a Newer-Generation 2.0 mm Drug-Eluting Stent	Objective/outcomes of study not relevant to decision problem.
52	O. Jensen Lisette; M. Maeng; B. Raungaard; J. Kahlert; J. Ellert; L. Jakobsen; A. B. Villadsen; K. T. Veien; S. D. Kristensen; O. Ahlehoff; S. Carstensen; M. K. Christensen; C. J. Terkelsen; T. Engstroem; K. N. Hansen; H. E. Bøtker; J. Aaroe; T. Thim; L. Thuesen; P. Freeman; A. Aziz; A. Eftekhari; A. Junker; S. E. Jensen; J. F. Lassen; H. S. Hansen; E. H. Christiansen	2020	Randomized Comparison of the Polymer-Free Biolimus-Coated BioFreedom Stent With the Ultrathin Strut Biodegradable Polymer Sirolimus-Eluting Orsiro Stent in an All-Comers Population Treated With Percutaneous Coronary Intervention: The SORT OUT IX Trial	Duplicate.
53	V. A. Jimenez; A. Iniguez; J. A. Baz; M. Valdes; A. Ortiz; A. Vuilliomenet; V. Mainar; D. Dudek; S. Banai; D. Tuller; J.-L. Bonnet; A. De Miguel; G. Bastos; W. Wijns; S. Saito	2016	A randomized comparison of novel bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent in patients with acute coronary syndromes: The CENTURY II high risk ACS substudy	Out of scope subgroup of included RCT.
54	V. A. Jiménez; A. Iñiguez; J. A. Baz; M. Valdés; A. Ortiz; A. Vuilliomenet; V. Mainar; D. Dudek; S. Banai; D. Tüller; J. L. Bonnet; A. De Miguel; G. Bastos; W. Wijns; S. Saito	2016	A randomized comparison of novel bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent in patients with acute coronary syndromes: The CENTURY II high risk ACS substudy	Duplicate.
55	A. Jurado-Román; J. Abellán-Huerta; J. A. Requena; I. Sánchez-Pérez; M. T. López-Lluva; R. Maseda-Uriza; J. Piqueras-Flores; P. Pérez-Díaz; R. Frías-García; F. Lozano-Ruíz-Poveda	2019	Comparison of Clinical Outcomes Between Very Long Stents and Overlapping Stents for the Treatment of Diffuse Coronary Disease in Real Clinical Practice	Bare metal stents included in intervention group.
56	E. Kandzari David; S. Kini Annapoorna; D. Karmpaliotis; W. Moses Jeffrey; E. Tummala Pradyumna; J. A. Grantham; C. Orr; W. Lombardi; J. Nicholson William; J. Lembo Nicholas; J. Popma Jeffrey; J. Wang; C. Larracas; R. Rutledge David	2015	Safety and Effectiveness of Everolimus-Eluting Stents in Chronic Total Coronary Occlusion Revascularization	Not a key subgroup in scope.
57	D. E. Kandzari; A. J. Kirtane; S. Windecker; A. Latib; E. Kedhi; R. Mehran; M. J. Price; A. Abizaid; D. I. Simon; S. G. Worthley; A. Zaman; J. W. Choi; R. Caputo; M. Kanitkar; B. McLaurin; S. Potluri; T. Smith; D. Spriggs; T. Tolleson;	2020	One-Month Dual Antiplatelet Therapy Following Percutaneous Coronary Intervention With Zotarolimus-Eluting Stents in High-Bleeding-Risk Patients	Duplicate.

#	Reference	Year	Title	Reason for exclusion
	T. Nazif; M. Parke; L. C. Lee; T. H. Lung; G. W. Stone			
58	S. H. Kang; W. Y. Chung; J. M. Lee; J. J. Park; C. H. Yoon; J. W. Suh; Y. S. Cho; J. H. Doh; J. M. Cho; J. W. Bae; T. J. Youn; I. H. Chae	2017	Angiographic outcomes of Orsiro biodegradable polymer sirolimus-eluting stents and Resolute Integrity durable polymer zotarolimus-eluting stents: results of the ORIENT trial	Less than 1 year follow-up.
59	P. P. Karjalainen; V. Varho; W. Nammas; J. Mikkelsson; M. Pietilä; A. Ylitalo; J. K. E. Airaksinen; J. Sia; K. Nyman; F. Biancari	2015	Early Neointimal Coverage and Vasodilator Response Following Biodegradable Polymer Sirolimus-Eluting vs. Durable Polymer Zotarolimus-Eluting Stents in Patients With Acute Coronary Syndrome–HATTRICK-OCT Trial–	Less than 1 year follow-up.
60	D. Karmpaliotis; R. Stoler; S. Walsh; S. El-Jack; S. Potluri; J. Moses; K. Oldroyd; A. Banning; M. Webster; A. Zaman; W. Wu; M. Ahmed; P. Underwood; D. Allocco	2022	Safety and efficacy of Everolimus-Eluting bioabsorbable Polymer-Coated stent in patients with long coronary lesions: The EVOLVE 48 study	Duplicate.
61	D. J. Kereiakes; I. Meredith; S. Windecker; A. Kabour; A. Bouchard; A. Kini; L. Janssens; M. Foster; R. Stoler; T. Stuckey; W. Batchelor; T. Christen; D. Allocco; K. Dawkins	2016	Late clinical outcomes after bioresorbable or permanent polymer everolimuseluting stents: 2-year results from the evolve II randomized trial	Abstract of included RCT.
62	Y. H. Kim; A.-Y. Her; M. H. Jeong; B.-K. Kim; S.-J. Hong; D.-H. Shin; J.-S. Kim; Y.-G. Ko; D. Choi; M.-K. Hong; Y. Jang	2019	Two-year clinical outcomes of zotarolimus- and everolimus-eluting durable-polymer-coated stents versus biolimus-eluting biodegradable-polymer-coated stent in patients with acute myocardial infarction with dyslipidemia after percutaneous coronary intervention: data from the KAMIR	Not a key subgroup in scope.
63	Y. Kim; S. S. Oh; M. H. Jeong; Y. Ahn; J. H. Kim; Y. J. Hong; D. S. Sim; M. C. Kim; H.-S. Kim; K. H. Yun; S. K. Oh; C. J. Kim; M. C. Cho	2019	Comparison of short-term clinical outcomes between Resolute Onyx zotarolimus-eluting stents and everolimus-eluting stent in patients with acute myocardial infarction: Results from the Korea Acute Myocardial infarction Registry (KAMIR)	Less than 1 year follow-up.
64	A. J. Kirtane; R. Stoler; R. Feldman; F.-J. Neumann; L. Boutis; N. Tahirkheli; R. Toelg; I. Othman; B. Stein; J. W. Choi; S. Windecker; R. W. Yeh; H. L. Dauerman; M. J. Price; P. Underwood; D. Allocco; I. Meredith; D. J. Kereiakes	2021	Primary Results of the EVOLVE Short DAPT Study	Duplicate.

#	Reference	Year	Title	Reason for exclusion
65	O. Kobo; M. Saada; P. Laanmets; D. Karageorgiev; H. Routledge; J. Crowley; P. Baello; J. B. Requena; F. Spano; L. Perez; J. M. Jimenez Mazuecos; M. A. Mamas; A. Roguin	2022	Impact of peripheral artery disease on prognosis after percutaneous coronary intervention: Outcomes from the multicenter prospective e-ULTIMASTER registry	Objective/outcomes of study not relevant to decision problem.
66	O. Kobo; M. Saada; C. von Birgelen; P. A. L. Tonino; A. Iniguez-Romo; O. Frobert; M. Halabi; R. M. Oemrawsingh; J. Polad; A. J. J. Ijsselmuiden; M. Roffi; A. Aminian; M. A. Mamas; A. Roguin	2023	Impact of multisite artery disease on clinical outcomes after percutaneous coronary intervention: an analysis from the e-Ultimaster registry	Objective/outcomes of study not relevant to decision problem.
67	R. Kornowski; K. Orvin; B. Merkely; G. Richardt; A. Colombo; J. L. Bonnet; W. Wijns	2016	Treatment of bifurcation lesions with a thin-strut DES with bioresorbable polymer: Three-year clinical outcomes of the CENTURY II trial	Abstract of included RCT.
68	K. Kozuma; Y. Kinoshita; H. Hioki; M. Nanasato; Y. Ito; J. Yamaguchi; N. Shiode; K. Hibi; K. Tanabe; J. Ako	2020	1-Year safety of 3-month dual antiplatelet therapy followed by aspirin or P2Y12 receptor inhibitor monotherapy using a bioabsorbable polymer sirolimus-eluting stent	Objective/outcomes of study not relevant to decision problem.
69	F. Krackhardt; V. Kočka; M. W. Waliszewski; A. Utech; M. Lustermann; M. Hudec; M. Studenčan; M. Schwefer; J. Yu; M. H. Jeong; T. Ahn; W. A. Wan Ahmad; M. Boxberger; A. Schneider; M. Leschke	2017	Polymer-free sirolimus-eluting stents in a large-scale all-comers population	Less than 1 year follow-up.
70	F. Krackhardt; M. Waliszewski; V. Kočka; P. Toušek; B. Janek; M. Hudec; F. Lozano; K. G.-S. Roman; B. G. del Blanco; J. Mauri; T. M. Heang; T. H. Ahn; M. H. Jeong; D. Herberger; V. Tomulic; G. Levy; L. Sebagh; J. Rischner; M. Pansieri	2020	Real-World Dual Antiplatelet Therapy Following Polymer-Free Sirolimus-Eluting Stent Implantations to Treat Coronary Artery Disease	Objective/outcomes of study not relevant to decision problem.
71	E. Kretov; I. Naryshkin; V. Baystrukov; I. Grazhdankin; A. Prokhorikhin; D. Zubarev; A. Biryukov; V. Verin; A. Boykov; D. Malaev; E. Pokushalov; A. Romanov; M. W. Bergmann	2018	Three-months optical coherence tomography analysis of a biodegradable polymer, sirolimus-eluting stent	Less than 1 year follow-up.
72	M. W. Krucoff; P. Urban; J.-F. Tanguay; T. McAndrew; Y. Zhang; S. V. Rao; M.-C. Morice; M. J. Price; D. J. Cohen; M. Abdel-Wahab; S. R. Mehta; B. Faurie; B. McLaurin; C. Diaz; H.-P. Stoll; S. Pocock; M. B. Leon	2020	Global Approach to High Bleeding Risk Patients With Polymer-Free Drug-Coated Coronary Stents	Comparator out of scope.

#	Reference	Year	Title	Reason for exclusion
73	A. Latib; L. Ferri; A. Ielasi; C. Godino; A. Chieffo; V. Magni; G. Bassanelli; A. S. P. Sharp; R. Gerber; I. Michev; M. Carlino; F. Airoldi; G. M. Sangiorgi; M. Montorfano; A. Colombo	2009	Clinical outcomes after unrestricted implantation of everolimus-eluting stents	Less than 1 year follow-up.
74	S. W. L. Lee; F. C. C. Tam; K. K. W. Chan; S. C. C. Lam; S.-L. Kong; C. P. Shea; M. K. L. Wong; A. Y. T. Wong; A. S. Y. Yung; L.-W. Zhang; Y.-M. Lam; G. S. Mintz; R. A. Costa; H.-P. Stoll; A. Maehara	2018	Establishment of healing profile and neointimal transformation in the new polymer-free biolimus A9-coated coronary stent by longitudinal sequential optical coherence tomography assessments: the EGO-BIOFREEDOM study	Less than 1 year follow-up.
75	T. Lefevre; M. Haude; F.-J. Neumann; K. Stangl; C. Skurk; T. Slagboom; M. Sabate; J. Goicolea; P. Barragan; S. Cook; J.-C. Macia; S. Windecker	2018	Comparison of a Novel Biodegradable Polymer Sirolimus-Eluting Stent With a Durable Polymer Everolimus-Eluting Stent: 5-Year Outcomes of the Randomized BIOFLOW-II Trial	RCT not powered to assess key clinical outcomes at a minimum of one year.
76	T. Lefèvre; M. Haude; F. J. Neumann; K. Stangl; C. Skurk; T. Slagboom; M. Sabaté; J. Goicolea; P. Barragan; S. Cook; J. C. Macia; S. Windecker	2018	Comparison of a Novel Biodegradable Polymer Sirolimus-Eluting Stent With a Durable Polymer Everolimus-Eluting Stent: 5-Year Outcomes of the Randomized BIOFLOW-II Trial	Duplicate.
77	Y. Levi; O. Kobo; M. Halabi; I. Al Haddad; B. Chevalier; J. Polad; P. Laanmets; A. Witkowski; J. Monsegu; A. R. Iniguez; M. A. Mamas; A. Roguin	2023	Treatment of Ostial Right Coronary Artery Narrowings: Outcomes From the Multicenter Prospective e-ULTIMASTER Registry	Objective/outcomes of study not relevant to decision problem.
78	C. Li; Y. Yang; Y. Han; D. Song; J. Xu; C. Guan; R. Gao; H. M. Garcia-Garcia; R. Waksman; B. Xu	2020	Comparison of the Ultrathin Strut, Biodegradable Polymer Sirolimus-eluting Stent With a Durable Polymer Everolimus-eluting Stent in a Chinese Population: The Randomized BIOFLOW VI Trial	Less than 1 year follow-up.
79	X. T. Li; H. Sun; D. P. Zhang; L. Xu; Z. H. Ni; K. Xia; Y. Liu; Y. H. Chi; J. F. He; W. M. Li; H. S. Wang; L. F. Wang; X. C. Yang	2014	Two-year clinical outcomes of patients with overlapping second-generation drug-eluting stents for treatment of long coronary artery lesions: Comparison of everolimus-eluting stents with resolute zotarolimus-eluting stents	Non-randomised study, comparator device not in scope.
80	A. Loch; J. P. Bewersdorf; R. S. Veeriah	2017	Early and aggressive ISR with a polymer- and carrier-free drug-coated stent system	Less than 1 year follow-up.
81	J. A. Mailey; M. Ahmed; M. Hogg; C. Cosgrove; J. C. Murphy; A. H. McNeice; J. C. Spratt; M. S. Spence; S. J. Walsh	2021	Initial Experiences of Percutaneous Coronary Intervention Using a New-Generation Everolimus-Eluting Stent Platform	Less than 1 year follow-up.
82	A. S. Mahmood Zuhdi; F. Krackhardt; M. W. Waliszewski; M. D. Ismail; M. Boxberger; W. A. Wan Ahmad	2018	Efficacy and Safety of Polymer-Free Ultrathin Strut Sirolimus-Probucol Coated Drug-Eluting Stents for Chronic Total Occlusions: Insights from the Coroflex ISAR 2000 Worldwide Registry	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
83	N. Mankerious; R. Hemetsberger; H. Traboulsi; R. Toelg; M. Abdel-Wahab; G. Richardt; A. Allali	2021	Outcomes of patients treated with a biodegradable-polymer sirolimus-eluting stent versus durable-polymer everolimus-eluting stents after rotational atherectomy	Subgroup not in scope.
84	S. Mansour; G. Guilbert-Vandal; M. J. Bertrand; R. Kouz; L. M. Stevens; N. Noiseux; A. Kokis; F. Gobeil	2013	Safety and efficacy of a novel drug-eluting stent with a bioresorbable polymer in a real life cohort	Abstract (does not meet criteria for inclusion).
85	I. B. A. Menown; M. A. Mamas; J. M. Cotton; D. Hildick-Smith; F. R. Eberli; G. Leibundgut; D. Tresukosol; C. Macaya; S. Copt; S. Sadozai Slama; H.-P. Stoll	2020	First clinical evidence characterizing safety and efficacy of the new CoCr Biolimus-A9 eluting stent: The Biomatrix Alpha TM registry	Less than 1 year follow-up.
86	I. T. Meredith; S. Verheye; C. L. Dubois; J. Dens; J. Fajadet; D. Carrie; S. Walsh; K. G. Oldroyd; O. Varenne; S. El-Jack; R. Moreno; A. A. Joshi; D. J. Allocco; K. D. Dawkins	2012	Primary endpoint results of the EVOLVE trial: a randomized evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent	Less than 1 year follow-up.
87	I. T. Meredith; S. Verheye; N. J. Weissman; P. Barragan; D. Scott; M. V. Chávarri; N. E. J. West; H. Kelbæk; R. Whitbourn; D. L. Walters; J. Kubica; L. Thuesen; M. Masotti; A. Banning; I. Sjögren; R. H. Stables; D. J. Allocco; K. D. Dawkins	2013	Six-month IVUS and two-year clinical outcomes in the EVOLVE FHU trial: a randomised evaluation of a novel bioabsorbable polymer-coated, everolimus-eluting stent	Primary outcome not a key clinical outcome.
88	M. O. Mohamed; J. Polad; D. Hildick-Smith; O. Bizeau; R. K. Baisebenov; M. Roffi; A. Iniguez-Romo; B. Chevalier; C. von Birgelen; A. Roguin; A. Aminian; M. Angioi; M. A. Mamas	2021	Impact of coronary lesion complexity in percutaneous coronary intervention: One-year outcomes from the large, multicentre e-Ultimaster registry	Objective/outcomes of study not relevant to decision problem.
89	M. R. Monjur; C. F. Said; P. Bamford; M. Parkinson; R. Szirt; T. Ford	2020	Ultrathin-strut biodegradable polymer versus durable polymer drug-eluting stents: a meta-analysis	Relevant primary trials already considered for inclusion separately.
90	J. Moreu; R. Moreno-Gómez; A. Perez de Prado; B. García del Blanco; R. Trillo; E. Pinar; E. Molina; J. Zueco; A. Merchán; J. F. Díaz-Fernández; I. J. Amat-Santos	2019	First-in-man randomised comparison of the Angiolite durable fluoroacrylate polymer-based sirolimus-eluting stent versus a durable fluoropolymer-based everolimus-eluting stent in patients with coronary artery disease: the ANGIOLITE trial	Duplicate.
91	Y. Morino; D. Terashita; H. Otake; T. Kikuchi; T. Fusazaki; N. Kuriyama; T. Suzuki; Y. Ito; K. Hibi; H. Tanaka; S. Ishihara; T. Kataoka; T. Morita; Y. Otsuka; T. Hayashi; K. Tanabe; T. Shinke	2019	Early vascular responses to everolimus-eluting cobalt–chromium stent in the culprit lesions of st-elevation myocardial infarction: results from a multicenter prospective optical coherence tomography study (MECHANISM-AMI 2-week follow-up study)	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
92	C. Musto; L. Paolucci; C. A. Pivato; L. Testa; A. Pacchioni; C. Briguori; G. Esposito; R. Piccolo; L. Lucisano; L. De Luca; F. Conrotto; J. Sanz-Sanchez; V. Cesario; F. De Felice; A. C. Latini; D. Regazzoli; G. Sardella; C. Indolfi; B. Reimers; G. Condorelli; G. Stefanini	2023	One-Month Dual Antiplatelet Therapy in Patients With Chronic and Acute Coronary Syndromes Treated With Bioresorbable Polymer Everolimus-Eluting Stents	Comparison between populations not relevant to decision problem.
93	A. A. B. Nuruddin; W. A. W. Ahmad; M. Waliszewski; T. M. Heang; L. H. Bang; A. K. M. Yusof; I. Z. Abidin; A. S. Zuhdi; F. Krackhardt	2021	Impact of Coronary Stent Architecture on Clinical Outcomes: Do Minor Changes in Stent Architecture Really Matter?	Comparison of device generations.
94	Y. Onuma; S. Tanimoto; P. Ruygrok; J. Neuzner; J. J. Piek; A. Seth; J. J. Schofer; G. Richardt; M. Wiemer; D. Carrié; L. Thuesen; C. Dorange; K. Miquel-Hebert; S. Veldhof; P. W. Serruys	2010	Efficacy of everolimus eluting stent implantation in patients with calcified coronary culprit lesions: Two-year angiographic and three-year clinical results from the SPIRIT II study	Non-comparative study with older generation device.
95	J. Y. Park; S.-W. Rha; Y.-K. Noh; B. G. Choi; J. Y. Hong; J.-W. Choi; S. K. Ryu; S.-H. Park; Y. H. Kim; M. H. Jeong	2021	Real-World Three-Year Clinical Outcomes of Biolimus-Eluting Stents versus Other Contemporary Drug-Eluting Stents in Patients with Acute Myocardial Infarction Patients: Data from the Korea Acute Myocardial Infarction Registry (KAMIR)	Comparing groups of stents with out of scope stents included in groups, results not reported per individual stent.
96	K. W. Park; J. M. Lee; S. H. Kang; H. S. Ahn; H. M. Yang; H. Y. Lee; H. J. Kang; B. K. Koo; J. Cho; H. C. Gwon; S. Y. Lee; I. H. Chae; T. J. Youn; J. K. Chae; K. R. Han; C. W. Yu; H. S. Kim	2013	Safety and efficacy of second-generation everolimus-eluting Xience v Stents versus zotarolimus-eluting resolute stents in real-world practice: Patient-related and stent-related outcomes from the multicenter prospective EXCELLENT and RESOLUTE-Korea registries	Out of scope comparator.
97	K. P. Patel; A. J. Lansky; H. Kelbaek; B. Xu; N. van Royen; T. W. Johnson; R. Anderson; W. Wijns; A. Baumbach	2024	Long-Term Percutaneous Coronary Intervention Outcomes in Chronic Versus Acute Coronary Syndromes (TARGET All Comers Trial)	Out of scope subgroup of included RCT.
98	S. Patra; R. N. Chakraborty; A. Pande; S. Banerjee; M. Jena; P. C. Mandal; S. K. De; A. Khan; S. S. Das; D. Ghosh; R. Nag	2017	Zotarolimus-eluting Resolute Integrity versus everolimus-eluting Xience Xpedition stents in the management of very long (>30mm) de novo coronary artery stenosis	Intervention not in scope.
99	S. V. Patted; A. S. Patted; P. K. Turiya; A. S. Thakkar	2018	Clinical Outcomes of World's Thinnest (50 mumr) Strut Biodegradable Polymer Coated Everolimus-Eluting Coronary Stent System in Real-World Patients	Less than 1 year follow-up.
100	R. Piccolo; G. G. Stefanini; A. Franzone; E. Spitzer; S. Blöchlinger; D. Heg; P. Jüni; S. Windecker	2015	Safety and Efficacy of Resolute Zotarolimus-Eluting Stents Compared With Everolimus-Eluting Stents	Systematic review, intervention is out of scope stent.

#	Reference	Year	Title	Reason for exclusion
101	T. Pilgrim; O. Muller; D. Heg; M. Roffi; D. J. Kurz; I. Moarof; D. Weilenmann; C. Kaiser; M. Tapponnier; S. Losdat; E. Eeckhout; M. Valgimigli; P. Jüni; S. Windecker; J. F. Iglesias	2021	Biodegradable- Versus Durable-Polymer Drug-Eluting Stents for STEMI: Final 2-Year Outcomes of the BIOSTEMI Trial	Duplicate.
102	T. Pilgrim; M. Rothenbühler; G. C. Siontis; D. E. Kandzari; J. F. Iglesias; M. Asami; T. Lefèvre; R. Piccolo; J. Koolen; S. Saito; T. Slagboom; O. Muller; R. Waksman; S. Windecker	2021	Biodegradable polymer sirolimus-eluting stents vs durable polymer everolimus-eluting stents in patients undergoing percutaneous coronary intervention: A meta-analysis of individual patient data from 5 randomized trials	Relevant primary trials already considered for inclusion separately.
103	C. A. Pivato; B. Reimers; L. Testa; A. Pacchioni; C. Briguori; C. Musto; G. Esposito; R. Piccolo; L. Lucisano; L. De Luca; F. Conrotto; A. De Marco; A. Franzone; P. Presbitero; G. Ferrante; G. Condorelli; V. Paradies; G. Sardella; C. Indolfi; G. Condorelli; G. G. Stefanini	2022	One-Month Dual Antiplatelet Therapy After Bioresorbable Polymer Everolimus-Eluting Stents in High Bleeding Risk Patients	Duplicate.
104	E. H. Ploumen; R. A. Buiten; P. Zocca; C. J. M. Doggen; G. A. J. Jessurun; C. E. Schotborgh; A. Roguin; P. W. Danse; E. Benit; A. Aminian; R. L. Anthonio; S. Somi; G. C. M. Linssen; M. Hartmann; M. M. Kok; C. von Birgelen	2021	Acute myocardial infarction treated with novel Resolute Onyx and Orsiro stents in the randomized BIONYX trial	Out of scope subgroup of included RCT.
105	E. H. Ploumen; T. H. Pinxterhuis; R. A. Buiten; P. Zocca; P. W. Danse; C. E. Schotborgh; M. Scholte; R. Gin; S. Somi; K. G. van Houwelingen; M. G. Stoel; H. A. F. de Man; M. Hartmann; G. C. M. Linssen; L. C. van der Heijden; M. M. Kok; C. J. M. Doggen; C. von Birgelen	2022	Final 5-Year Report of the Randomized BIO-RESORT Trial Comparing 3 Contemporary Drug-Eluting Stents in All-Comers	Duplicate.
106	W. Postma; E. Fabris; M. Van der Ent; R. Hermanides; P. Buszman; C. Von Birgelen C; S. Cook; H. Wedel; G. De Luca; R. Delewi; F. Zijlstra; E. Kedhi	2020	Resolute zotarolimus-eluting stent in ST-elevation myocardial infarction (resolute-STEMI): A prespecified prospective register from the DAPT-STEMI trial	Less than 1 year follow-up.
107	R. Puri; I. Otaegui; M. Sabaté; A. Serra-Peñaranda; M. Puigfel; A. Perez de Prado; L. Nombela-Franco; J. M. de la Torre Hernandez; R. Ortas Nadal; A. Iniguez-Romo; et al.	2018	Three- and 6-month optical coherence tomographic surveillance following percutaneous coronary intervention with the Angiolite® drug-eluting stent: the ANCHOR study	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
108	R. Puri; I. Otaegui; M. Sabaté; A. Serra-Peñaranda; M. Puigfel; A. Perez de Prado; L. Nombela-Franco; J. M. de la Torre Hernandez; R. Ortas Nadal; A. Iniguez-Romo; G. Jiménez; F. Fernandez-Vazquez; C. Cuellas-Ramon; N. Gonzalo; V. Alfonso Jiménez Diaz; L. Duocastella; M. Molina; M. Amoros; I. Perez; A. Barria Perez; E. Pelletier Beaumont; S. J. Nicholls; B. Garcia del Blanco; J. Rodés-Cabau	2018	Three- and 6-month optical coherence tomographic surveillance following percutaneous coronary intervention with the Angiolite® drug-eluting stent: The ANCHOR study	Duplicate.
109	J. Qian; B. Xu; A. J. Lansky; Y. J. Yang; S. B. Qiao; Y. J. Wu; J. Chen; F. H. Hu; W. X. Yang; G. S. Mintz; M. B. Leon; R. L. Gao	2012	First report of a novel abluminal groove filled biodegradable polymer rapamycin-eluting stent in de novo coronary artery disease: Results of the first in man FIREHAWK trial	Less than 1 year follow-up.
110	T. Roleder; E. Kedhi; B. Berta; P. Gasior; W. Wanha; M. Roleder; J. Fluder; G. Smolka; A. Ochala; W. Wojakowski	2019	Short-term stent coverage of second-generation zotarolimus-eluting durable polymer stents: Onyx one-month optical coherence tomography study	Less than 1 year follow-up.
111	A. Roguin; D. E. Kandzari; E. Marcusohn; J. J. Koolen; G. Doros; J. M. Massaro; H. M. Garcia-Garcia; J. Bennett; E. G. Gharib; D. E. Cutlip; R. Waksman	2018	Subgroup Analysis Comparing Ultrathin, Bioresorbable Polymer Sirolimus-Eluting Stents Versus Thin, Durable Polymer Everolimus-Eluting Stents in Acute Coronary Syndrome Patients	Out of scope subgroup of included RCT.
112	M. Saada; O. Kobo; F. Kauer; O. Sakhov; P. Laanmets; R. Abhaichand; I. Lozano; J. Crowley; G. S. Wander; M. A. Mamas; A. Roguin	2022	Prognosis of PCI in the Older Adult Population: Outcomes From the Multicenter Prospective e-ULTIMASTER Registry	Objective/outcomes of study not relevant to decision problem.
113	M. Saada; O. Kobo; J. Polad; M. Halabi; I. J. AJJ; Á. Puentes; J. Monségu; D. Austin; R. K. Baisebenov; F. Spanó; A. Roguin	2022	Prognosis of PCI in AMI setting in the elderly population: Outcomes from the multicenter prospective e-ULTIMASTER registry	Objective/outcomes of study not relevant to decision problem.
114	Y. Saito; W. Wijns; A. Baumbach; B. Xu; H. Kelbaek; M. Zheng; M.-A. Morel; R. Anderson; V. Schachinger; A. Lansky	2022	Differential impact of abluminal groove-filled biodegradable-polymer sirolimus-eluting stent versus durable-polymer everolimus-eluting stent on and off dual antiplatelet therapy	Out of scope subgroup of included RCT.
115	S. Saito; K. Ando; Y. Ito; T. Tobaru; J. Yajima; T. Kimura; K. Kadota	2019	Two-year results after coronary stenting of small vessels in Japanese population using 2.25-mm diameter sirolimus-eluting stent with bioresorbable polymer: primary and long-term outcomes of CENTURY JSV study	Longer term results available.

#	Reference	Year	Title	Reason for exclusion
116	S. Saito; N. Hagiwara; A. Seki; K. Igarashi; T. Muramatsu; J. Yajima; H. Yokoi; M. Nakamura; K. Fujii; T. Isshiki; G. W. Stone; P. S. Teirstein; I. T. Meredith; D. J. Allocco; K. D. Dawkins	2014	Japanese and non-Japanese patient outcomes in the PLATINUM randomized trial comparing the PROMUS Element and XIENCE V everolimus-eluting stents	Out of scope subgroup of included RCT.
117	Y. Saito; A. Baumbach; W. Wijns; B. Xu; H. Kelbaek; M. Zheng; M.-A. Morel; R. Anderson; V. Schachinger; A. Lansky	2020	Clinical outcomes of complex lesions treated with an abluminal groove-filled biodegradable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent	Relevant data already included in main trial publication.
118	G. Sarno; B. Lagerqvist; G. Olivecrona; C. Varenhorst; M. Danielewicz; K. Hambraeus; D. Lindholm; T. Råmunddal; N. Witt; S. James	2017	Real-life clinical outcomes with everolimus eluting platinum chromium stent with an abluminal biodegradable polymer in patients from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR)	Duplicate.
119	G. G. Secco; A. Mattesini; R. Fattori; R. Parisi; F. Castriota; M. Vercellino; G. Dall'Ara; L. Uguccioni; L. Marinucci; G. De Luca; P. N. Marino; G. Pistis; C. Di Mario	2016	Time-related changes in neointimal tissue coverage of a novel Sirolimus eluting stent: Serial observations with optical coherence tomography	Less than 1 year follow-up.
120	A. Seth; R. Costa; U. Kaul; G. Wander; A. Mullasari; C. Nanjappa; P. Heggunje-Shetty	2016	Late angiographic and clinical outcomes of the novel BioMime™ sirolimus-eluting coronary stent with ultra-thin cobalt–chromium platform and biodegradable polymer for the treatment of diseased coronary vessels: results from the prospective, multicentre meriT-2 clinical trial	Longer term results available.
121	A. Seth; G. Singh; M. Sankardas; M. Nanjappa; P. Heggunje; T. Alexander; S. Hardas; M. Kalaricka; S. Abraham; S. Vijan; R. Kumar; A. Abizaid	2017	Three-year clinical outcomes of biomime sirolimus-eluting coronary stent system with a biodegradable polymer in coronary artery disease patients: A long-term follow-up of the merit-2 study	Abstract of single-arm study.
122	A. Sethi; V. Kodumuri; V. Prasad; J. Kassotis	2021	Ultrathin biodegradable polymer sirolimus-eluting stent versus contemporary durable polymer everolimus-eluting stent for percutaneous coronary intervention: a meta-analysis of randomized trials	Relevant primary trials already considered for inclusion separately.
123	R. Shetty; J. Prajapati; U. Pai; K. Shetty	2016	Preliminary Evaluation of Clinical and Angiographic Outcomes with Biodegradable Polymer Coated Sirolimus-Eluting Stent in De Novo Coronary Artery Disease: Results of the MANIPAL-FLEX Study	Less than 1 year follow-up.
124	S. Silber; S. Windecker; P. Vranckx; P. W. Serruys	2011	Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial	Intervention not in scope.

#	Reference	Year	Title	Reason for exclusion
125	G. G. Stefanini; P. W. Serruys; S. Silber; A. A. Khattab; R. J. van Geuns; G. Richardt; P. E. Buszman; H. Kelbæk; A. J. van Boven; S. H. Hofma; A. Linke; V. Klauss; W. Wijns; C. Macaya; P. Garot; C. Di Mario; G. Manoharan; R. Kornowski; T. Ischinger; A. L. Bartorelli; P. Gobbens; S. Windecker	2011	The impact of patient and lesion complexity on clinical and angiographic outcomes after revascularization with zotarolimus- and everolimus-eluting stents: a substudy of the RESOLUTE All Comers Trial (a randomized comparison of a zotarolimus-eluting stent with an everolimus-eluting stent for percutaneous coronary intervention)	Intervention not in scope.
126	S. Stojkovic; A. N. Neskovic; Z. Mehmedbegovic; S. Kafedzic; M. Ostojic; M. Nedeljkovic; D. Orlic; B. Ilisic; I. Ilic; A. Aleksic; M. Cerovic; I. Nikolajevic; A. Vlahovic-Stipac; Z. Stajic; B. Putnikovic; M. Hamilos	2015	Reduced sirolimus systemic exposure and improved bioresorbable polymer properties: new allies for the treatment of patients with coronary artery disease	Objective/outcomes of study not relevant to decision problem.
127	Y. Tadano; J.-I. Kotani; Y. Kashima; D. Hachinohe; T. Watanabe; T. Sugie; U. Kaneko; K. Kobayashi; D. Kanno; T. Fujita	2019	Predictors of clinical outcomes after coronary implantation of bioresorbable polymer sirolimus-eluting Ultimaster stents in all-comers: A report of 1,727 cases	Objective/outcomes of study not relevant to decision problem.
128	N. Taglieri; G. Bruno Antonio; G. Ghetti; C. Marrozzini; F. Saia; N. Galié; T. Palmerini	2020	Target Lesion Failure With Current Drug-Eluting Stents	Duplicate.
129	G. Tarantini; F. Cardaioli; G. De Iaco; B. Tuccillo; M. C. De Angelis; C. Mauro; M. Boccalatte; A. Trivisonno; F. Ribichini; G. Vadalà; G. Caramanno; M. Caruso; M. Lombardi; D. Fischetti; A. Danesi; L. Abbracciavento; G. Lorenzoni; D. Gregori; A. Panza; L. Nai Fovino; G. Esposito	2024	A more-Comers populAtion trEated with an ultrathin struts polimer-free Sirolimus stent: an Italian post-maRketing study (the CAESAR registry)	Duplicate.
130	K. Teeuwen; E. M. Spoormans; J. Bennett; C. Dubois; W. Desmet; G. J. Ughi; A. Belmans; J. C. Kelder; J. G. P. Tijssen; P. Agostoni; M. J. Suttorp; T. Adriaenssens	2017	Optical coherence tomography findings: insights from the “randomised multicentre trial investigating angiographic outcomes of hybrid sirolimus-eluting stents with biodegradable polymer compared with everolimus-eluting stents with durable polymer in chronic total occlusions” (PRISON IV) trial	Less than 1 year follow-up.
131	K. Teeuwen; R. J. van der Schaaf; T. Adriaenssens; J. J. Koolen; P. C. Smits; J. P. Henriques; P. H. Vermeersch; R. M. Tjon Joe Gin; B. E. Schölzel; J. C. Kelder; J. G. Tijssen; P. Agostoni; M. J. Suttorp	2017	Randomized Multicenter Trial Investigating Angiographic Outcomes of Hybrid Sirolimus-Eluting Stents With Biodegradable Polymer Compared With Everolimus-Eluting Stents With Durable Polymer in Chronic Total Occlusions: The PRISON IV Trial	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
132	P. Teirstein; G. W. Stone; I. T. Meredith; A. C. Rabinowitz; V. J. Pompili; T. C. Lee; L. A. Cannon; D. J. Kereiakes; M. Mooney; D. Carrie; S. Saito; D. J. Allocco; K. D. Dawkins	2015	Final five-year outcomes following implantation of the promus element platinum chromium everolimus-eluting stent in de novo coronary artery lesions in small vessels (SV) and long lesions (LL): Results of the PLATINUM small vessel and long lesion trials	Abstract of included RCT.
133	R. Toelg; T. Slagboom; J. Waltenberger; T. Lefèvre; S. Saito; D. E. Kandzari; J. Koolen; G. Richardt	2021	Individual patient data analysis of the BIOFLOW study program comparing safety and efficacy of a bioresorbable polymer sirolimus eluting stent to a durable polymer everolimus eluting stent	Relevant primary trials already considered for inclusion separately.
134	T. Tsujimura; T. Ishihara; O. Iida; Y. Hata; T. Toyoshima; N. Higashino; N. Kurata; M. Asai; M. Masuda; S. Okamoto	2021	Arterial Healing 10 Months After Implantation of an Ultrathin-Strut, Biodegradable-Polymer, Sirolimus-Eluting Stent—An Angioscopic Study—	Less than 1 year follow-up.
135	E. Valero; L. Consuegra-Sanchez; G. Minana; S. Garcia-Blas; J. C. Rodriguez; P. Moyano; J. Sanchis; J. Nunez	2018	Initial experience with the novel BioMime 60 mm-long sirolimus-eluting tapered stent system in long coronary lesions	Less than 1 year follow-up.
136	C. von Birgelen; M. W. Basalus; K. Tandjung; K. G. van Houwelingen; M. G. Stoel; J. H. Louwerenburg; G. C. Linssen; S. A. Saïd; M. A. Kleijne; H. Sen; M. M. Löwik; J. van der Palen; P. M. Verhorst; F. H. de Man	2012	A randomized controlled trial in second-generation zotarolimus-eluting Resolute stents versus everolimus-eluting Xience V stents in real-world patients: the TWENTE trial	Duplicate.
137	C. von Birgelen; M. M. Kok; L. C. van der Heijden; P. W. Danse; C. E. Schotborgh; M. Scholte; R. Gin; S. Somi; K. G. van Houwelingen; M. G. Stoel; F. de Man; J. H. W. Louwerenburg; M. Hartmann; P. Zocca; G. C. M. Linssen; J. van der Palen; C. J. M. Doggen; M. M. Löwik	2016	Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial	Duplicate.
138	C. von Birgelen; H. Sen; M. K. Lam; P. W. Danse; G. A. Jessurun; R. W. Hautvast; G. K. van Houwelingen; A. R. Schramm; R. M. Gin; J. W. Louwerenburg; F. H. de Man; M. G. Stoel; M. M. Löwik; G. C. Linssen; S. A. Saïd; M. B. Nienhuis; P. M. Verhorst; M. W. Basalus; C. J. Doggen; K. Tandjung	2014	Third-generation zotarolimus-eluting and everolimus-eluting stents in all-comer patients requiring a percutaneous coronary intervention (DUTCH PEERS): a randomised, single-blind, multicentre, non-inferiority trial	Duplicate.
139	R. Waksman; E. Shlofmitz; S. Windecker; J. J. Koolen; S. Saito; D. Kandzari; P. Kolm; M. J. Lipinski; R. Torguson	2019	Efficacy and Safety of Ultrathin, Bioresorbable-Polymer Sirolimus-Eluting Stents Versus Thin, Durable-Polymer Everolimus-Eluting Stents for Coronary Revascularization of Patients With Diabetes Mellitus	Relevant primary trials already considered for inclusion separately.

#	Reference	Year	Title	Reason for exclusion
140	J. Waltenberger; J. Brachmann; J. van der Heyden; G. Richardt; O. Fröbert; M. Seige; A. Erglis; W. Dewilde; M. Winkens; C. Hegeler-Molkewehrum; N. Klein; S. Hoffmann	2016	Real-world experience with a novel biodegradable polymer sirolimus-eluting stent: twelve-month results of the BIOFLOW-III registry	Longer term results available.
141	T. Williams; A. Mittal; D. Karageorgiev; A. Iniguez Romo; A. Aminian; J. Fernandez Portalese; E. Kharrat; J. A. Gomez-Hospital; D. Firman; R. Trillo Nouche; D. Hildick-Smith	2022	Complete revascularization optimizes patient outcomes in multivessel coronary artery disease: Data from the e-Ultimaster registry	Objective/outcomes of study not relevant to decision problem.
142	J. Wohrle; S. Markovic; W. Rottbauer; T. Muramatsu; K. Kadota; N. Vazquez-Gonzalez; J. Odenstedt; A. Serra; D. Antoniucci; O. Varenne; S. Saito; W. Wijns	2016	Bioresorbable polymer sirolimus-eluting coronary stent compared with permanent polymer everolimus-eluting coronary stent implantation for treatment of small vessel coronary artery disease: CENTURY II trial	Out of scope subgroup of included RCT.
143	S. G. Worthley; A. Abizaid; A. J. Kirtane; D. I. Simon; S. Windecker; S. Brar; I. T. Meredith; S. Shetty; A. Sinhal; A. P. Almonacid; D. Chamie; A. Maehara; G. W. Stone	2017	First-in-Human Evaluation of a Novel Polymer-Free Drug-Filled Stent: Angiographic, IVUS, OCT, and Clinical Outcomes From the RevElution Study	Less than 1 year follow-up.
144	B. Xu; R. L. Gao; R. Y. Zhang; H. C. Wang; Z. Q. Li; Y. J. Yang; C. S. Ma; Y. L. Han; A. J. Lansky; Y. Huo; W. Li; M. B. Leon	2013	Efficacy and safety of FIREHAWK abluminal groove filled biodegradable polymer sirolimus-eluting stents for the treatment of long coronary lesions: Nine-month angiographic and one-year clinical results from TARGET I trial long cohort	Less than 1 year follow-up.
145	W. Yeh Robert; S. Silber; L. Chen; S. Chen; S. Hiremath; F.-J. Neumann; S. Qiao; S. Saito; B. Xu; Y. Yang; L. Mauri	2017	5-Year Safety and Efficacy of Resolute Zotarolimus-Eluting Stent	Device out of scope.
146	R. W. Yeh; S. Silber; L. Chen; S. Chen; S. Hiremath; F. J. Neumann; S. Qiao; S. Saito; B. Xu; Y. Yang; L. Mauri	2017	5-Year Safety and Efficacy of Resolute Zotarolimus-Eluting Stent: The RESOLUTE Global Clinical Trial Program	Duplicate.
147	C. Zanchin; Y. Ueki; T. Zanchin; J. Häner; T. Otsuka; S. Stortecky; C. Koskinas Konstantinos; C. M. Siontis George; F. Praz; A. Moschovitis; L. Hunziker; M. Valgimigli; T. Pilgrim; D. Heg; S. Windecker; L. Räber	2019	Everolimus-Eluting Biodegradable Polymer Versus Everolimus-Eluting Durable Polymer Stent for Coronary Revascularization in Routine Clinical Practice	Duplicate.
148	Y. J. Zhang; W. Wu; D. R. Pan; B. Xu; J. Kan; Y. X. Chen; S. Pang; W. You; J. J. Zhang; F. Ye; S. L. Chen	2015	Feasibility of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent in patients with complex anatomical and clinical scenarios	Less than 1 year follow-up.
149	C. Zivelonghi; J. P. van Kuijk; V. Nijenhuis; E. Poletti; M. J. Suttorp; J. A. S. van der	2018	First report of the use of long-tapered sirolimus-eluting coronary stent for the treatment of chronic total occlusions with the hybrid algorithm	Less than 1 year follow-up.

#	Reference	Year	Title	Reason for exclusion
	Heyden; F. D. Eefting; B. J. Rensing; J. M. ten Berg; L. Azzalini; F. S. van den Brink; F. Ribichini; A. Colombo; J. P. S. Henriques; P. Agostoni			
150	C. Zivelonghi; K. Teeuwen; P. Agostoni; R. J. van der Schaaf; F. Ribichini; T. Adriaenssens; J. C. Kelder; J. G. P. Tijssen; J. P. S. Henriques; M. J. Suttorp	2018	Impact of ultra-thin struts on restenosis after chronic total occlusion recanalization: Insights from the randomized PRISON IV trial	Less than 1 year follow-up.
151	P. Zocca; M. M. Kok; K. Tandjung; P. W. Danse; G. A. J. Jessurun; R. W. M. Hautvast; K. G. van Houwelingen; M. G. Stoel; A. R. Schramm; R. M. Tjon Joe Gin; F. de Man; M. Hartmann; J. H. W. Louwerenburg; G. C. M. Linssen; M. M. Löwik; C. J. M. Doggen; C. von Birgelen	2018	5-Year Outcome Following Randomized Treatment of All-Comers With Zotarolimus-Eluting Resolute Integrity and Everolimus-Eluting PROMUS Element Coronary Stents: Final Report of the DUTCH PEERS (TWENTE II) Trial	Duplicate.

Late-stage assessment

Drug-eluting coronary stents for treating coronary artery disease

Assessment report overview

This overview summarises key information from the assessment and sets out points for discussion in the committee meeting. It should be read together with the final scope, the external assessment report and the user preference report. List of abbreviations used in this overview is in appendix A.

Technologies

In coronary artery disease, the heart's blood supply may become reduced by a build-up of fatty substances in the coronary arteries. To restore the blood flow, a drug-eluting stent may be inserted in coronary arteries during percutaneous coronary intervention (PCI).

Drug-eluting stents are made from metal and coated with an antiproliferative drug. These vary between the stents. In some stents the drug is applied on a durable or absorbable polymer, some are polymer-free. Each drug-eluting stent has an instruction for use (IFU) document that includes the indications for which the device can be used. The indications for use vary and may or may not specify subpopulations or lesion types. They often specify the sizes of vessels the stent can be used for. Some stents may be purchased for use in specific cases because they are indicated for use in a subpopulation or lesion type, or because they have certain design features.

This assessment included 29 drug-eluting coronary stents available through the NHS Supply Chain.

Table 1 Drug-eluting stents in the NHS Supply Chain framework

Manufacturer	Technology	Scaffold material	Polymer type	Drug
Abbott Medical	XIENCE PRO 48	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE PRO S	Cobalt chromium	Durable	Everolimus
Abbott Medical	Skypoint	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE Skypoint 48	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE Skypoint LV	Cobalt chromium	Durable	Everolimus
B. Braun Medical	Coroflex ISAR NEO	Cobalt chromium	Polymer-free	Sirolimus
Biosensors International	BioFreedom	Stainless steel	Polymer-free	Biolimus A9
Biosensors International	BioMatrix Alpha	Cobalt chromium	Biodegradable	Biolimus A9
Biosensors International	BioFreedom Ultra	Cobalt chromium	Polymer-free	Biolimus A9
Biotronik	Orsiro Mission	Cobalt chromium	Biodegradable	Sirolimus
Biotronik	Synsiro Pro	Cobalt chromium	Biodegradable	Sirolimus
Boston Scientific	Promus ELITE	Platinum chromium	Durable	Everolimus
Boston Scientific	Synergy MEGATRON	Platinum chromium	Biodegradable	Everolimus
Boston Scientific	Synergy XD	Platinum chromium	Biodegradable	Everolimus
Cardionovum	XLIMUS	Cobalt chromium	Biodegradable	Sirolimus
IHT	ihtDEStiny BD	Cobalt chromium	Biodegradable	Sirolimus

iVascular	Angiolite	Cobalt chromium	Durable	Sirolimus
Medtronic	Onyx Frontier	Cobalt chromium, platinum-iridium core	Durable	Zotarolimus
Meril	BioMime	Cobalt chromium	Biodegradable	Sirolimus
Meril	BioMime Branch	Cobalt chromium	Biodegradable	Sirolimus
Meril	BioMime Morph	Cobalt chromium	Biodegradable	Sirolimus
Meril	EverMine 50	Cobalt chromium	Biodegradable	Everolimus
Microport	Firehawk	Cobalt chromium	Biodegradable	Sirolimus
Microport	Firehawk Liberty	Cobalt chromium	Biodegradable	Sirolimus
QualiMed	MAGMA	Stainless steel	Biodegradable	Sirolimus
Sahajanand Medical Technologies	Supraflex Cruz	Cobalt chromium	Biodegradable	Sirolimus
Sahajanand Medical Technologies	Supraflex Cruz Nevo	Cobalt chromium	Biodegradable	Sirolimus
Terumo	Ultimaster Nagomi	Cobalt chromium	Biodegradable	Sirolimus
Terumo	Ultimaster Tansei	Cobalt chromium	Biodegradable	Sirolimus

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope.

Clinical effectiveness

The external assessment group (EAG) decided not to use real-world evidence from the National Audit of Percutaneous Coronary Interventions (NAPCI),

hosted by the National Institute for Cardiovascular Outcomes Research (NICOR). Details of the limitations of this data for the purpose of this assessment are in section 4.1.1 of the external assessment report (EAR).

The EAG did targeted literature searches to identify relevant published clinical evidence. The search and selection methods are in section 4.1.3 of the EAR. If this evidence was not available on a stent in the scope, the EAG looked for evidence on the clinically equivalent predecessors. The clinical equivalence summary is in table 3 in section 4.1.2 of the EAR.

Overview of key studies

The EAG identified 22 key randomised controlled trials (RCTs) comparing a stent in the scope to another stent in the scope. Of the 22 studies, 18 provided evidence in a mixed coronary artery disease population, 1 in people with ST-segment elevation myocardial infarction (STEMI), 1 in people with left main lesions and 2 in people with high bleeding risk.

Of the 22 studies, 21 were designed as non-inferiority studies to determine if the stent studied works as well as the stent it is compared to. In most studies, the comparator was a XIENCE stent. No randomised evidence comparing to another device in scope were identified for 8 of the 29 stents (BioMime Branch, BioMime Morph, Coroflex ISAR NEO, EverMine 50, Firehawk Liberty, ihtDEStiny BD, MAGMA and Synergy Megatron).

Table 2 summarises the study results. Most studies showed or suggested similar clinical outcomes between the different stents. In a superiority study (BIOSTEMI), Orsiro showed lower rates of target lesion failure compared with XIENCE. In 1 study (SORT OUT IX), between BioFreedom and Orsiro, the non-inferiority target was not met. Details of the studies and study results are in section 5.1 of the EAR.

Table 2 Summary of clinical outcome results from key studies

Trial name (reference)	Trial type	Population	Stents compared	Results
ANGIOLITE (Moreu et al. 2019)	Non-inferiority	Coronary artery disease	Angiolite with XIENCE Xpedition (Pro 48)	Suggests (not powered) similar target lesion failure (TLF) rates at 2 years
BIODEGRADE (Yoon et al. 2023)	Non-inferiority	Coronary artery disease	Orsiro with BioMatrix	Suggests (not powered) lower TLF rates at 3 years
BIOFLOW-DAPT (Valgmigli et al. 2023)	Non-inferiority	High bleeding risk (participants had 1-month dual antiplatelet therapy [DAPT])	Orsiro Mission with Resolute Onyx	Non-inferiority in a composite of death from cardiac causes, myocardial infarction (MI) or stent thrombosis (ST) at 1 year
BIOFLOW IV (Slagboom et al. 2023)	Non-inferiority	Coronary artery disease (excluding acute MI)	Orsiro with XIENCE Prime or XIENCE Xpedition (Pro 48)	Non-inferiority in target vessel failure (TVF) at 1 year. Suggests (not powered) similar TVF rates at 5 years.
BIOFLOW V (Kandzari et al. 2022)	Non-inferiority	Coronary artery disease (excluding STEMI)	Orsiro with XIENCE	Similar (not powered) TLF rates and lower target vessel myocardial infarction (TVMI) rates at 5 years.
BioFreedom QCA (Sabaté et al. 2021)	Non-inferiority	Coronary artery disease	BioFreedom Ultra with BioFreedom	Suggests (not powered) similar rates of death, MI, TLF and ST at 2 years
BIONYX (van Vliet et al. 2024)	Non-inferiority	Coronary artery disease	Resolute Onyx vs Orsiro	Non-inferiority in TVF and its components cardiac death, TVMI and target vessel revascularisation (TVR) at 5 years

Trial name (reference)	Trial type	Population	Stents compared	Results
BIO-RESORT (Ploumen et al. 2022)	Non-inferiority	Coronary artery disease	Synergy with Orsiro	Suggests (not powered) similar outcomes rates of death, MI and repeat revascularisation at 5 years
BIOSCIENCE (Pilgrim et al. 2018)	Non-inferiority	Coronary artery disease	Orsiro with XIENCE Prime	Non-inferiority in TLF at 1 year. Suggests (not powered) similar rates of TLF at 5 years.
BIOSTEMI (Iglesias et al. 2023)	Superiority	STEMI	Orsiro with XIENCE Prime or XIENCE Xpedition (Pro 48)	Superiority in TLF at 1 year. Lower rates of TLF at 5 years.
CASTLE (Nakamura et al. 2022)	Non-inferiority	Coronary artery disease	Orsiro with XIENCE Sierra (Pro S) or XIENCE Xpedition (Pro 48)	Non-inferiority in TLF at 1 year
CENTURY II (Wijns et al. 2018, Orvin et al. 2016)	Non-inferiority	Coronary artery disease	Ultimaster with XIENCE	Non-inferiority in TLF at 9 months. Suggests (not powered) similar TLF, TVF, patient-oriented composite endpoint (POCE), ST and bleeding rates at 5 years.
EVOLVE II (Kereiakes et al. 2019)	Non-inferiority	NSTEMI or stable angina	Synergy with Promus Element Plus	Non-inferiority in TLF at 1 year. Suggests (not powered) similar TLF rate at 5 years.
IDEAL-LM (van Geuns et al. 2022)	Non-inferiority	Left main lesions	Synergy (4-month DAPT) with XIENCE (1-year DAPT)	Non-inferiority in (major adverse cardiovascular events (MACE) at 2 years
MERIT-V (Abizaid et al. 2023)	Non-inferiority	Coronary artery disease	BioMime with XIENCE V	Suggests (not powered) similar MACE rates at 2 years (powered for 9 months)

Trial name (reference)	Trial type	Population	Stents compared	Results
Onyx ONE (Windecker et al. 2022)	Non-inferiority	High bleeding risk (participants had 1-month DAPT)	Resolute Onyx with BioFreedom	Non-inferiority in a composite of cardiac death, MI or ST at 1 year. Suggests (not powered) similar rates of a composite of cardiac death, MI or ST at 2 years.
PLATINUM (Kelly et al. 2017)	Non-inferiority	Stable or unstable angina or silent ischemia (excluding acute MI)	Promus Element with XIENCE V	Non-inferiority in TLF at 1 year. Suggests (not powered) lower rate of cardiac death or MI and definite or probable ST at 1 year. Suggests (not powered) similar TLF rates at 5 years.
SORT OUT IX (Ellert-Gregersen et al. 2022, Hansen et al. 2022)	Non-inferiority	Coronary artery disease	BioFreedom with Orsiro	Non-inferiority not achieved in MACE at 1 year (higher target lesion revascularisation [TLR] rate). Suggests (not powered) similar TLF but higher TLR rates at 2 years.
SORT OUT VIII (Maeng et al. 2019)	Non-inferiority	Coronary artery disease	BioMatrix NeoFlex with Synergy	Non-inferiority in TLF at 1 year
TALENT (de Winter et al. 2022)	Non-inferiority	Coronary artery disease	Supraflex with XIENCE family	Non-inferiority in device-oriented composite end point (DOCE) at 1 year. Suggests (not powered) similar DOCE rates at 3 years.
TARGET-AC (Lanksy et al. 2023)	Non-inferiority	Coronary artery disease	Firehawk with XIENCE family	Non-inferiority in TLF at 1 year. Suggests (not powered) similar TLF rates at 5 years.
XLIMIT (Testa et al. 2023)	Non-inferiority	Coronary artery disease (excluding STEMI)	XLIMUS with Synergy	Suggests (not powered) similar cardiac death, TVMI and TLR rates at 1 year

Non-randomised comparative studies

In addition to the key RCTs, the EAG identified a large volume of other types of evidence related to the stents in scope. Results of the 14 non-randomised or observational comparative studies are summarised in section 6.1 and a brief description of the 54 single-arm studies are in appendix H of the EAR.

Data on subgroups

The EAG looked if any of the 22 key RCTs reported outcome data for the subgroups in the scope. Of the 22 studies:

- 2 studies reported subgroup results for women and 10 studies if sex affected clinical outcomes between stents
- 5 studies reported subgroup results for people with diabetes and 8 studies if having diabetes affected clinical outcomes between stents
- 1 study reported subgroup results for people with bifurcation lesions and 4 studies if having a bifurcation lesion affected clinical outcomes between stents
- 2 studies were in people with high bleeding risk
- 1 study was in people with left main stem lesions and 4 studies reported if having a left main lesion affected clinical outcomes between stents
- No studies reported results by ethnicity or its effect on clinical outcomes between stents

The subgroup results in these studies were similar to the overall study results. None of the subgroup characteristics had a significant effect on the clinical outcomes between stents. More information on subgroup data is in section 5.1.2 and appendix E of the EAR.

Network meta-analysis

To present the comparative effectiveness of multiple stents in a single analysis, the EAG did a network meta-analysis (NMA) of outcomes at 1 year and after longer-term follow up from the initial stenting. An NMA estimates relative effects between any pair of interventions in the network. Because it synthesises evidence from multiple studies, it may generate more precise estimates than individual studies. Through common comparators in the network, it can provide information for comparisons between pairs of interventions that have not yet been evaluated in individual RCTs. The NMA methods are described in section 4.3 of the EAR.

Of the 22 key RCTs, the EAG's NMA included those 14 RCTs that:

- had at least 1 year follow-up
- compared 2 or more stents in the scope

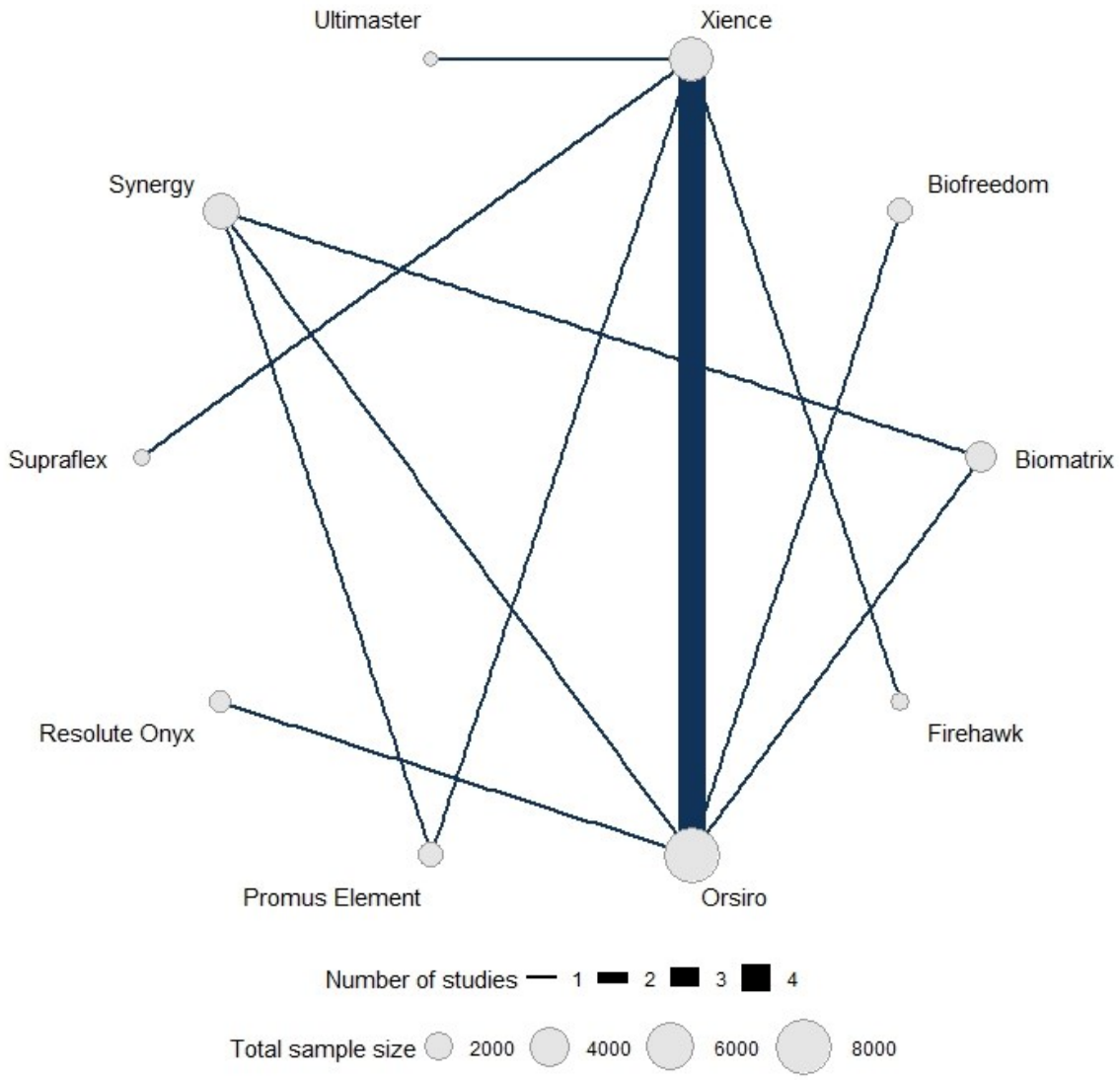
The EAG excluded trials that were powered only for short-term angiographic outcomes (for example in-stent late lumen loss) and trials that included only high-risk participants (for example people with high bleeding risk, STEMI or left main lesions).

The NMA for outcomes at 1 year included 25,974 participants. The size of the 14 studies ranged from 190 to 1,579 participants. Of the 14 trials, 2 were done partly in the UK, and 9 included other locations in Europe. Nine of the trials described the included population as 'all comers'. Five trials excluded high risk participants such as people with STEMI or acute MI. The NMA covered 18 stents in the scope (some through clinically equivalent predecessors). Follow-up in the trials ranged from 1 to 5 years. All studies reported on target lesion revascularisation and target vessel-related myocardial infarction. In all the studies, rates of these outcomes were less than 10%. The NMA synthesised evidence for these outcomes.

Figure 1 presents the network plot for 1-year outcomes. This shows how the stents were connected through common comparators between the RCTs in the analysis. The thick line between the XIENCE and Orsiro nodes shows that this comparison was the most common in the included studies. Orsiro has the largest node in the figure because the largest number of participants in the NMA were randomised to this stent. An overview of the studies in the NMA is in table 7 and a summary of the study participants is in table 8 in section 5.2.2 of the EAR.

The network plot for longer-term follow up is shown in figure 4 in section 5.2.4 of the EAR. For the long-term follow-up NMA, 2 trials that only reported 1-year follow-up data were excluded (CASTLE and SORT OUT VIII). Therefore, data from 12 RCTs with all together 21,770 participants contributed to the long-term analysis.

Figure 1 Network meta-analysis plot for 1-year outcomes (stents names in the plot reflect the stents or stent families in the studies)



Quality of studies in the network meta-analysis

The EAG assessed risk of bias using the Joanna Briggs Institute (JBI) checklist for RCTs. The EAG had most concerns over high risk of bias because participants and those delivering the treatments were not always

unaware of the treatment assignment. High risk of bias was also a concern because of incomplete follow up and that differences between groups in terms of their follow up were not always adequately described and analysed. Details of the risk of bias and quality assessment of the 14 RCTs in the NMA are in section 5.2.3 of the EAR.

Results of the network meta-analysis

Table 3 shows the relative effect estimates for the different stents compared to a XIENCE stent (XIENCE Xpedition, XIENCE V or XIENCE Prime) on target lesion revascularisation and target vessel related myocardial infarction at 1 year. Figures 2 and 3 present the results graphically in forest plots. The wide 95% confidence intervals around the effect estimates indicate that the estimates were uncertain. But like the results of the individual primary studies, most results of the NMA suggested that the 2 clinical outcomes were similar between the different stents. The NMA estimated a slightly higher risk of target lesion revascularisation with BioFreedom compared with XIENCE. Risk of target vessel related myocardial infarction with all the stents was similar to that with the XIENCE stent.

Table 3 Risk of target lesion revascularisation and target vessel-related myocardial infarction at 1 year comparing different drug-eluting coronary stents to a XIENCE stent

Drug-eluting coronary stent	Hazard ratio (HR) of target lesion revascularisation 95% credible interval (95% CrI)	HR of target vessel related myocardial infarction (95% CrI)	Evidence from (if not from the stent being compared)
BioFreedom	3.70 (1.83 to 6.80)	0.88 (1.83 to 6.80)	
BioFreedom Ultra	3.70 (1.83 to 6.80)	0.88 (1.83 to 6.80)	BioFreedom
BioMatrix Alpha	1.87 (0.94 to 3.32)	1.05 (0.94 to 3.32)	Biomatrix
Firehawk	0.54 (0.20 to 1.11)	1.19 (0.20 to 1.11)	
Orsiro Mission	1.25 (0.84 to 1.81)	0.84 (0.84 to 1.81)	Orsiro

Synsiro Pro	1.25 (0.84 to 1.81)	0.84 (0.84 to 1.81)	Orsiro
Promus Elite	1.00 (0.52 to 1.77)	0.59 (0.52 to 1.77)	Promus Element
Onyx Frontier	1.71 (0.80 to 3.20)	0.89 (0.80 to 3.20)	Resolute Onyx
Supraflex Cruz	0.70 (0.36 to 1.22)	0.94 (0.36 to 1.22)	Supraflex
Supraflex Cruz Nevo	0.70 (0.36 to 1.22)	0.94 (0.36 to 1.22)	Supraflex
Synergy XD	1.51 (0.81 to 2.54)	0.68 (0.81 to 2.54)	Synergy
Ultimaster Nagomi	0.99 (0.48 to 1.85)	0.63 (0.48 to 1.85)	Ultimaster
Ultimaster Tansei	0.99 (0.48 to 1.85)	0.63 (0.48 to 1.85)	Ultimaster

Figure 2 Risk of target lesion revascularisation at 1 year comparing different drug-eluting coronary stents to a XIENCE stent

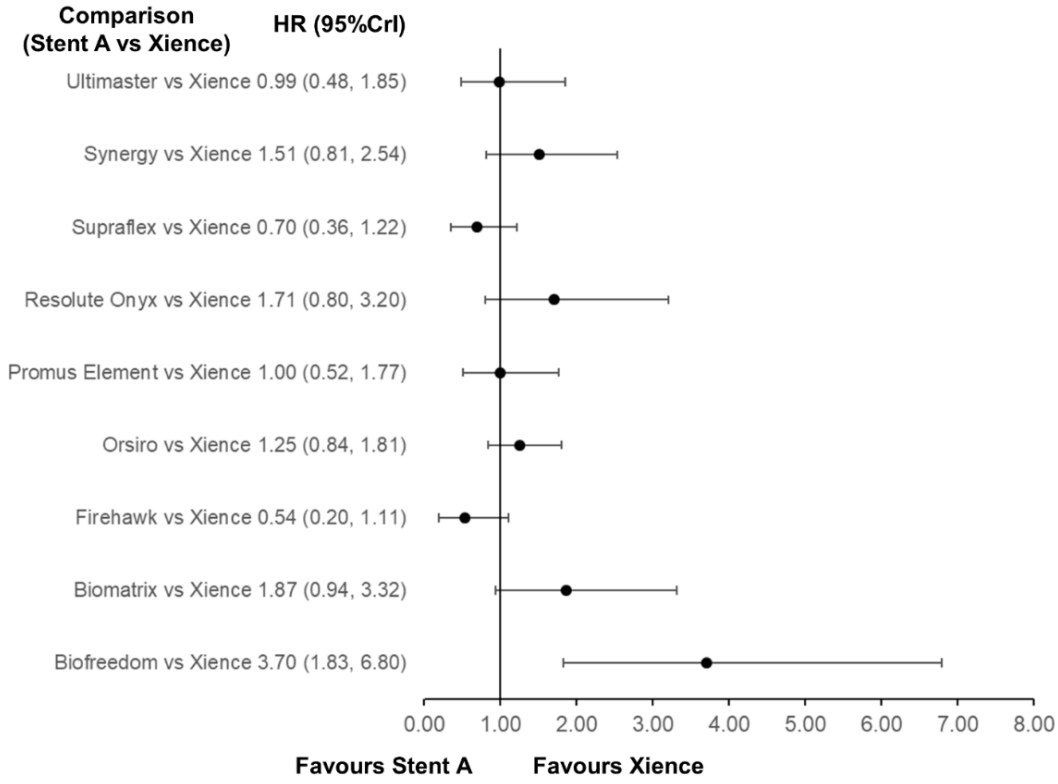
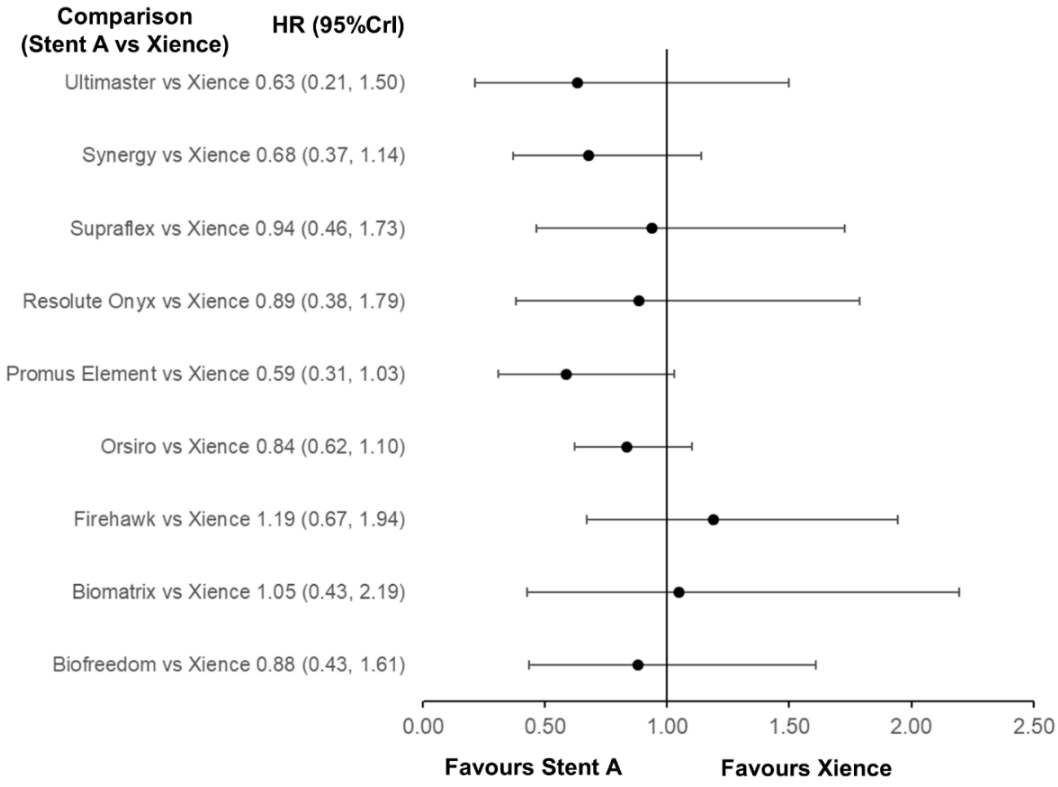


Figure 3 Risk of target vessel related myocardial infarction at 1 year comparing different drug-eluting coronary stents to a XIENCE stent



In the analysis of the longer-term follow-up, the effect estimates were even more uncertain. These long-term results suggested the outcomes were similar between the stents. The relative effect estimates for the different stents compared to a XIENCE stent on target lesion revascularisation and target vessel related myocardial infarction using long-term data are in table 12 and the forest plots of the long-term results in figure 6 in section 5.2.4 of the EAR.

The EAG compared the results from their NMA to an earlier NMA by Taglieri et al. (2020). This was an NMA of target lesion failure and its individual outcomes at 1 year and long-term follow-up using 77 RCTs with 99,039 participants. A total of 10 devices were compared in this NMA, including 5 stents in the scope (BioMatrix, Orsiro, Resolute, Synergy and XIENCE). The

study did not report comparisons between all the devices but the relative effect between Orsiro and XIENCE was reported. Taglieri et al. (2020) had similar findings to EAG's NMA. There were no significant differences in terms of target lesion revascularisation and target vessel-related myocardial infarction but Taglieri reported narrower confidence intervals for the estimate. This may have been because the study used different NMA methods and inclusion criteria for the stents and studies in the NMA.

Ongoing studies

Table 4 lists 4 potentially relevant ongoing RCTs comparing a stent in the scope to another stent in the scope the EAG identified. The EAG noted that SMART-CHOICE4 and ONE-PASS would likely be eligible for inclusion in the NMA. Further study details are in table 31 in appendix E of the EAR.

Table 4 Ongoing studies

Trial name	Trial type	Status	Population	Stents compared
NCT04500912	Not specified	Completed September 2023	High bleeding risk (participants had 1-month dual antiplatelet therapy [DAPT])	Supraflex Cruz with Ultimaster Tansei
NCT05240781 ZEVS-HBR	Non-inferiority	Recruiting	High bleeding risk (participants had 1-month DAPT)	Resolute Onyx with Ultimaster Tansei (or Ultimaster)
NCT05066789 SMART-CHOICE4	Non-inferiority	Recruiting	Acute coronary syndrome (participants had 1-month or 12-month DAPT)	BioFreedom Ultra with Orsiro Mission
NCT05305482 ONE-PASS	Non-inferiority	Recruiting	Acute coronary syndrome (participants had 1-month DAPT)	BioFreedom Ultra with Ultimaster

Cost effectiveness

The external assessment group (EAG) did a review to identify suitable health economic models. They found 3 NICE clinical guidelines and 19 economic evaluations that reported an economic model. An overview of these 22 models is in section 8.1 and appendix I of the external assessment report (EAR).

Health economic model

The EAG developed a Markov model that included 7 health states:

- no further event
- Target lesion revascularisation (TLR)
- Target vessel-related myocardial infarction (TVMI)
- TVMI-repeat revascularisation
- post-revascularisation
- post-myocardial infarction (post-MI) and
- death.

The model estimated cost-effectiveness estimates for the 18 stents covered by the NMA. All 29 stents in scope were included in a cost-comparison analysis. Figure 4 shows the model structure schematic. People would enter the model through the ‘no further event’ -state after having a drug-eluting coronary stent inserted during a percutaneous coronary intervention (PCI). They could then either continue not have further events, or they could have a target lesion revascularisation (because of a restenosis in the stented lesion) or a target vessel-related myocardial infarction or they could die. People who had a target lesion revascularisation and survived the procedure, would move to the ‘post-revascularisation’ -state and stay in that state until they died. Those who had a target vessel-related myocardial infarction could survive or die. Those who survived would have a repeat revascularisation. If they

survived the procedure, they would then move to the ‘post-MI’ -state and stay in that state until they died. The model assumed that the choice of revascularisation strategy was always PCI with stenting (in practice, alternative treatments could include for example coronary artery bypass grafting). In the model, the minimum stay in a health state (cycle length) was 1 year. In the base case, the model ran for 1 year (time horizon). The EAG explored a longer time horizon in the scenario analyses. Further details of the economic modelling are in section 9 of the EAR.

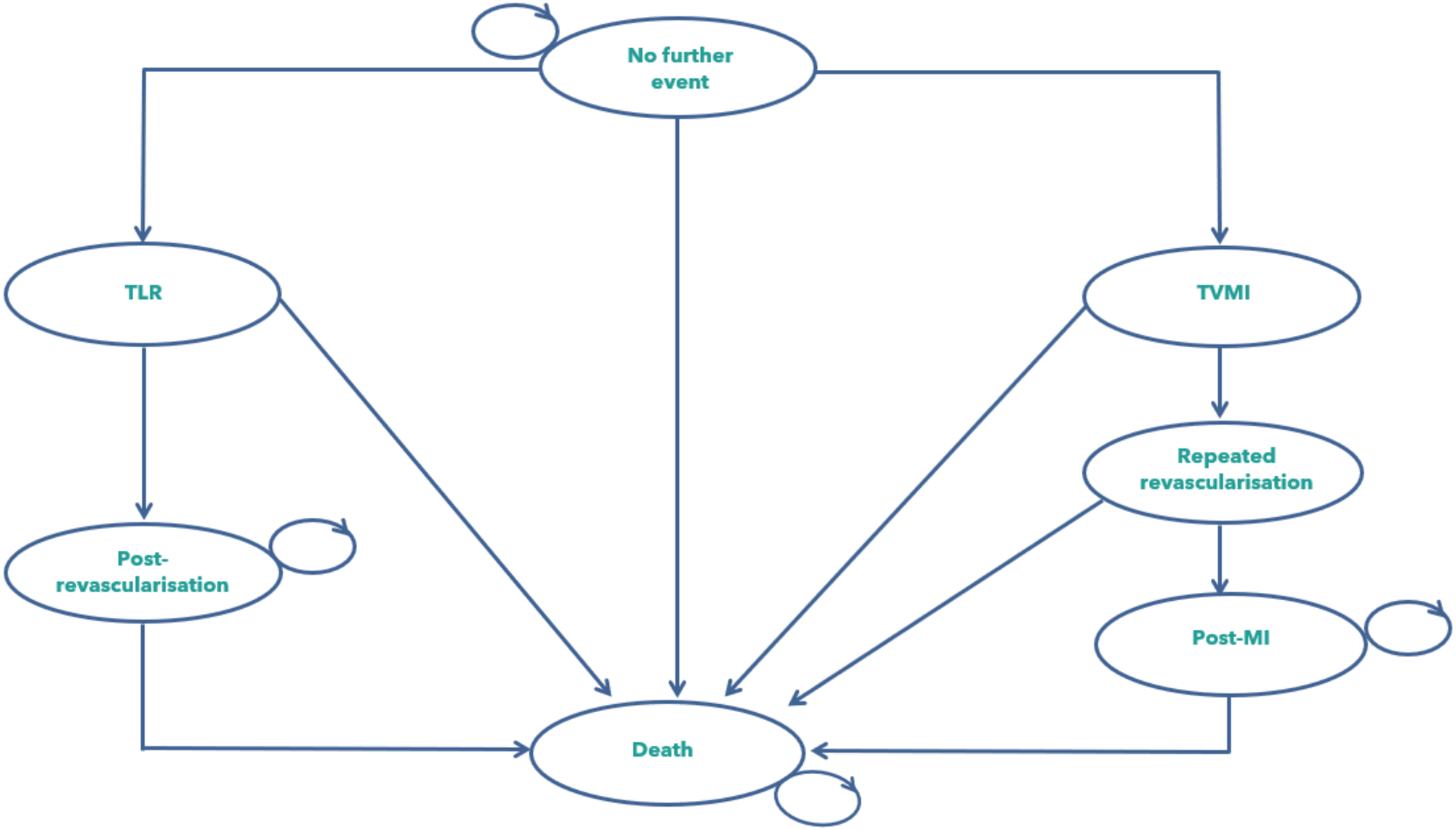
Population

People entering the model had coronary artery disease. Based on the NICOR PCI Annual report 2022 data, they were 66 years old. Most participants (72.5%) were men.

Comparator

The comparator in the economic model was XIENCE Pro S. This was the cheapest XIENCE stent in the assessment. XIENCE stents were the most common comparators in the 22 key studies and the 14 of the 22 key studies included in the EAG’s network meta-analysis (NMA).

Figure 4. Model structure



Model inputs

Probability of target lesion revascularisation and target vessel related myocardial infarction

Table 5 shows the probability of target lesion revascularisation and target vessel-related myocardial infarction at 1 year with XIENCE stents. The 5-year probabilities are in table 20 in section 9.3 of the EAR. The EAG calculated the probabilities using events at year 1 and year 5 in the XIENCE-arm in the 5-year studies (BIOFLOW IV, BIOFLOW V, BIOSCIENCE, CENTURY II, PLATINUM). Long-term event rates after the first year were converted into yearly probabilities. The risk of clinical events was constant after the first year. The EAG calculated the probabilities for the other stents using the probability with XIENCE and the risks (hazard ratios) from the NMA. For example, the probability of target lesion revascularisation at 1 year for BioFreedom was calculated as: 2.322% (probability with XIENCE Pro S) multiplied by 3.70 (HR for BioFreedom) equals to 8.591%.

Table 5 Outcome probabilities at 1 year with XIENCE stents

Drug-eluting coronary stent	Probability of target lesion revascularisation at 1 year (95% CI)	Probability of target vessel-related myocardial infarction at 1 year (95% CI)
XIENCE Pro 48 XIENCE Pro S XIENCE Skypoint XIENCE Skypoint 48 XIENCE Skypoint LV	2.322% (2.320 to 2.323%)	3.184% (3.182-3.186%)

Costs

Stent costs

Table 6 shows the stent costs used in the model. In the base case, the costs were NHS Supply Chain weighted average of the 2023 purchase costs. For devices with no 2023 sales through NHS Supply Chain, the model used the framework price. The minimum and maximum costs based on NHS Supply Chain 2023 purchase data were explored in the scenario analyses. Based on

NICOR PCI audit data 2022, the index (first) PCI and each repeat revascularisation procedure used a mean of 1.33 stents per procedure. The model assumed that the repeat procedures used the same stents that were used in the index PCI.

Table 6 Stent costs

Drug-eluting coronary stent	NHS Supply Chain weighted average of the 2023 purchase costs or framework price	NHS Supply Chain 2023 minimum and maximum costs	Model analyses
Angiolite	[redacted]	[redacted]	Cost comparison
BioFreedom	[redacted]	[redacted]	Cost effectiveness and cost comparison
BioFreedom Ultra	[redacted]	[redacted]	Cost effectiveness and cost comparison
BioMatrix Alpha	[redacted]	[redacted]	Cost effectiveness and cost comparison
BioMime	[redacted]	[redacted]	Cost comparison
BioMime Branch	[redacted]	[redacted]	Cost comparison
BioMime Morph	[redacted]	[redacted]	Cost comparison
Coroflex ISAR NEO	[redacted]	[redacted]	Cost comparison
EverMine 50	[redacted]	[redacted]	Cost comparison
Firehawk	[redacted]	[redacted]	Cost effectiveness and cost comparison
Firehawk Liberty	[redacted]	[redacted]	Cost comparison
ihtDEStiny BD	[redacted]	[redacted]	Cost comparison
MAGMA	[redacted]	[redacted]	Cost comparison
Onyx Frontier	[redacted]	[redacted]	Cost effectiveness and cost comparison

Drug-eluting coronary stent	NHS Supply Chain weighted average of the 2023 purchase costs or framework price	NHS Supply Chain 2023 minimum and maximum costs	Model analyses
Orsiro Mission	[redacted]	[redacted]	Cost effectiveness and cost comparison
Promus ELITE	[redacted]	[redacted]	Cost effectiveness and cost comparison
Supraflex Cruz	[redacted]	[redacted]	Cost effectiveness and cost comparison
Supraflex Cruz Nevo	[redacted]	[redacted]	Cost effectiveness and cost comparison
Synergy MEGATRON	[redacted]	[redacted]	Cost comparison
Synergy XD	[redacted]	[redacted]	Cost effectiveness and cost comparison
Synsiro Pro	[redacted]	[redacted]	Cost effectiveness and cost comparison
Ultimaster Nagomi	[redacted]	[redacted]	Cost effectiveness and cost comparison
Ultimaster Tansei	[redacted]	[redacted]	Cost effectiveness and cost comparison
XIENCE PRO 48	[redacted]	[redacted]	Cost effectiveness and cost comparison
XIENCE PRO S	[redacted]	[redacted]	Cost effectiveness and cost comparison
XIENCE SKYPOINT	[redacted]	[redacted]	Cost effectiveness and cost comparison
XIENCE Skypoint 48	[redacted]	[redacted]	Cost effectiveness and cost comparison

Drug-eluting coronary stent	NHS Supply Chain weighted average of the 2023 purchase costs or framework price	NHS Supply Chain 2023 minimum and maximum costs	Model analyses
XIENCE Skypoint LV	[redacted]	[redacted]	Cost effectiveness and cost comparison
XLIMUS	[redacted]	[redacted]	Cost comparison

Other treatment and follow-up costs

Other costs in the model included:

- PCI procedure costs
- treatment costs after PCI (cardiac rehabilitation, 1 outpatient appointment, 12 months of dual antiplatelet therapy [DAPT])
- costs after no further events
- myocardial infarction-related costs for those who have target vessel-related myocardial infarction and
- post-revascularisation costs.

Details of other treatment and follow-up costs are in table 22 in section 9.4 of the EAR.

Health-related quality of life

People had different health-related quality of life at different health states in the model. The model assumed that only 'no further events' and the 'post-repeat revascularisation' state were associated with the same quality of life. Details of the utility values at the different health states are in table 23 in section 9.5 of the EAR.

Mortality

The model included:

- general population mortality

- mortality risk after repeat revascularisation (30 days)
- additional risks of death at the 'no further events', 'post- revascularisation' (after TLR), 'target vessel-related myocardial infarction', 'repeat revascularisation' (after TVMI) and 'post-MI' health states

Details of mortality risk are in table 20 in section 9.3 of the EAR.

Model results

Base case

There was considerable uncertainty around the net monetary benefit (NMB) estimates. In the base case analysis, at 1 year after the index PCI at a £20,000 per QALY willingness-to-pay threshold, the net monetary benefit per QALY (NMB) ranged from [redacted] to [redacted] (probabilistic analysis). Figure 5 graphically presents these results. It shows that the 95% confidence intervals (horizontal lines) around the NMB average estimates (diamond shaped spots) for all the 18 stents in the model were wide and largely overlapped. Figure 6 presents the cost-effectiveness acceptability curve graphically showing the probabilities of any of the stents being the most cost-effective stent. At the £20,000 threshold, the probability of any of the stents being the most cost-effective drug-eluting stent of the stents in the analysis was low (less than 30%).

The probabilistic results are in table 25 in section 10.2 and the deterministic results in table 24 in section 10.1 of the EAR.

Figure 5 Net monetary benefits (NMB) at 1 year after the index PCI at a £20,000 per QALY willingness-to-pay threshold [the figure has been partly redacted]

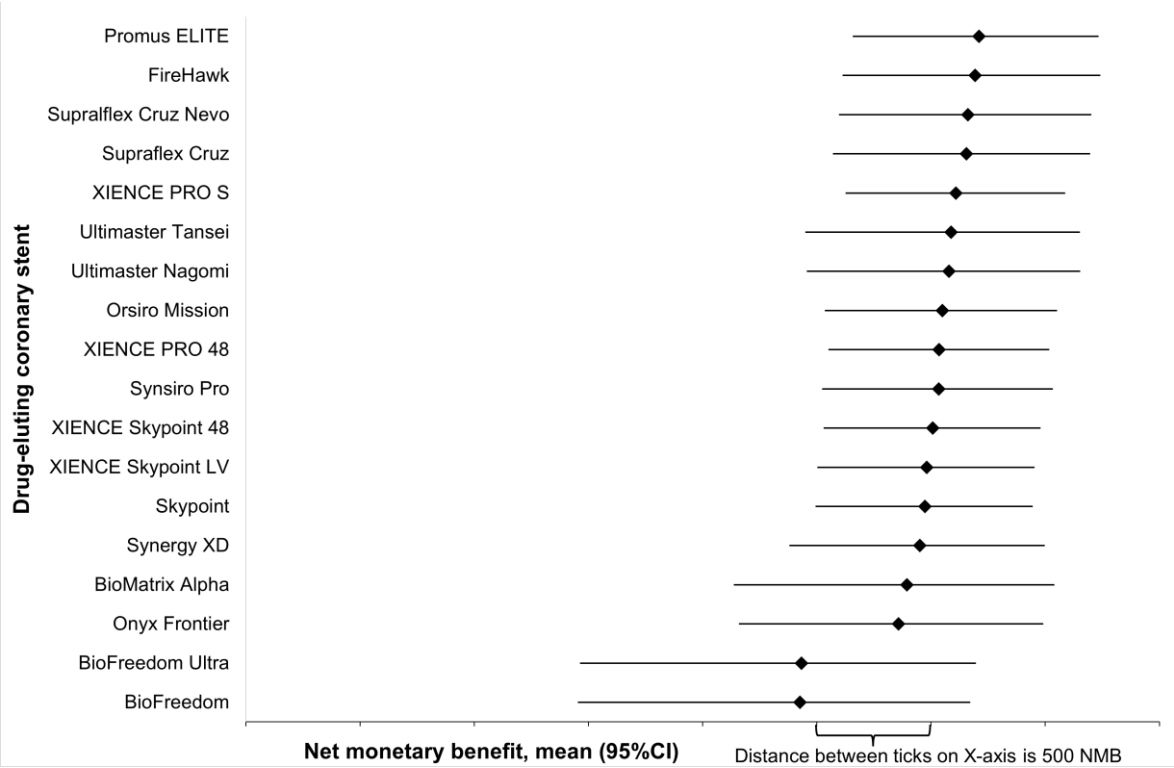
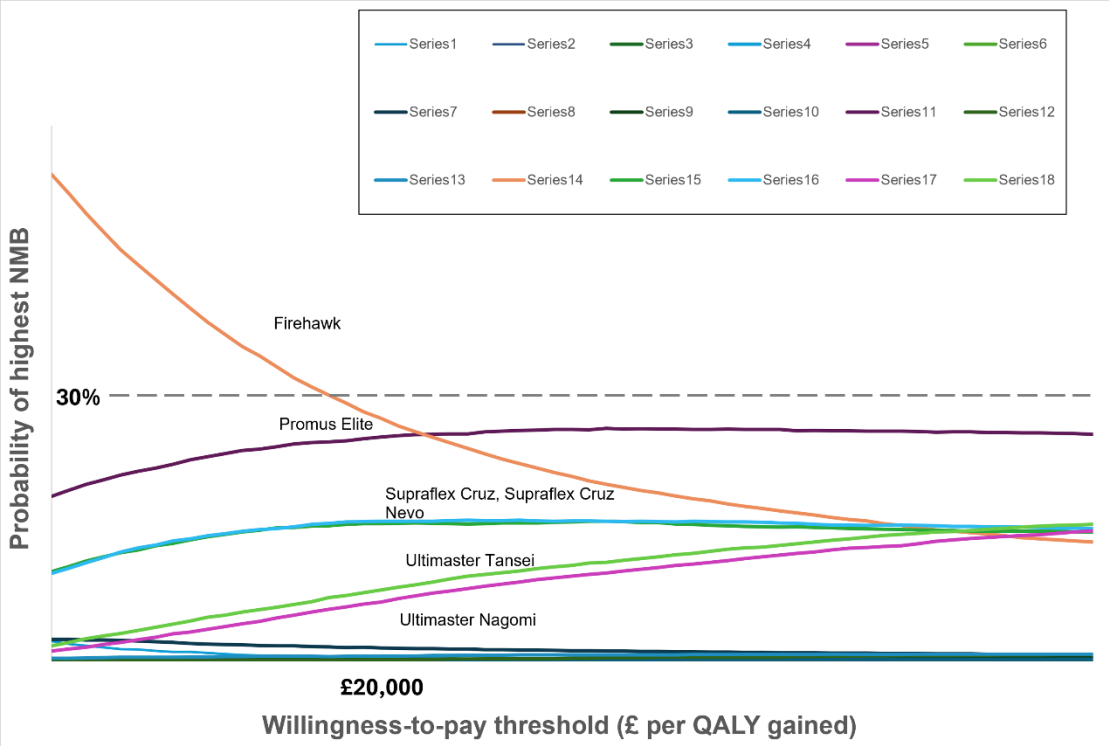


Figure 6 Cost-effectiveness acceptability curve at 1 year after the index PCI [the figure has been partly redacted]



Scenario analyses

The EAG analysed alternative scenarios using:

- relative treatment effects for the stents generated using the higher prior heterogeneity distribution in the NMA (slightly higher effects with slightly wider confidence intervals)
- a longer, 5-year time horizon in the model using the relative treatment effects in the long-term follow-up from the NMA (prior heterogeneity distribution 0.1 and 1.0)
- a more favourable treatment effect with less uncertainty around it for Orsiro Mission and Synsiro Pro reported in the NMA by Taglieri et al. (2020)
- the minimum and maximum stent costs or for stents with no NHS Supply Chain sales in 2023 the framework price plus or minus 20%
- a higher, £30,000 per QALY willingness-to-pay threshold

In all the alternative scenarios, like in the base case, the variation in NMBs across all the stents was small. The NMBs from the scenario with the 5-year time horizon were very uncertain. This was because the quantity of data in the long-term NMA was very limited and events rare, and so the relative effect estimates used to calculate the event probabilities for the 5-year time horizon scenario were very uncertain. The EAG noted that these results should be interpreted with caution. Scenario analysis results are in section 10.3 of the EAR.

Cost-comparison analysis

Because the EAG's NMA did not show significant differences between devices and most primary studies were non-inferiority studies, the EAG explored cost-comparison analysis. This analysis assumed no differences in treatment effect between stents and estimated total costs and NMBs for all 29 stents in the scope. Like in the base case, the variation in NMBs across stents was small. Cost-comparison results are in section 10.3 of the EAR.

User preferences

A group of 7 interventional cardiologists participated NICE's user preference assessment to explore what is important when they consider which drug-eluting coronary stent to use. They identified a set of 4 criteria at the patient-level after the decision about the treatment with stents has been made. They also identified a set of 6 criteria that are important when choosing typically 2 to 3 different stents to have available to cover most cases they expect to treat. High on both lists were stent failure and suitable stent size. Suitability for people having abbreviated 1-month dual antiplatelet therapy (DAPT) and procedural success also featured on both lists. Clinical evidence was key for measuring performance against most criteria.

Details on the identified user preferences are on pages 6 to 11 of the user preference report. Table 2 in this assessment report overview summarises clinical outcomes, including those that indicate stent failure (such as target

lesion failure), in the 22 key studies comparing 2 or more stents in scope. These key studies in table 2 include 2 studies in which people had abbreviated DAPT. Table 4 in this overview includes 4 ongoing studies in which people will have abbreviated DAPT. Information on 6 additional RCTs comparing different length DAPT regimens for people having PCI with a stent or stents in the scope of this late-stage assessment is in section 6.2 and a summary of the procedural outcomes in the 22 key studies is in section 6.3 of the external assessment report (EAR).

Equality considerations

The final scope and the scoping equality impact assessment describe equality considerations for this assessment. Page 8 of this assessment report overview summarises the data the external assessment group (EAG) found on subgroups including women and people with diabetes. The key studies in this assessment did not report subgroup data or study participant information on ethnicity. The EAG did not identify additional equality issues.

Limitations and key issues

Clinical effectiveness

Limitations

- Most clinical trials comparing stents had been designed for non-inferiority so could only suggest but not demonstrate superiority
- Not all stents had randomised evidence where the stent had been compared to another stent (or an accepted predecessor) in scope and so they could not be included in the network meta-analysis (NMA)
- Not all stents had an RCT that was powered to assess clinical outcomes at a minimum follow-up of 1 year and so they were excluded from the NMA
- Information about clinical equivalence between stents was not available for all the stents

- Some studies were excluded from the NMA because they were not in the main population (this did not result in any stents being excluded from the NMA)
- The quantity of data available for each comparison for the 18 of the 29 stents in the NMA was limited, even more so for the long-term, making the results uncertain
- The NMA only included 2 clinical outcomes
- The EAG noted that having some of the data in the model from previous generations of devices may have introduced further uncertainty
- There was not enough evidence to do an NMA in subgroups.

Key issues:

- Are RCTs the best source of data for looking at comparative effectiveness between the stents?
- What can the published studies tell us about the comparative effectiveness between the stents?
- What can the published studies tell us about the comparative effectiveness in the subgroups in scope?
- What can the EAG's NMA tell us about the comparative effectiveness between the stents that were included in it?

Cost effectiveness

Limitations:

- Cost-effectiveness model included only 18 of the 29 devices (those in the NMA)
- There was not enough data to do health economic analyses in subgroups.
- The economic model structure and model inputs were guided by the trial data and the nature and quality of trial reporting may have affected the accuracy of the model results

- Because of limited quantity of evidence comparing effectiveness between the stents and therefore uncertainty in the treatment effects from the NMA, there was considerable uncertainty in the model results
- The EAG noted that the results of the health economic analysis may not be generalisable to the NHS setting because only 2 studies in the NMA were done partly in the UK and the baseline event probabilities for the comparator stent in the model came from studies outside of the UK

Key issues:

- Are the economic model structure, assumptions and clinical and cost parameters suitable to answer the decision question (see final scope) for this assessment?
- What can the model results tell about the comparative cost-effectiveness of the stents?

User preferences

Limitations:

- Some participants ranked items they expected to differentiate between the stents higher than items they expected to be similar between the stents (for example stent failure or procedural success)
- The user preference assessment only focused on the main population
- People involved in purchasing were not involved in the assessment (although not users of stents, they could bring in further factors that are important in the decision-making on which stents to have available)

Key issues:

- What conclusions can be drawn from the user preference assessment?

Appendix A Abbreviations

DAPT	Dual antiplatelet therapy
DOCE	Device-oriented composite end point
EAG	External assessment group
EAR	External assessment report
HR	Hazard ratio
LSA	Late-stage assessment
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
NAPCI	National Audit of Percutaneous Coronary Intervention
NICOR	The National Institute for Cardiovascular Outcomes Research
NMA	Network meta-analysis
NMB	Net monetary benefit
NSTEMI	non-ST-segment elevation myocardial infarction
PCI	Percutaneous coronary intervention
POCE	Patient-oriented composite endpoint
QALY	Quality adjusted life year
RCT	Randomised controlled trial
ST	Stent thrombosis
STEMI	ST-segment elevation myocardial infarction
TLF	Target lesion failure
TLR	Target lesion revascularisation
TVF	Target vessel failure
TVR	Target vessel revascularisation
TVMI	Target vessel related myocardial infarction

HealthTech Programme

Drug-eluting coronary stents for treating coronary artery disease: late-stage assessment

Section A: External Assessment Report - Comments collated table:

Any confidential sections of the information provided should be underlined and highlighted. Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in blue and all that is 'academic in confidence' in yellow

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
1.	B. Braun Medical	99-100	Section 9.4, Table 21	As the costs in the table are redacted, it is not possible to comment on whether the costs are representative. However, from the narrative under the heading "Stent costs" it appears that these costs are taken from NHS Supply Chain (NHSSC). As not all DESs are purchased via NHSSC, it is unclear whether the true range of costs charged to the NHS are reflected in the economic model. The EAG should clarify whether the model is able to reflect the variation in price charged to different NHS Organisations for the same DES.	Thank you for your comment. The price provided by NHS SC is weighted based on the purchases in 2023, and has considered the varying pricing levels awarded at individual trusts. The EAG acknowledges the cost variation across different trusts, however the significant uncertainty with relative treatment effect would outweigh this cost impact. A related limitation is now added in the EAG report (p129).
2.	Boston Scientific	N/A	N/A	Thank you for undertaking this work to trial your new approach to Late Stage Assessment. Having reviewed the documentation sent to us, we wish to raise a number of points related to the limitations of any conclusions that can be drawn, which are outlined below. • Limited integration and recognition of the user preference report, giving uncertainty into how user preference has been considered in any conclusions drawn	EAG responses are individually given against each point below.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				• Exclusion of relevant evidence in the assessment • Limited number of clinical outcomes considered in the NMA and economic model • Limited consideration of evidence for stents not included in the NMA • Heterogeneity between PCI techniques in trials which impact clinical outcomes for PCI patients	
3.	Boston Scientific	N/A	N/A	**Integration and recognition of user preference** We welcome the inclusion of the user preference analysis in this assessment, and the recognition in the user preference report of the importance of stent size, stent failure, and suitability for people having abbreviated 1-month DAPT. This is line with what was outlined in the scope, in which user preference / multi-criteria decision analysis was specified as a relevant approach to adopt. However, we are concerned that despite this user preference study being specified and conducted, it is infrequently referred to in the final EAG report or included in the economic model, casting some doubt into the role user preference will play in the discussion and subsequent recommendation. We request that, as a specified approach in the scope, user preference is given more consideration.	Thank you for this comment. The EAG report and NICE user preference report are standalone pieces of work. The EAG understands that both reports will be presented for consideration by the committee.
4.	Boston Scientific	128	12	**Exclusion of relevant evidence: trial design** We note the EAG's analysis was restricted to evidence from RCTs on the basis that "Taking results	The EAG acknowledge the volume of non-RCT evidence available, and have referred to this evidence at various points in the report and in the appendices. Reference to this evidence has

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				from an RCT setting, as opposed to a 'real world' setting, increases the likelihood that the incidence of clinical events observed can be directly attributed to the type of DES used." However, the EAG do acknowledge that "there are still multiple patient-specific and operator-specific factors that may influence outcomes and this should be taken into consideration when interpreting the evidence." We also note that the objective of the LSA as described in the EAG report – "to assess whether there is evidence of superior clinical effectiveness for any of the devices that justify a higher cost" – is narrower than the objective of the LSA as defined in the scope – "to assess whether price variations between technologies are justified by the incremental differences and advancements, and which technologies represent value for money." We feel the restriction of the considered evidence to RCTs has meant that valuable evidence from non-randomised interventional and observational studies that could address the wider question as posed in the original scope has been omitted. Modern PCI trials tend to investigate modern PCI techniques as a whole (e.g. imaging techniques, plaque modification, use of balloons, DAPT, etc); this means that non-RCT evidence is likely to be required to understand the impact of incremental differences and advancements related to modern stents. We suggest that the potential impact of the restriction of the evidence base to RCTs should be considered by the committee.	now been added to the executive summary. The EAG has prioritised the evidence it believes to be most relevant to the decision problem, in line with NICE LSA interim methods and processes. The EAG encourage discussion of the limitations of the analysis at committee.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
5.	Boston Scientific	52	5.2.1	**Exclusion of relevant evidence: disease severity** Further to comment number 3, though we understand that trials including only high-risk patients would likely introduce bias to the main NMA, high-risk patients such as STEMI are a significant portion of PCI patients in modern practice (NICOR registry data suggests 24.7% of PCIs were in STEMI in 2022/23), and we are concerned that automatically excluding these trials from discussion in the report downplays the importance of this evidence. Consideration of the evidence for stents in high-risk groups or in particular anatomies (e.g. IDEAL LM trial[1], Synergy AMI (SCAAR Registry)[2]) could help to make the report more meaningful. **References**: **(1)** van Geuns RJ, Chun-Chin C, McEntegart MB, et al. Bioabsorbable polymer drug-eluting stents with 4-month dual antiplatelet therapy versus durable polymer drug-eluting stents with 12-month dual antiplatelet therapy in patients with left main coronary artery disease: the IDEAL-LM randomised trial. *EuroIntervention*. 2022;17(18):1467-1476. doi:10.4244/EIJ-D-21-00514. **(2)** Buccheri S, Sarno G, Lagerqvist B, et al. Bioabsorbable polymer everolimus-eluting stents in patients with acute myocardial infarction: a report from the Swedish Coronary Angiography and Angioplasty Registry. *EuroIntervention*. 2018;14(5):e562-e569. Published 2018 Aug 3. doi:10.4244/EIJ-D-18-00392.	The EAG accepts that STEMI patients are a significant proportion of those who undergo PCI. The EAG would like to highlight Table 8 in the report which indicates the percentage of participants with STEMI of the trials that were included in the NMA. The EAG commented on the percentage of STEMI in the trials in comparison with 2022/23 NICOR data in Section 5.2.2 of the report. Results of the IDEAL LM trial (Van Geuns et al. 2022) are reported in Section 5.1.1. The Synergy AMI trial (Buccheri et al. 2022) is reported on briefly in Section 6.1. The EAG have added a statement to the executive summary regarding subgroups.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
6.	Boston Scientific	63	5.2.4	**Limited number of clinical outcomes considered and importance of clinical choice** The EAG acknowledges in the report that the NMA does not capture all relevant clinical outcomes, as it is restricted to only two endpoints (target lesion revascularisation [TLR] and target vessel-related myocardial infarction [TVMI]). Similarly, the economic model, in addition to mortality, considers only these outcomes. We understand the constraints that led to the analyses focusing on a limited range of outcomes. However, the exclusion of important outcomes such as MACE, bleeding and others listed in the NICE scope further increases the high degree of uncertainty as to whether the analyses are a reliable basis for decision-making. It is important to recognise that a wide range of outcomes need to be considered when choosing a stent, as recognised by NICE in the appraisal scope. Making decisions on access to technologies based on a narrow range of outcomes is not only uncertain but risks limiting clinical choice, i.e. the clinician's ability to choose their preferred stent for the individual patient case. Restricting clinical choice is potentially detrimental to patients. Given the high degree of uncertainty around the NMA and modelling, we believe that clinicians should continue to be able to exercise choice in their selection of stents.	Thank you for this comment. There were insufficient data to incorporate additional endpoints into the analysis. The EAG has stated this as a limitation and encourages discussion of this at committee.
7.	Boston Scientific	66	5.2.4	**Reliability of NMA results based on limiting endpoints**	Thank you for this comment. The EAG has stated this as a limitation and encourages discussion of this at committee.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				The EAG's NMA was restricted to only two endpoints: target lesion revascularisation (TLR) and target vessel-related myocardial infarction (TVMI), omitting the majority of endpoints listed in the scope. There are a number of statements regarding the comparisons with Firehawk and Supraflex stents such as "Compared to BioMatrix, there is clear evidence that Firehawk and Supraflex have a lower TLR rate" and "There is weak evidence that Firehawk and Supraflex may reduce TLR rate, compared to Xience". We note that although the hazard ratio for TLR at one year for Firehawk compared with Xience is estimated in the NMA as 0.54 (95%CrI 0.20 to 1.11), based on the results of TARGET trial, the reported hazard ratio from TARGET (Lansky 2018) for target lesion failure (TLF, primary endpoint) is 1.04 (0.69–1.57,p=0.86), cardiac death 1.3 (0.49–3.5, p=0.60) and target vessel myocardial infarction1.15 (0.71–1.88, 0.58). Likewise although the estimated hazard ratio for TLR at one year for Supraflex compared with Xience is 0.70 (0.36 to 1.22) based on the results of the TALENT trial; the reported hazard ratio for the device-oriented composite (primary) endpoint of cardiac death, target-vessel myocardial infarction, or clinically indicated target lesion revascularisation was 0.94 (0.59–1.5, p=0.801).	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Given the limitations of the NMA, acknowledged in the report ("This leads to serious implications on the precision and robustness in NMA, which is then translated in the economic findings. In addition, the EAG recognises that the NMA does not capture all relevant clinical outcomes") and the results of the two RCTs comparing these stents (Firehawk and Supraflex) to Xience, we suggest any statements of superiority for these stents should be viewed with caution. **References**: Lanksy A et al. Targeted therapy with a localised abluminal groove, low-dose sirolimus-eluting, biodegradable polymer coronary stent (TARGET All Comers): a multicentre, open-label, randomised non-inferiority trial. Lancet (London, England), 392(10153), 1117-1126.	
8.	Boston Scientific	39	5.1	**Exclusion of stents outside of the NMA** We understand that not all stents could be included in the NMA. However, we are concerned about the consequent absence of the Synergy Megatron from the entire report and ask that its clinical benefits should be discussed and given consideration, as published evidence is available, information was requested and provided in the RFI, and in line comment number 3, this evidence is relevant to the decision problem. Synergy Megatron is purpose built for large proximal vessels, including left main, bifurcations and ostial lesions. It uses a 12-peak stent scaffolding design to	The EAG have acknowledged there are non-RCT types of evidence available for devices. The study by De Silva et al. (2023) is listed in Appendix H. The study by Stoler et al. (2023) is reported in a conference abstract and has been excluded in line with criteria outlined in the report. The study by Mailey et al. (2021) had less than one year of follow-up and has also been excluded in line with criteria outlined in the report. The EAG have added a statement to the executive summary regarding subgroups.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				minimise tissue prolapse, which when coupled with its overexpansion range and limit provides a unique solution for large proximal vessels. Its benefit has been demonstrated in several registries and trials.[1,2,3] We believe it is important that clinicians retain access to this specialist stent as an option for use in large proximal vessels, and are concerned that the omission of any evidence of its efficacy could lead to recommendations being made counter to this. **References: (1)** Stoler, R, Wood, F, Hawa, Z. et al. CRT-100.52 Primary Clinical Outcomes of the Bioabsorbable Polymer-Coated, Everolimus-Eluting Synergy Megatron Stent in the Treatment of Large Coronary Vessels. J Am Coll Cardiol Intv. 2023 Feb, 16 (4_Supplement) S24–S25. https://doi.org/10.1016/j.jcin.2023.01.095. **(2)** De Silva K, Li Kam Wa ME, Wells T, et al. The everolimus eluting Synergy Megatron™ drug-eluting stent platform: Early outcomes from the European Synergy Megatron™ Implanters' Registry. *Catheter Cardiovasc Interv*. 2023;102(7):1222-1228. doi:10.1002/ccd.30902. **(3)** Mailey JA, Ahmed M, Hogg M, et al. Initial Experiences of Percutaneous Coronary Intervention Using a New-Generation Everolimus-Eluting Stent Platform. J Invasive Cardiol. 2021;33(10):E784-E790. doi:10.25270/jic/20.00663.	
9.	Boston Scientific	N/A	N/A	**Variability in PCI technique between trials in the network** It is important to note that patients and procedures are not the same today as they were a decade ago. PCI outcomes are not only associated with the performance of the stent, but a range of other	Thank you for this comment. The EAG encourages discussion of this at committee.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				variables in the patient and during the procedure. The PCI trial ecosystem is highly complex which creates severe limitations when attempting to compare stents indirectly using trials from over 10 years ago and more recent trials. For example, variation in imaging and debulking techniques will influence the outcomes of the trials. For example, the journal article “Evolution of drug-eluting coronary stents: a back-and-forth journey from the bench to bedside” discusses how techniques have evolved. It suggests that contemporary studies should, besides the conventional target vessel-related endpoints, evaluate the role of optimal stent deployment as an endpoint using currently available state-of-the-art imaging technologies. https://doi.org/10.1093/cvr/cvac105 This limitation is currently not called out clearly enough in the report, and we request it be given consideration in the review of how comparable all the selected studies are in order to prevent potential oversimplification of a downstream recommendation.	
10.	BIOTRONIK	19	2	The strut thickness for Orsiro Mission should have an upper thickmess measurement of 80 µm. i.e. the information in the column should read 60-80 µm	Thank you for this comment. The EAG has updated the report to reflect this change.
11.	BIOTRONIK	41	5.1.1	Clinical results addition to Iglesius, et al (2023): This study previously demonstrated the superiority of the Orsiro BP-DES over the Xience Prime/Xpedition DP-DES for the primary endpoint at 1 year. The study also demonstrated a significantly lower rates of TLF (driven by lower risk of TLR) in the Orsiro group	The EAG has added this information.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				compared to the Xience Prime/Xpedition group at a follow-up duration of five years.	
12.	BIOTRONIK	42	5.1.1	Clinical results for Nakumura et al. (2022) should read one year (6.0% versus 5.7%, p=0.843, p for non-inferiority = 0.040).	The EAG has added this information.
13.	BIOTRONIK	51	5.1.2	The author of the BIOSCIENCE trial in table 6 should read Franzone et al. 2019	The EAG identified and extracted results from the following publication: Iglesias, J. F., Heg, D., Roffi, M., Tüller, D., Lanz, J., Rigamonti, F., Muller, O., Moarof, I., Cook, S., Weilenmann, D., Kaiser, C., Cuculi, F., Valgimigli, M., Jüni, P., Windecker, S., & Pilgrim, T. (2019a). Five-Year Outcomes in Patients With Diabetes Mellitus Treated With Biodegradable Polymer Sirolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents. *Journal of the American Heart Association*, *8*(22), e013607. https://doi.org/10.1161/JAHA.119.013607 The EAG have designated this reference as Iglesias 2019**a** to differentiate from Iglesias 2019**b** in the reference list which was a publication that reported on one year outcomes of the BIOSTEMI trial. It is unclear which publication the stakeholder is referring to in this comment. The EAG did identify a publication by Franzone et al., from **2015**, which was excluded due to longer term follow-up being reported by Iglesias et al. (2019a).
14.	BIOTRONIK	52	5.2.1	There are minor typs in this section, it should read "or they focussed solely on 'high-risk' populations	Thank you for this comment. The EAG has updated the report to reflect this change.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				(BIOFLOW-DAPT, BIOSTEMI, IDEAL-LM and ONYX ONE).”	
15.	Abbott Medical	12	Executive summary	The report says, “The NMA at the first year demonstrated some evidence that Promus Elite may have meaningful effect in reducing TVMI rate at 1 year compared to Xience [hazard ratio (HR) 0.59, 95% credible interval (CrI) 0.31 to 1.03].”. We do not believe this statement is correct as the 95% CrI crosses 1 and this implies there is no statistically significant difference. The document goes on to mentioned the unreliability of this data but this statement is misleading and we suggest it is removed to avoid incorrect assumptions being drawn.	The EAG undertook a Bayesian approach, where a posterior distribution of the relative treatment effect was estimated based on observed data and prior distributions specified in the report. The Bayesian approach does not assume null and alternative hypotheses, and is not intended to be used to decide whether to accept or reject a hypothesis based on the statistical significance level (which in any case is arbitrary). It is therefore not appropriate to interpret the EAG NMA results based on the significance level. The EAG have made changes in the executive summary to reflect the overall uncertainty with NMA (p14) and added the criteria used to determine the strength of the NMA evidence in the EAG report (p71).
16.	Abbott Medical	13	Executive summary	The report says, “The economic analyses (both deterministic and probabilistic) demonstrate that there is a lot of uncertainty surrounding the NMB findings, which outweigh the small NMB difference between devices”. We very much agree with this statement as we do not agree with the outcome of the NMB ranking and suggest the NMB ranking are not used to reflect which stent is truly the most cost-effective.	Thank you for this comment. The NMB approach was used because it was more intuitive than ICER when multiple devices are compared. NMB considers costs, effects and the WTP threshold, therefore reflecting the stent cost-effectiveness. No changes made.
17.	Abbott Medical	14	Executive summary	The report says, “however Promus Elite appeared to yield the highest NMB.”	The EAG performed base case analysis and a number of sensitivity analyses including probabilistic sensitivity analysis and scenario analysis. The EAG believe that the probabilistic

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				We believe this to be based on a non-statistically significant difference within the NMA and therefore disagree with this statement.	sensitivity analysis has sufficiently captured the uncertainty with treatment effect, where the 95%CrI of relative effect has been considered. All economic findings were reported and discussed in the report. No changes made.
18.	Abbott Medical	14	Executive summary	The report says, “The EAG believes the following issues should be considered by decision makers” We very much agree with the points made here.	Thank you for the comment. No changes made.
19.	Abbott Medical	15	Executive summary	The report says, “The NMA found that any evidence at 1 year was weak and had considerable uncertainty. However, there was some indication that Promus Elite may reduce TVMI rates at 1 year.” We agree with the first sentence above and therefore believe that the second sentence should not be stated. This second sentence being present in a summary risks non-statistically significant data being taken out of context and incorrect assumptions being drawn.	See EAG response to comment #15.
20.	Abbott Medical	15	Executive summary	The report says, “The robustness of the economic findings could not be established, given the uncertainty with respect to treatment effect. This has therefore prevented firm conclusions on cost-effectiveness being drawn. From the base case economic analysis, there were small NMB differences between devices. Promus Elite appeared to yield the highest NMB across devices, by a small amount.” We agree with the first two sentences above and therefore believe that the last sentence should not be stated. This final sentence being present in a summary risks non-statistically significant data being	See EAG response to comment #15.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				taken out of context and incorrect assumptions being drawn.	
21.	Abbott Medical	25	3. Clinical context	The report says, “A decision was made in conjunction with NICE to not pursue using NICOR registry data for the purposes of this LSA, due the aforementioned limitations.” We agree with this decision due to the aforementioned limitations.	Thank you for the comment. No changes made.
22.	Abbott Medical	39	5. Key clinical evidence results	The report says, “The EAG notes the majority of the 22 RCTs were designed as non-inferiority studies and are therefore only powered to demonstrate that the intervention device is ‘not worse’ than the comparator, and are not designed to detect superiority.” Due to this we do not believe it is possible to make claims such as “Promus Elite may have meaningful effect in reducing TVMI rate at 1 year compared to Xience”. Non-inferiority studies should not be used to claim superiority.	The absolute number of events and sample size were used in an NMA to generate the posterior distribution for each pairwise comparison in the network. Despite study design being important, and the different statistical tests used for non-inferiority and superiority studies, it is not appropriate to ignore any quantitative findings based on statistical significance level. Therefore, the decision was made to include all available data that meet the predefined inclusion criteria in the NMA. The EAG have added this limitation (p81).
23.	Abbott Medical	41	5. Key clinical evidence results	The study by Iglesias et al. (2023) (BIOSTEMI) should be reviewed and considered with caution because: - Outcomes at 5 years show Xience has significantly lower all-cause mortality than Orsiro - Outcomes at 5 years show Xience has significantly lower binary restenosis and TLR in complex patients. Outcomes at 5 years were only available for 85% of participants and this suggests a poor study design	The EAG has reviewed this study and is unable to identify the results reported in this comment. No changes made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
24.	Abbott Medical	41	5. Key clinical evidence results	The study by Kandzari et al. (2022) (BIOFLOW V) should be reviewed and considered with caution because it utilises Bayesian Analyses. Extra caution is warranted when interpreting the results and conclusions of studies that utilize Bayesian Analyses. FDA published guidance in 2020 highlighting the potentially erroneous conclusions resulting from Bayesian Statistics. FDA Guidance for Industry - 2020. FDA-2019-D-3679.	The EAG has reviewed the paper, and found no evidence that the authors performed a Bayesian analysis. No changes made.
25.	Abbott Medical	53	5. Key clinical evidence results	The report says, “The 14 RCTs included in the network meta-analysis were all designed to assess the non-inferiority of one DES against another DES.” Due to this we do not believe it is possible to make claims such as “Promus Elite may have meaningful effect in reducing TVMI rate at 1 year compared to Xience”. Non-inferiority studies should not be used to claim superiority.	See EAG response to comment #22.
26.	Abbott Medical	61	5. Key clinical evidence results	In table 9, we believe Q12 for BIOFLOW V should be a NO, not a yes. The study by Kandzari et al. (2022) (BIOFLOW V) should be reviewed and considered with caution because it utilises Bayesian Analyses. Extra caution is warranted when interpreting the results and conclusions of studies that utilize Bayesian Analyses. FDA published guidance in 2020 highlighting the potentially erroneous conclusions resulting from Bayesian Statistics.	See EAG response to comment #24. No changes made.

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				FDA Guidance for Industry - 2020. FDA-2019-D-3679.	
27.	Abbott Medical	64	5. Key clinical evidence results	The PLATINUM trial is the only existing RCT comparing Promus Elite and Promus (Xience V platform), whereas Xience has been studies in more than 150 trials worldwide. PLATINUM was powered for non-inferiority of the composite endpoint TLF, where TVMI is only one component of TLF, obviously underpowered to show either non-inferiority or superiority. Underpowered sub-analysis of secondary endpoints cannot generate meaningful comparisons in a NMA. The PLATINUM trial was designed to meet regulatory requirements for FDA approval, and as such excluded high-risk patients including ACS, CTOs, bifurcations, Left Main etc. The results therefore are not applicable to a wider population. At 5 years follow-up, TVMI was in-fact numerically lower for Promus (Xience V), probably confirming the play of chance. The 5-year results are published in JACC VOL. 10. NO. 23, 2017 See figure 2 Major Secondary Endpoints at 5 Years in the Main PLATINUM Trial: Five-year time-to-event curves for (A) target vessel (TV)-related cardiac death, (B) target vessel-related myocardial infarction (TV-MI), (C) ischemia-driven target lesion revascularization (ID-TLR), and (D) definite or probable stent thrombosis (ST).	The EAG recognise the limitation of underpowered outcomes and the impact on statistical power. However, excluding underpowered outcome data whether they are statistically significance or not, would ignore potentially useful results. The EAG have added this limitation (p81). It is common that studies are only powered for the primary outcome, which in the case of most studies included in the NMA, was a composite outcome. However, it is not possible to obtain a single utility value and cost value for the composite outcome, which consists of a number of different individual outcomes with varying proportion. This needs to be split into individual outcomes to fit into the economic model, in order to attach different costs and utilities to each individual outcome. Hence the EAG decision to use individual outcome in the EAG economic model, given the complex nature of this multi-technology assessment. In this assessment, the limited evidence base led to the EAG decision to use the best available data to evaluate both clinical and cost-effectiveness of the devices. However, the EAG acknowledge the economic findings are influenced by underpowered studies. This limitation is now added to the report (p133).

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				 Other than PLATINUM, EVOLVE II is the only other trial included that looks at a Promus stent. EVOLVE II was designed to support regulatory approval of Synergy in the United States. The aim was to show non-inferiority for TLF to Promus Element and did not study an all-comers population. Specific complex patient and target lesion subsets were excluded from the study. EVOLVE II is not powered to evaluate the individual components of TLF such as TVMI. Underpowered sub-analysis of secondary endpoints cannot generate meaningful comparisons to other stents and not applicable to a wider population. Due to the above reasons, we disagree with the consist messaging throughout the documents regarding “some evidence that Promus Elite may	The EAG would encourage the discussion of this at the committee.

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				have meaningful effect in reducing TVMI rate at 1 year compared to Xience". We believe that this evidence should be reconsidered, and the implications of 'chance' be re-assessed.	
28.	Abbott Medical	66	5. Key clinical evidence results	The report says, "Given that Xience is used as the comparator in the economic analysis, the relative treatment effect of each device compared to Xience is primarily discussed in this section." We believe there should be some information to explain why Xience is the comparator and emphasise the vast amount of data for Xience in comparison to all other stents on the market.	Not factual inaccuracy. No changes made.
29.	Abbott Medical	66	5. Key clinical evidence results	The report says, "At 1 year, results from the NMA suggest there is some evidence that Promus Elite has meaningful beneficial effect on TVMI rate when compared to Xience (HR 0.59, 95%CrI 0.31 to 1.03)." We do not believe this statement is correct as the 95% CrI crosses 1 and this implies there is no statistical difference. As the data is not statistically significant, we do not think conclusions should be drawn and therefore this statement should not be made.	See EAG response to comment #15.
30.	Abbott Medical	66	5. Key clinical evidence results	The report says, "There is weak evidence that Firehawk and Supraflex may reduce TLR rate, compared to Xience – Firehawk: HR 0.54 (95%CrI 0.20 to 1.11), Supraflex: HR 0.70 (95%CrI 0.36 to 1.22). For TVMI, there is some weak evidence that Synergy and Orsiro may lower TVMI rate compared to Xience – Synergy: HR 0.68 (95%CrI 0.37 to 1.14), Orsiro: HR 0.84 (95%CrI 0.62 to 1.10). The 95%CrIs	See EAG response to comment #15.

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				are wide and therefore the direction of effect is uncertain." We very much agree with the final sentence and believe that this data should not be classed as relevant / these conclusions not drawn due to the wide 95% CrIs. If the data is not statistically significant, we do not think conclusions should be drawn and included in the report.	
31.	Abbott Medical	70	5. Key clinical evidence results	The report says, "In the long-term follow-up, the NMA results suggest there is no evidence for meaningful differences in TLR and TVMI rate between devices (Table 12). There is weak evidence suggesting that Resolute Onyx and Promus Element have an effect on TLR compare to Xience – Promus Element: HR 0.80 (95%CrI 0.48 to 1.25), Resolute Onyx: HR 0.72 (95%CrI 0.40 to 1.20), whereas Supraflex may result in lower TVMI (HR 0.46, 95%CrI 0.13 to 1.11). Forest plots are shown in Figure 6." We agree with the first sentence and therefore do not think that the rest of the statement should be made. If the data is not statistically significant, we do not think conclusions should be drawn and included in the report.	See EAG response to comment #15.
32.	Abbott Medical	75	5. Key clinical evidence results	The report says, "This is evident in the EAG NMA where data were sparse coming from 14 studies and the only available data source for most devices in the NMA was a single study." We believe that the wealth of evidence on some stents and lack of evidence of on others has not been addressed. In our opinion we do not think it is right	The relevant limitation on data sparsity was acknowledged and discussed in the EAG report. The EAG encourage the discussion on this limitation at the committee meeting. No changes made.

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				that clinical conclusions have been drawn between two stents when one stent has masses of data and the other only has one study showing a non-statistically significant result.	
33.	Abbott Medical	75	5. Key clinical evidence results	The report says, “Given the caveats and uncertainties associated with meta analyses of sparse data, the EAG would advise that the NMA results should be interpreted with great caution.” We agree with this statement, and it needs to be very clear in any summaries / conclusions drawn.	Thank you for the comment. No changes made.
34.	Abbott Medical	93	9. Economic modelling methods	The report says, “To minimise double-counting, ST and in-stent restenosis (ISR) were not modelled explicitly in the EAG model.” We believe that a subgroup analysis on ST would have been very valuable to be included in the model.	The EAG recognise that ST is a clinically-important outcome, however given the nature of trial reporting, it is impossible to separate ST-related MI from TVMI trial data. This limitation was acknowledged in the EAG report. No changes made.
35.	Abbott Medical	94	9. Economic modelling methods	The report says, “This is because of the short time horizon used in the analysis, and the lack of information on the time needed to recuperate from the event to enable utility to be adjusted in the model. Therefore, the total QALYs might be underestimated.” Underestimating the QALY has an impact on the outcome and results of the economic analysis. We would recommend that a sensitivity analysis should be performed to assess the impact of this underestimation.	The EAG believe the uncertainty of the relative effect between devices outweighs the impact of QALY underestimation. As the evidence on recovery time is lacking, more assumptions would be needed, thus introducing more uncertainty into the model. No changes made.
36.	Abbott Medical	96	9. Economic	The report says, “The baseline TLR and TVMI probabilities are taken from Xience arm of 5-year	See EAG response to comment #24. No changes made.

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			modelling methods	RCTs in the EAG NMA (BIOFLOW IV, BIOFLOW V, BIOSCIENCE, CENTURY II, PLATINUM)." The study by Kandzari et al. (2022) (BIOFLOW V) should be reviewed and considered with caution because it utilises Bayesian Analyses. Extra caution is warranted when interpreting the results and conclusions of studies that utilize Bayesian Analyses. FDA published guidance in 2020 highlighting the potentially erroneous conclusions resulting from Bayesian Statistics. FDA Guidance for Industry - 2020. FDA-2019-D-3679.	
37.	Abbott Medical	98	9. Economic modelling methods	The report says, "All stent costs have been provided by NHS Supply Chain, and are calculated as a weighted average of the purchase costs for all stents purchased through NHS Supply chain in 2023" [redacted]	See EAG response to comment #1.

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				[redacted]	

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				[redacted]	
38.	Abbott Medical	100	9. Economic modelling methods	In Table 22 there is reference to cost of revascularisation but there is no reference to where those costs are from. We recommend these references are added.	This is subject to NICE discretion. No changes made.
39.	Abbott Medical	102	9. Economic modelling methods	In table 23, we believe there should be utility costs for the treatment of stent thrombosis as this can be very expensive.	See EAG response to comment #34.
40.	Abbott Medical	105	10. Economic modelling results	The report says, “Although Promus Elite is found to yield the highest NMB of XXXX at the WTP threshold, there is a modest NMB difference of XX between Promus Elite and Firehawk. Promus Elite accrues the lowest costs (XXXX) and the highest QALYs (XXXX) at 1-year follow-up (Table 24). This might be driven by Promus Elite effect on TVMI reduction.”. The final sentence suggests that the use of non-statistically significant data has led to this stent yielding the highest NMB. As this TVMI reduction is based on a 95% CrI that crosses 1, we do not believe that this should lead to this stent having the highest NMB. Only statistically significant data should be considered when calculating the NMB.	Thank you for the comment. No changes made.

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41.	Abbott Medical	106	10. Economic modelling results	The report says, “Results from the PSA show that Promus Elite yields the highest NMB of mean XXXXX (95% CI XXXXX to XXXXX) (Table 25). When results are summarised graphically in Figure 8, it shows that 95%CI NMB for all devices are overlapping. This reflects the considerable uncertainty associated with the model inputs, which is likely due to the wide CrI in relative treatment effect of each device.” We very much agree with the final sentence and for this reason do not believe NMB can be accurately calculated or assigned to different stents.	Thank you for the comment. No changes made.
42.	Abbott Medical	106	10. Economic modelling results	The report says, “Promus Elite is associated with a XXX chance of having the highest NMB, despite generating the highest NMB in base case analysis. Apart from the variation in treatment effects, this might be driven by the stent price range used in the PSA where an arbitrary ±20% was used for Firehawk and the NHS Supply Chain maximum and minimum price for Promus Elite.” [redacted]	See EAG response to comment #1.

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				[redacted]	

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				[redacted]	
43.	Abbott Medical	111	10. Economic modelling results	The report says, “In all scenarios, there are small NMB differences across all devices, ranging between XX to XXX in 1-year time horizon and between XXXXXXXXX in 5-year time horizon. However, it is noted that Promus Elite results in the highest NMB, except in the scenario using the maximum stent price.” We want to reiterate that this is based on non-statistically significant data and therefore the conclusion should not be drawn.	Not factual inaccuracy. No changes made.
44.	Abbott Medical	121	10. Economic modelling results	[redacted]	See EAG response to comment #1.

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				[redacted]	

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				[redacted]	
45.	Abbott Medical	124	11. Combined summary and interpretation of the clinical and economic evidence	The report says, “Non-inferiority with respect to clinically meaningful endpoints was demonstrated for the following devices against the Xience device: Orsiro Mission (demonstrated in four RCTs), Promus Elite (demonstrated in one RCT), Supraflex Cruz/Supraflex Cruz Nevo (demonstrated in one RCT), Firehawk (demonstrated in one RCT) and Ultimaster (demonstrated in one RCT).” This statement emphasises our earlier concern that the two stents showing with the highest NMB only have 1 RCT included each, whilst other stents have a much larger evidence base.	The EAG agree that combining data from several studies can improve precision of the pooled estimates. Factors such as sample size and variance are also taken into account, which can influence the magnitude and direction of the pooled effect size. However, the main challenge with the NMA is the issue of data sparsity with very few studies, leading to unreliable estimate for treatment effect and between-studies heterogeneity. The EAG acknowledged and discussed this limitation throughout the report.
46.	Abbott Medical	125	11. Combined summary and interpretation of the clinical and economi	The report says, “At 1-year, NMA results suggest there is some evidence that Promus Elite may have beneficial effect on reducing TVMI when compared to Xience (HR 0.59, 95%CrI 0.31 to 1.03).” We do not believe this statement is correct as the 95% CrI crosses 1 and this implies there is no statistically significant difference.	Not factual inaccuracy. No changes made.

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			c evidence		
47.	Abbott Medical	126	11. Combined summary and interpretation of the clinical and economic evidence	The report says, “The economic evidence from both deterministic and probabilistic analyses suggest that there is substantial uncertainty with the NMB results, which outweighs the small NMB differences between devices.” We very much agree that the uncertainty with the NMB results outweighs the small NMB differences between devices and therefore suggest these NMB outputs are not considered as truth.	Not factual inaccuracy. No changes made.
48.	Abbott Medical	126	11. Combined summary and interpretation of the clinical and economic evidence	The report says, “In the 1-year base case analysis, there was a modest NMB difference between Promus Elite and Firehawk, though Promus Elite appeared to yield the highest NMB. When the impact of parameter uncertainty was examined, the PSA results showed that 95%CI of NMB for all devices were overlapping and CEAC suggested that Firehawk and Promus Elite had the highest probability of achieving the greatest NMB. This indicates the high degree of parameter uncertainty driven by the wide treatment effect CrI.” We very much agree with this point and therefore suggest these NMB outputs are not considered as truth.	Not factual inaccuracy. No changes made.
49.	Abbott Medical	129	11. Combine	The report says, “In addition, the EAG recognises that the NMA does not capture all relevant clinical	See EAG response to comment #34.

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			d summary and interpretation of the clinical and economic evidence	outcomes, a limitation which is shared by the subsequent economic analysis. Events such as stent thrombosis are associated with high morbidity and mortality, thus costs are underestimated and utilities are overestimated when this is not available for consideration in the economic analysis." We very much agree with this statement and feel that inclusion of events such as stent thrombosis would improve the outcome and detail of the assessment.	
50.	Abbott Medical	129	11. Combined summary and interpretation of the clinical and economic evidence	The report says, "Additionally, a key limitation is the lack of subgroup analyses, which was precluded by a lack of published data available to populate these into the economic analysis." We very much agree with this and believe that there should be reference made to the fact that only some stents have evidence in specific subgroups and some stents have no evidence in these subgroups. Some stents have evidence in these different subgroups and a lack of evidence from other stents should not lead to assumed equivalence in these subgroups. We believe this should specifically be called out in the report and be valorised for the fact that companies invest in evidence generation.	The EAG has stated this as a limitation and encourages discussion at committee. No changes required.
51.	TERUMO	25	4.1.1 Real-world evidence and registry data	"*A decision was made in conjunction with NICE to not pursue using NICOR registry data for the purposes of this LSA, due the aforementioned limitations*." Having in mind the limitations presented by the EAG around the NICOR registry data, Terumo Europe proposes to consider the e-Ultimaster registry which was subject to	The EAG has prioritised the evidence it believes to be most relevant to the decision problem, in line with NICE LSA interim methods and processes. Limitations of using registry data are outlined in the report. The EAG encourage discussion of the limitations of the analysis at committee.

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				multiple peer reviewed publications (list below). To date, it is the largest international registry available with more than 35,000 patients included. It is noteworthy that 5,701 patients in this registry were from the UK, and they represented 15.3% of the total cohort which makes the UK the largest contributor in terms of patient number included in this registry. Having in mind the limited high quality UK specific data, Terumo Europe believes that the e-Ultimaster registry is very relevant for the EAR and should be considered a in the assessment. ***e-ULTIMASTER publications (to date)*** 1. Kobo, O. *et al.* Impact of the number of modifiable risk factors on clinical outcomes after percutaneous coronary intervention: An analysis from the e-Ultimaster registry. *IJC Heart & Vasculature* 101370 (2024) doi:10.1016/j.ijcha.2024.101370. 2. Mamas, M. A. *et al.* Predicting target lesion failure following percutaneous coronary intervention through machine learning risk assessment models. *European Heart Journal - Digital Health* ztad051 (2023) doi:10.1093/ehjdh/ztad051. 3. Levi, Y. *et al.* Treatment of Ostial Right Coronary Artery Narrowing: Outcomes From the Multicenter Prospective e-ULTIMASTER Registry. *Journal of the Society for Cardiovascular Angiography & Interventions* 100604 (2023) doi:10.1016/j.jscai.2023.100604. 4. Gautier, A. *et al.* Complementary evidence on the performance of coronary stents generated by a randomized controlled trial and a worldwide registry. *American Heart Journal* S0002870323000613 (2023) doi:10.1016/j.ahj.2023.02.016.	

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				5. Doolub, G. *et al.* Sex-based treatment and outcomes for coronary bifurcation stenting: A report from the e-ULTIMASTER registry. *Cathet Cardio Intervent* ccd.30770 (2023) doi:10.1002/ccd.30770. 6. Saada, M. *et al.* Prognosis of PCI in AMI setting in the elderly population: Outcomes from the multicenter prospective e-ULTIMASTER registry. *Clinical Cardiology* clc.23902 (2022) doi:10.1002/clc.23902. 7. Saada, M. *et al.* Prognosis of PCI in the Older Adult Population: Outcomes From the Multicenter Prospective e-ULTIMASTER Registry. *Journal of the Society for Cardiovascular Angiography & Interventions* **1**, 100442 (2022). 8. Mohamed, M. O. *et al.* Clinical Outcomes of Percutaneous Coronary Intervention for Bifurcation Lesions According to Medina Classification. *JAHA* **11**, e025459 (2022). 9. Kobo, O. *et al.* Impact of multisite artery disease on clinical outcomes after percutaneous coronary intervention: an analysis from the e-Ultimaster registry. *European Heart Journal - Quality of Care and Clinical Outcomes* qcac043 (2022) doi:10.1093/ehjqcco/qcac043. 10. Kobo, O. *et al.* Impact of peripheral artery disease on prognosis after percutaneous coronary intervention: Outcomes from the multicenter prospective e-ULTIMASTER registry. *Atherosclerosis* **344**, 71–77 (2022). 11. Doolub, G. *et al.* Impact of Sex on Clinical Outcomes in Patients undergoing Complex Percutaneous Coronary Angioplasty (from the e-ULTIMASTER Study). *The American Journal of Cardiology* **186**, 71–79 (2022). 12. Cimci, M. *et al.* Outcomes and regional differences in practice in a worldwide coronary stent registry. *Heart* **108**, 1310–1318 (2022). 13. Williams, T. *et al.* Complete revascularization optimizes patient outcomes in multivessel coronary artery	

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				disease: Data from the e-Ultimaster registry. *Cathet Cardio Intervent* **99**, 961–967 (2021). 14. Vlieger, S. *et al.* One-year performance of thin-strut cobalt chromium sirolimus-eluting stent versus thicker strut stainless steel biolimus-eluting coronary stent: a propensity-matched analysis of two international all-comers registries. *Coronary Artery Disease* **32**, 391–396 (2021). 15. Chevalier, B. *et al.* Clinical outcomes of the proximal optimisation technique (POT) in bifurcation stenting. *EuroIntervention* **17**, e910–e918 (2021). 16. Scholz, S. S. *et al.* One-year clinical outcomes in patients with renal insufficiency after contemporary PCI: data from a multicenter registry. *Clin Res Cardiol* **109**, 845–856 (2020). 17. Mohamed, M. O. *et al.* Impact of coronary lesion complexity in percutaneous coronary intervention: one-year outcomes from the large, multicentre e-Ultimaster registry. *EuroIntervention* **16**, 603–612 (2020). Codner, P. *et al.* Proximal Left Anterior Descending Artery Treatment Using a Bioresorbable Polymer Coating Sirolimus-Eluting Stent: Real-World Outcomes From the Multicenter Prospective e-Ultimaster Registry. *JAHA* **8**, e013786 (2019).	
52.	TERUMO	31	4.1.1 Assessment of clinical equivalence	In “Table 3: Summary of device generations and clinical equivalence”, Ultimaster Nagomi™ stent launch is mentioned as being in 2018 and that of Ultimaster Tansei™ in 2023. This information should be corrected as follows: Ultimaster Tansei™ was launched in 2018 (CE mark 13 april 2018) and Ultimaster Nagomi™ is the latest iteration of the sirolimus eluting coronary stents and was launched in 2023 (CE mark 28 June 2023).	Thank you for this comment. The EAG have amended the launch dates for Ultimaster Tansei and Nagomi respectively. Ultimaster Tansei and Ultimaster Nagomi are both represented by evidence for Ultimaster in the NMA, which is in line with the stakeholder’s comment relating to clinical equivalence.

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				Separately, a letter received by Terumo from the Notified Body, DNV MEDCERT, dated December 2nd, 2022 confirmed the equivalence of both devices from clinical, biological and technical perspective, per Appendix XIV (A(3)) of the EU Regulation 2017/747 on medical device. Ultimaster Nagomi™ is the 3rd generation of the Ultimaster sirolimus eluting coronary stent. The main differences compared to the previous generation consists in the optimization of the stent design of small and large stents, including an optimization of the delivery system to further enhance the deliverability to the lesion and meet the physicians' need to treat more complex lesions in daily practice: - Small nominal stent diameter items have improved flexibility for better deliverability and vessel conformability. - Large nominal stent diameter items have increased overexpansion capabilities for better vessel conformability and to minimize the risk of stent strut malposition. The size range is expanded to the availability of longer stents (44mm and 50mm) to reduce the need for using multiple – potentially overlapping – stents in the treatment of long lesions. Smaller and larger stent nominal diameters are available to allow better alignment with the vessel size and vessel geometry. The delivery balloon has a higher nominal pressure and a higher rated burst pressure to improve stent apposition.	
53.	TERUMO	64	5.2.4 NMA results	"Table 10: TLR and TVMI events in RCTs included in NMA".	Data at 1-year and the study final follow-up were used in the respective NMA. The different length of follow-up time in each trial was accounted for in the EAG NMA using Poisson rate model with

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				The table show the results of the CENTURY II studies comparing Ultimaster™ sirolimus eluting coronary stent versus Xience with regards to the TLR and TVMI events at final follow up. However, this table is comparing the results at different points in time i.e. 1 year and 5 year follow-up. The consideration of the different timepoints would impact the rates of TLR and TVMI. The results imply a higher likelihood of TVMI adverse events with Ultimaster™, which is in contradiction with the Wijns et al. (2018) publication which reported TVMI rates of 1.3% for Ultimaster™ and 2.2% for Xience at one year, and 1.8% vs. 2.4% at five years. Also, having in mind the wide confidence intervals which indicate high level of variability and uncertainty, we are surprised with the interpretation made with such poor methodological result leading us to question the statistical value of such data. We would request to have more details about the methodologies that were used in the NMA in order to mitigate this major follow-up timeframe difference in the analysis and have a high quality and methodologically sound comparison approach. We would like to highlight also that the CENTURY II trial resulted in multiple peer reviewed publications: ***CENTURY II publications*** 1. Iñiguez, A. et al. Comparison of long-term clinical outcomes in multivessel coronary artery disease patients treated either with bioresorbable polymer sirolimus-eluting stent or permanent polymer everolimus-eluting stent: 5-year results of the CENTURY II randomized clinical trial. Catheter Cardiovasc Interv 95, 175–184 (2020).	cloglog link, when estimating Y1 and long-term HR. This is in line with the recommendation outlined in NICE DSU TSD 2. The EAG have now added outcome data at 1-year to Table 10.

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				2. Wijns, W. et al. Long-term clinical outcomes after bioresorbable and permanent polymer drug-eluting stent implantation: final five-year results of the CENTURY II randomised clinical trial. EuroIntervention 14, e343–e351 (2018). 3. Wöhrle, J. et al. Bioresorbable polymer sirolimus-eluting coronary stent compared with permanent polymer everolimus-eluting coronary stent implantation for treatment of small vessel coronary artery disease: CENTURY II trial. EuroIntervention 12, e167–e174 (2016). 4. Orvin, K. et al. Comparison of sirolimus eluting stent with bioresorbable polymer to everolimus eluting stent with permanent polymer in bifurcation lesions: Results from CENTURY II trial: Sirolimus DES With Bioresorbable Polymer for Bifurcation. Cathet. Cardiovasc. Intervent. 87, 1092–1100 (2016). 5. Lesiak, M. et al. Long Coronary Lesions Treated With Thin Strut Bioresorbable Polymer Drug Eluting Stent: Experience From Multicentre Randomized CENTURY II Study. J Interven Cardiology 29, 47–56 (2016). 6. Jiménez, V. A. et al. A randomized comparison of novel bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent in patients with acute coronary syndromes: The CENTURY II high risk ACS substudy. Cardiovascular Revascularization Medicine 17, 355–361 (2016). 7. Kuramitsu, S. et al. Vascular response to bioresorbable polymer sirolimus-eluting stent vs. permanent polymer everolimus-eluting stent at 9-month follow-up: an optical coherence tomography sub-study from the CENTURY II trial. Eur Heart J Cardiovasc Imaging jev203 (2015) doi:10.1093/ehjci/jev203. 8. Saito, S. et al. A randomized, prospective, intercontinental evaluation of a bioresorbable polymer sirolimus-eluting coronary stent system: the CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting Coronary	

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				Stent System in the Treatment of Patients with Coronary Artery Disease) trial. European Heart Journal 35, 2021–2031 (2014).	
54.	TERUMO	70	5.2.4 NMA results Outcomes in the long-term follow up(>1 year)	The long term follow up seems to be calculating HR based on the longest follow-up timeframe observed in the study, excluding from the calculation events already taken into account during the first year of follow-up. This approach represents a biased one. We would request to have more details about the methodologies that were used in the NMA in order to mitigate the major follow-up timeframe difference in the analysis. This can only bring more transparency and build a methodologically sound comparison approach.	The EAG believe that sufficient details of the NMA approach have been included in the report. In addition, the different study period was considered in the HR calculation (see EAG response to comment #53). No changes made.
55.	TERUMO	71	5.2.4 NMA Results	“Table 12: Results from NMA RE models using long-term follow-up data” In addition to the comment #3 highlighted above, the relative treatment effect of Ultimaster™ sirolimus eluting coronary stent vs Xience is shown in Table 12 as an outlier with regards to the TLR and TVMI events. This is in contradiction with the conclusion of the EAR which states that "*the NMA results suggest there is no evidence for meaningful differences in TLR and TVMI rate between devices*". We would request to have more details about the methodologies that were used in the NMA in order to mitigate the major follow-up timeframe difference in the analysis on one hand and have a clarification of the relative treatment effect outlier figures calculated in Table 12 on the other hand. This can only bring more transparency and build a methodologically sound comparison approach.	See EAG response to comment #15 regarding the criteria used to determine the strength of the NMA evidence.

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56.	TERUMO	73	5.2.4 NMA Results	"Figure 6: Forest plots: Long-term follow-up (HR with 95% CrI)" Same feedback as in comments #3 and #4. The relative treatment effect of Ultimaster™ sirolimus eluting coronary stent vs Xience is shown Figure 6 as an outlier with regards to the TVMI events which is very surprising. This is in contradiction with the conclusion of the EAR which states that "*the NMA results suggest there is no evidence for meaningful differences in TLR and TVMI rate between devices*". We would request to have more details about the methodologies that were used in the NMA in order to mitigate the major follow-up timeframe difference in the analysis on one hand and have a clarification of the relative treatment effect outlier figures calculated in Table 12 and for the Forest plot (Figure 6) on the other hand. This can only bring more transparency and build a methodologically sound comparison approach.	Thank you for the comment. Data sparsity is the key issue with the NMA. Further, in the situation when the events are very rare (as reported in CENTURY II), the estimates generated are unreliable and unstable. This is because of the skew posterior distribution pushing the posterior mean (HR) to a higher number. The EAG have decided not to pursue in reporting posterior median which is less affected by the skewness, because the fundamental issue here is the data are too sparse to draw any firm conclusions whether it is a mean or median. The EAG have made changes to the report and added this limitation. The EAG encourage the discussion of the data sparsity issue at committee.
57.	TERUMO	77	6 A dditional clinical evidence	"…*the EAG identified a large volume of other types of evidence which related to the devices in scope, but were not considered to be key studies for this assessment*". "*Results were not extracted from the non-comparative studies, as this was not considered useful in answering the decision problem by the EAG and NICE. However, clinical experts indicated that the volume of clinical efficacy evidence available for specific stents, and whether there is evidence of clinical efficacy and safety in particular populations (e.g. high bleeding risk), could be useful context for decision-making".*	The EAG has prioritised the evidence it believes to be most relevant to the decision problem, in line with NICE LSA interim methods and processes. The EAG have added a statement to the executive summary with respect to subgroups. The EAG note that the MASTER DAPT study referenced below is included in the EAG report. The EAG encourage discussion of the limitations of the analysis at committee, where translation of any findings into advice for clinicians will be discussed.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				"*DAPT duration required post-procedure was of importance to clinicians involved in selecting and implanting drug-eluting stents*." We are very surprised that the EAR considered only RCT type of evidence, excluding other types of studies from peer reviewed publications. And this, in spite of the clinical experts' opinion on the importance of the availability of clinical efficacy and safety evidence especially in high bleeding risk (HBR) patient populations. Moreover, in this same HBR patient group, the DAPT duration required post-procedure is of critical importance as it is association with bleeding risk, which was highlighted by the clinical experts. Excluding from this assessment additional type of clinical studies, especially in special patient groups like HBR patients, and excluding the DAPT duration post-procedure as an important comparative outcome between the various stents may result in misleading treatment recommendations. Ultimately this would put the patients' life at risk. ***MASTER DAPT publications (to date)*** 1. Landi, A. *et al.* Consecutive or selectively included high bleeding risk patients in the MASTER DAPT screening log and trial. *European Journal of Internal Medicine* S0953620524001766 (2024) doi:10.1016/j.ejim.2024.04.016. 2. Landi, A. *et al.* Abbreviated or Standard Antiplatelet Therapy in HBR Patients. *JACC: Cardiovascular Interventions* **16**, 798–812 (2023). 3. Landi, A. *et al.* Abbreviated or Standard Dual Antiplatelet Therapy by Sex in Patients at High Bleeding	

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				Risk: A Prespecified Secondary Analysis of a Randomized Clinical Trial. *JAMA Cardiol* (2023) doi:10.1001/jamacardio.2023.4316. 4. Valgimigli, M. *et al.* Duration of antiplatelet therapy after complex percutaneous coronary intervention in patients at high bleeding risk: a MASTER DAPT trial sub-analysis. *European Heart Journal* **43**, 3100–3114 (2022). 5. Valgimigli, M. *et al.* Impact of Medication Nonadherence in a Clinical Trial of Dual Antiplatelet Therapy. *Journal of the American College of Cardiology* **80**, 766–778 (2022). 6. Smits, P. C. *et al.* Abbreviated Antiplatelet Therapy After Coronary Stenting in Patients With Myocardial Infarction at High Bleeding Risk. *Journal of the American College of Cardiology* **80**, 1220–1237 (2022). 7. Valgimigli, M. *et al.* Dual Antiplatelet Therapy after PCI in Patients at High Bleeding Risk. *N Engl J Med* **385**, 1643–1655 (2021). 8. Smits, P. C. *et al.* Abbreviated Antiplatelet Therapy in Patients at High Bleeding Risk With or Without Oral Anticoagulant Therapy After Coronary Stenting: An Open-Label, Randomized, Controlled Trial. *Circulation* **144**, 1196–1211 (2021). Frigoli, E. *et al.* Design and rationale of the Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen (MASTER DAPT) Study. *American Heart Journal* **209**, 97–105 (2019).	
58.	TERUMO	82	6.2 RCTs comparing DAPT regimens	Table 15: Summary of RCTs comparing DAPT regimens in trials using in-scope DES. One of the major outcomes and conclusions from the MASTER DAPT study (Valgimigli et al. 2021) and which is missing in this table, is that abbreviated DAPT is associated with significantly lower bleeding risk.	Thank you for this comment. The EAG have added this information.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				For the MASTER DAPT study (Valgimigli et al. 2021), we request to add in the column "Summary of differences observed between regimens" the following: • "Abbreviated DAPT non-inferior to standard DAPT with respect to NACE and MACCE • **Abbreviated DAPT is associated with significantly lower bleeding risk**".	
59.	TERUMO	100	9.4 Resource use and cost parameters	"*Follow-up costs post-PCI:* *Follow up costs after PCI include cardiac rehabilitation, one outpatient appointment and 12 months of DAPT therapy*" This assumption considers a 12 months DAPT therapy for all patients. This assumption does not reflect the difference between the patient groups and bleeding risk, nor does it consider the proportion of HBR patient who could benefit from a DAPT therapy duration as short as one month. A DAPT therapy of 12 months is not recommended clinically in HBR patient and puts at risk the patient's safety. Moreover this assumption creates a meaningful bias in the cost input. Ultimaster Tansei™ and Ultimaster Nagomi™ are the only DES that have **proven to have the shortest DAPT duration, 1-month, post-procedure, with no additional safety risk or adverse events reported.** As a consequence, the costs associated with DAPT treatment and the consequent bleeding are not taken into account in the hypothesis.	The EAG economic analysis did not include HBR subgroup analysis, given the lack of relevant data. In addition, the EAG acknowledged that some clinically-important outcomes were not captured in the NMA and economic model. The EAG encourage the discussion of this limitation at committee. No changes made.
60.	TERUMO	111	10.3 Scenario analysis results	"*It is noted that Ultimaster Tansei and Ultimaster Nagomi incur the highest costs but accumulate the least QALYs. This is because Ultimaster is found to increase TVMI by 7-fold compared to Xience (HR 7.30) in the long-term, however as previously discussed in Section 5.2.4, the*	See EAG response to comment #56.

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				NMA was not able to estimate long-term HR reliably due to data sparsity." This conclusion is based on a biased calculation and should be revised accordingly. As mentioned in the comment above, we would request to have more details about the methodologies that were used in the NMA in order to mitigate the major follow-up timeframe difference in the analysis on one hand and have a clarification of the relative treatment effect outlier figures calculated in Table 12 and for the Forest plot (Figure 6) on the other hand. This can only bring more transparency and build a methodologically sound comparison approach.	
61.	TERUMO	130	12 D iscussion	"*The EAG and NICE chose to focus on published evidence to inform this analysis, primarily from RCTs, as it was decided that real-world evidence in the form of registry data was subject to confounding that would be difficult to mitigate*." We are very surprised that the EAR considered only RCT type of evidence, excluding other types of studies like registries, subject to peer reviewed publications. And this, in spite of the clinical experts' opinion on the importance of the availability of clinical efficacy and safety evidence especially in high bleeding risk (HBR) patient populations. Given the aim of the LSA "*is not to compare 'types' of DES, but to attribute outcomes to individual devices*" then the assessment should consider, in addition to long term follow-up data available, the safety and efficacy of the devices in special populations at risk of high bleeding. As mentioned in the comments above, the DAPT duration required post-procedure is of critical importance as it is associated with bleeding risk, which was highlighted by the	The EAG has prioritised the evidence it believes to be most relevant to the decision problem, in line with NICE LSA interim methods and processes. The EAG acknowledge the volume of non-RCT evidence available, and have referred to this evidence at various points in the report and in the appendices. Reference to this evidence has now been added to the executive summary. The EAG encourage discussion of the limitations of the analysis at committee, where translation of any findings into advice for clinicians will be discussed.

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				clinical experts. Ultimately this would put the patients' life at risk. As presented in the many publications from the MASTER DAPT study (Valgimigli et al. 2021), not all drug eluting stents have similar impact on the DAPT duration post-procedure. Actually an abbreviated DAPT is associated with significantly lower bleeding risk. Ultimaster™ sirolimus eluting coronary stent is the **only stent which has proven to have the shortest DAPT duration, 1-month, post-procedure**.	
62.	TERUMO	158	14.Appendices Appendix A: Innovative features of included devices	Table 28 Innovative features of included devices Ultimaster Nagomi™ stent launch is mentioned as being in 2018 and that of Ultimaster Tansei™ in 2023. This information should be corrected as follows: **Ultimaster Tansei™ was launched in 2018 and Ultimaster Nagomi™ is the latest iteration of the sirolimus eluting coronary stents and was launched in 2023 (**CE mark 28 June 2023)**.** Separately, a letter received by Terumo from the Notified Body, DNV MEDCERT, dated December 2nd, 2022 confirmed the equivalence of both devices from clinical,, biological and technical perspective, per Appendix XIV (A(3)) of the EU Regulation 2017/747 on medical device. Moreover, the following additional features (in bold text) should be added for the "Three key innovative features were described that apply to both technologies: 1) Innovative PDLLA-PCL copolymer bioresorbable coating.	Thank you for this comment. The EAG have amended the launch dates for Ultimaster Tansei and Nagomi respectively. The EAG has added some further detail on innovative features of the technologies.

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				2) Open cell, 2-link platform 3) Additional sizes in the range of 2.00 mm to 4.5 mm and lengths from 9 to 50 mm. **4) platforms specifically designed to meet the needs of each vessel size** **5) Optimized overexpansion capability, up to 6.25 mm (for 3.5 mm to 4.5 mm diameter stents)** **6) The largest size line-up in the Ultimaster™ family with the new Ø 2.00 & Ø 4.50 mm and 44 & 50 mm lengths** **7) Inherited open-cell, 2-link design, for flexible stent platforms** **New hydrophilic coating for enhanced deliverability**"	
63.	TERUMO	214	14.Appendices Appendix H: Non-comparative studies	Table 33: Prospective studies (34 studies, reported across in 36 publications) The table reports only four prospective studies for **Ultimaster Tansei™ and Ultimaster Nagomi™, while there is much more evidence published to date:** ***e-ULTIMASTER publications (to date)*** 18. Kobo, O. *et al.* Impact of the number of modifiable risk factors on clinical outcomes after percutaneous coronary intervention: An analysis from the e-Ultimaster registry. *IJC Heart & Vasculature* 101370 (2024) doi:10.1016/j.ijcha.2024.101370. 19. Mamas, M. A. *et al.* Predicting target lesion failure following percutaneous coronary intervention through machine learning risk assessment models. *European Heart Journal - Digital Health* ztad051 (2023) doi:10.1093/ehjdh/ztad051. 20. Levi, Y. *et al.* Treatment of Ostial Right Coronary Artery Narrowing: Outcomes From the Multicenter Prospective e-ULTIMASTER Registry. *Journal of the Society for Cardiovascular Angiography & Interventions* 100604 (2023) doi:10.1016/j.jscai.2023.100604.	The EAG has prioritised the evidence it believes to be most relevant to the decision problem, in line with NICE LSA interim methods and processes. Criteria for inclusion in this assessment is outlined in Section 4.1.3 (Table 4). As a result, this assessment does not represent a systematic review of all relevant literature relating to devices.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				21. Gautier, A. *et al.* Complementary evidence on the performance of coronary stents generated by a randomized controlled trial and a worldwide registry. *American Heart Journal* S0002870323000613 (2023) doi:10.1016/j.ahj.2023.02.016. 22. Doolub, G. *et al.* Sex-based treatment and outcomes for coronary bifurcation stenting: A report from the e-ULTIMASTER registry. *Cathet Cardio Intervent* ccd.30770 (2023) doi:10.1002/ccd.30770. 23. Saada, M. *et al.* Prognosis of PCI in AMI setting in the elderly population: Outcomes from the multicenter prospective e-ULTIMASTER registry. *Clinical Cardiology* clc.23902 (2022) doi:10.1002/clc.23902. 24. Saada, M. *et al.* Prognosis of PCI in the Older Adult Population: Outcomes From the Multicenter Prospective e-ULTIMASTER Registry. *Journal of the Society for Cardiovascular Angiography & Interventions* **1**, 100442 (2022). 25. Mohamed, M. O. *et al.* Clinical Outcomes of Percutaneous Coronary Intervention for Bifurcation Lesions According to Medina Classification. *JAHA* **11**, e025459 (2022). 26. Kobo, O. *et al.* Impact of multisite artery disease on clinical outcomes after percutaneous coronary intervention: an analysis from the e-Ultimaster registry. *European Heart Journal - Quality of Care and Clinical Outcomes* qcac043 (2022) doi:10.1093/ehjqcco/qcac043. 27. Kobo, O. *et al.* Impact of peripheral artery disease on prognosis after percutaneous coronary intervention: Outcomes from the multicenter prospective e-ULTIMASTER registry. *Atherosclerosis* **344**, 71–77 (2022). 28. Doolub, G. *et al.* Impact of Sex on Clinical Outcomes in Patients undergoing Complex Percutaneous Coronary Angioplasty (from the e-ULTIMASTER Study). *The American Journal of Cardiology* **186**, 71–79 (2022).	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				29. Cimci, M. *et al.* Outcomes and regional differences in practice in a worldwide coronary stent registry. *Heart* **108**, 1310–1318 (2022). 30. Williams, T. *et al.* Complete revascularization optimizes patient outcomes in multivessel coronary artery disease: Data from the e-Ultimaster registry. *Cathet Cardio Intervent* **99**, 961–967 (2021). 31. Vlieger, S. *et al.* One-year performance of thin-strut cobalt chromium sirolimus-eluting stent versus thicker strut stainless steel biolimus-eluting coronary stent: a propensity-matched analysis of two international all-comers registries. *Coronary Artery Disease* **32**, 391–396 (2021). 32. Chevalier, B. *et al.* Clinical outcomes of the proximal optimisation technique (POT) in bifurcation stenting. *EuroIntervention* **17**, e910–e918 (2021). 33. Scholz, S. S. *et al.* One-year clinical outcomes in patients with renal insufficiency after contemporary PCI: data from a multicenter registry. *Clin Res Cardiol* **109**, 845–856 (2020). 34. Mohamed, M. O. *et al.* Impact of coronary lesion complexity in percutaneous coronary intervention: one-year outcomes from the large, multicentre e-Ultimaster registry. *EuroIntervention* **16**, 603–612 (2020). Codner, P. *et al.* Proximal Left Anterior Descending Artery Treatment Using a Bioresorbable Polymer Coating Sirolimus-Eluting Stent: Real-World Outcomes From the Multicenter Prospective e-Ultimaster Registry. *JAHA* **8**, e013786 (2019).	
64.	Medtronic		General	Thank you for the opportunity to comment. We acknowledge the complexity of the task assigned to the EAG in this pilot late-stage assessment.	Thank you for this comment. No changes made.
65.	Medtronic	10-15	Executive	**Given the serious limitations of the clinical and economic evaluations highlighted by the EAG, we ask that these limitations are strongly stated in**	Not factual inaccuracy, no changes made. The EAG encourage discussion of the limitations of the analysis at committee, where translation of

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			summary	**the executive summary and that the EAG considers the addition of a conclusion highlighting that the level of uncertainty means that the NMA and resulting economic model are unreliable for LSA committee decision making.** The overarching aim of this LSA is to demonstrate whether there is evidence of superior clinical effectiveness for any of the devices that justify a higher cost. We agree with the EAG conclusion that there are serious limitations in the NMA and economic findings. EAG stated: • *"the relative effect was too uncertain to establish any conclusions"* • *"Insufficient prior information to enable NMA model to estimate reliably"* • *"NMA using long-term data is highly dependent on the prior distribution, meaning the reliability of the estimate is a concern".* • *"Economic findings are impacted by the underlying issue in the NMA, and this key source of uncertainty prevented a firm conclusion to be drawn"* • *"The economic results informed by the current evidence on treatment effect can have serious biases"* Given the EAG identified serious limitations of the clinical and economic evaluations we believe that the results from the EAG assessment are not reliable for committee decision making and a conclusion cannot	any findings into advice for clinicians will be discussed.

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				be made on the relative effectiveness or cost effectiveness of the drug eluting stents in scope based on the EAR report. **We ask that any reference to superior results of one device over another be deleted from the executive summary**, for example, • Page 12: remove reference to "*weak evidence*" when confidence intervals cross 1 to ensure consistency and completeness in interpretation of level of evidence for NMA. • Page 13: remove reference to Promus Elite and Firehawk in paragraph 2 - this is potentially misleading. • Page 14: remove 2nd paragraph: "*When all devices were assumed to be clinically equivalent …., Firehawk appeared to yield the highest NMB. This indicates that Firehawk may offer the cheapest option when only the cost per device is considered*." • Page 15: remove 2nd paragraph: "*there was some indication that Promus Elite may reduce TVMIR rates ...and BioFreedom has increased TLR rates…compared to Xience*". Remove 3rd paragraph: "*Promus Elite appeared to yield the highest NMB across devices...in a cost comparison analysis, Firehawk may offer the cheapest option if…"*	
66.	Medtronic	34	4. Study selection	The EAG excluded the trials in high-risk patients from the network meta-analysis (NMA) and a separate	Evidence for high-risk groups has been excluded from the NMA, but is discussed narratively in the EAG report.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
		10-15	Executive summary	qualitative review of the evidence for high-risk groups was not conducted. A significant proportion of patients are in this high-risk category e.g. up to 40% of patients are at high bleeding risk, ~30% of PCI involve a bifurcation, more than 80% of left main disease involves the bifurcation, and left main coronary artery (LMCA) disease is discovered in 5-8% of patients undergoing coronary angiography. High-risk patients have higher risk of mortality, increased procedural time, repeat revascularisations and are more complex to treat and therefore it is particularly important for patients' safety that decision making is done based on specific clinical evidence in these patient groups. Whilst we understand the rationale for excluding high-risk patient studies from the main NMA to ensure transitivity, we believe that the studies in high-risk population should have been subject to further analysis within the evaluation, as they meet the population inclusion criteria and these high-risk subgroups were identified in the scope to be considered "*where data permits".* High-risk groups have also been highlighted as important by the clinical experts: "*in people who are considered of high-bleeding risk, there would be preference for a device that has evidence to demonstrate compatibility with shorter DAPT regimens*" and *"evidence of clinical efficacy and*	The EAG have added a statement to the executive summary with regard to subgroups. The EAG encourage discussion of the limitations of the analysis at committee, where translation of any findings into advice for clinicians will be discussed.

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				safety in particular populations (e.g., high bleeding risk)… could be useful for decision making". Any conclusions drawn from the clinical and economic analyses included in the NMA cannot be assumed applicable to high-risk populations as the evidence in these groups has not been assessed. **As there is a significant body of evidence in high-risk patient groups available for assessment, as outlined in comment 4, we request that the EAG assess this evidence to enable the committee to make recommendations specifically for high-risk subgroups and identify which DES are supported with evidence**. **If the evidence in high-risk groups is not assessed, we ask that the exclusion of high-risk patients from the EAG assessment is flagged as a key limitation in the executive summary and in the "key point for decision makers" section, to ensure that committee members are clear that high-risk groups have not been assessed and therefore any conclusions regarding relative treatment effects in this analysis are confined to the population assessed in the NMA and not generalisable to the high-risk population.**	
67.	Medtronic	34 10-15	4. Study selection Executive	**We would like to remind the EAG the key studies in high-risk patient groups, and given this was a relevant subgroup identified in the evaluation scope, we kindly ask the EAG to review and summarise this evidence in the clinical evidence**	Relevant studies conducted in high-risk groups have been included in this assessment and summarised narratively in the report.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			summary	**section as well as the evidence summary and in the executive summary.** One RCT data in high bleeding risk patients (Onyx ONE) was identified in the EAG evidence review but this was excluded from the NMA and not adequately reviewed elsewhere. The EAG appears to have excluded all the data that do not compare different stent technologies, such as EBC MAIN trial in left main lesions (Hildick-Smith 2021) and KISS trial in bifurcation lesions (Chevalier 2023). While they do not compare different stent technologies, these trials are relevant as they provide evidence of clinical safety and efficacy in these patient groups that are complex to treat. This has also been flagged by the clinical experts to have "*evidence of clinical efficacy and safety in particular populations (e.g., high bleeding risk)… could be useful for decision making*". **High-bleeding risk** • Windecker (2020) Polymer-based or Polymer-free Stents in Patients at High Bleeding Risk (Onyx ONE Trial) https://www.nejm.org/doi/10.1056/NEJMoa1911002 • Windecker (2022) Polymer-Based Versus Polymer-Free Stents in High Bleeding Risk Patients: Final 2-Year Results From Onyx ONE https://pubmed.ncbi.nlm.nih.gov/35680195/ • Kandzari (2020) One-month dual antiplatelet therapy following percutaneous coronary	The EAG has prioritised the evidence it believes to be most relevant to the decision problem, in line with NICE LSA interim methods and processes.

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				Intervention with Zotarolimus-eluting stents in high-bleeding-risk patients. (Onyx ONE Clear Trial) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7665241/ • Kandzari (2021) One-Month Dual Antiplatelet Therapy After PCI With Resolute Onyx DES: Final 2-Year Results From Onyx ONE Clear. https://doi.org/10.1016/j.jacc.2021.09.885 **Left main lesions** • Hildick-Smith (2021) The European bifurcation club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN) https://pubmed.ncbi.nlm.nih.gov/34002215/ • Hildick-Smith (2023) The European Bifurcation Club Left Main Coronary Stent Study - A Randomized Comparison of Stepwise Provisional versus Systematic Dual Stenting Strategies (EBC Main) 3-year results. https://media.pcronline.com/diapos/EuroPCR2023/86-20230516_1655_Room_Maillot_Hildick-Smith_David_1111100_(10139)/Hildick-Smith_David_20230516_1645_Room_Maillot.pdf • Tarantini (2023) A large, prospective, multicentre study of left main PCI using a latest-generation zotarolimus-eluting stent:	

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				the ROLEX study. https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-22-00454 • Tarantini (2023) A large, prospective, multicentre study of left main PCI using a latest-generation zotarolimus-eluting stent: the ROLEX study 2-year results. https://media.pcronline.com/diapos/EuroPCR2023/86-20230516_1647_Room_Maillot_Tarantini_Giuseppe_1111100_(10136)/Tarantini_Giuseppe_20230516_1645_Room_Maillot.pdf **Bifurcation lesions** • Chevalier (2023) Keep bifurcation stenting simple (KISS) Trial 1-month results. https://media.pcronline.com/diapos/EuroPCR2023/1263-20230516_1213_Room_Maillot_Chevalier_Bernard_1111100_(8747)/Chevalier_Bernard_20230516_1200_Room_Maillot.pdf • Chevalier (2024) Keep bifurcation stenting simple (KISS) Trial 1-year results. https://media.pcronline.com/diapos/EuroPCR2024/87-20240515_1632_Theatre_Havane_Chevalier_Bernard_1111100_(669)/Chevalier_Bernard_20240515_1630_Theatre_Havane.pdf • Price (2021) ONE YEAR CLINICAL OUTCOMES IN PATIENTS WITH CORONARY BIFURCATION LESIONS: RESULTS FROM THE RESOLUTE ONYX	

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				BIFURCATION STUDY (Post-Approval Study). https://www.jacc.org/doi/10.1016/S0735-1097%2821%2902324-X • Price (2022) Two-Year Outcomes in Patients with Bifurcation Lesions treated with Resolute ONYX ZES: Final Results from the RESOLUTE ONYX Bifurcation Study. https://doi.org/10.1016/j.jscai.2022.100132 • Price (2023) The Resolute Onyx Bifurcation Study: 3-Year Outcomes in Patients with Coronary Bifurcation Lesions. https://doi.org/10.1016/j.jscai.2023.100736 • Hildick-Smith (2021) The European bifurcation club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN) https://pubmed.ncbi.nlm.nih.gov/34002215/ • Hildick-Smith (2023) The European Bifurcation Club Left Main Coronary Stent Study - A Randomized Comparison of Stepwise Provisional versus Systematic Dual Stenting Strategies (EBC Main) 3-year results. https://media.pcronline.com/diapos/EuroPCR2023/86-20230516_1655_Room_Maillot_Hildick-Smith_David_1111100_(10139)/Hildick-Smith_David_20230516_1645_Room_Maillot.pdf	

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68.	Medtronic		General	We are concerned that generalisation of conclusions regarding relative treatment effects to this high-risk group could drive poorer outcomes for high-risk patients if clinically appropriate stents were unavailable as an option due to the flawed assumption that there is no difference in efficacy between stents in all groups. **We ask that this is highlighted as an equity issue.**	There was a lack of evidence to draw conclusions of any differences in outcomes between stents in any subgroups in scope. The EAG have added a statement to the executive summary with respect to subgroups.
69.	Medtronic	10-15	Executive summary	**We ask the EAG to add a section in the executive summary outlining the indication and evidence available for DES approved in high-risk subgroups to ensure clarity in the report that not all the DES in scope have CE approval or specific evidence in high-risk patients.** **This would help avoid off-label use recommendations for DES without CE mark approval or relevant evidence in that indication and ensure that those DES with evidence in high-risk patients are differentiated.** For example, 1-month DAPT in high-bleeding risk was identified as a population that requires specific evidence in the user preference report, where experts concluded that *"they would want to see clinical evidence as a measure of suitability"* **We ask the EAG to highlight that not all stents have a CE mark in this indication.**	The EAG have added a statement to the executive summary with respect to subgroups. The EAG encourage discussion of the limitations of the analysis at committee, where translation of any findings into advice for clinicians will be discussed.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Onyx Frontier (via Resolute Onyx) is one of the DES that has provided RCT evidence to support the clinical efficacy and safety for high-risk patients, which led to the CE mark approval in 12 indications including 1-month DAPT in high bleeding risk patients, bifurcation lesions, and left main**.**	
70.	Medtronic	130	12. Discussion	**We ask the EAG to rephrase the wording on page 130 to "there is published RCT evidence available to demonstrate that 21 of the devices in scope are effective in some of the populations of interest."** The EAG report has concluded that "*there is published evidence available to demonstrate that **27** of the devices in scope are effective in the population of interest*". However, the EAG also states that "***No RCTs** drawing comparisons against another device in scope were identified for the following devices: BioMime Branch, BioMime Morph, Coroflex ISAR NEO, EverMine 50, Firehawk Liberty, ihtDEStiny BD, MAGMA and Synergy Megatron. Therefore, the EAG is unable to comment on any differences in outcomes between these devices and any comparator devices from a controlled setting*", and "*Based on the company information on clinical equivalence between their predecessor and the device in the scope, the NMA results could be used to inform the relative treatment effect of 18 devices in the scope*." It is therefore misleading to state that 27 devices are equally considered effective when evidence of the	The EAG has not stated that 27 devices are considered to be equally effective. The EAG has amended this sentence to avoid misinterpretation.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				effectiveness of 8 devices has not been identified in this assessment. **We ask the EAG to add a sentence to clarify the availability of published RCT evidence in the key subgroups identified in the scope,** e.g. There is published RCT evidence available for Onyx Frontier that demonstrate effectiveness in high-risk populations such as ….”	
71.	Medtronic	12 124	Executive summary 11. Combined summary	The sentence below in bold is missing from the executive summary and the summary of the clinical and economic evidence sections where the EAG comments on lack of RCTs for these technologies. **We ask this conclusion is also added in these sections for consistency**. On page 38, the EAG commented “*No RCTs drawing comparisons against another device in scope were identified for the following devices: BioMime Branch, BioMime Morph, Coroflex ISAR NEO, EverMine 50, Firehawk Liberty, ihtDEStiny BD, MAGMA and Synergy Megatron*. ***Therefore, the EAG is unable to comment on any differences in outcomes between these devices and any comparator devices from a controlled setting.***”	Not factual inaccuracy. No changes made.
72.	Medtronic	65 69	Outcomes at first-year follow-up.	**We ask that the EAG remove all references to “weak evidence” where there is no statistical difference.** In numerous places on pages 65 and 69, the EAG report uses terms such as “*there is some evidence*”	See EAG response to comment #15.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			Outcomes in the long-term follow-up	or "*there is weak evidence*" when discussing the treatment effects calculated in the NMA. **We request that the report be updated in these sections to note only those differences that are statistically significant**. Furthermore, given the uncertainties in the NMA estimates, it is inappropriate to refer to a hazard ratio of less than 1 as demonstrating benefit (however weak it may be). Discussion of differences in treatment effects should be restricted to cases where statistical significance has been demonstrated. **We also ask that the EAG update an inaccurate interpretation of a CrI indicating non-significance (crossing 1**).For example, on page 65 "*At 1 year, results from the NMA suggest there is **some evidence** that Promus Elite has **meaningful beneficial effect** on TVMI rate when compared to Xience (HR 0.59, 95%CrI 0.31 to 1.03).",*	
73.	Medtronic	13 104-107	Executive Summary 10. Economic modelling results	**We ask that statements relating to ranking of devices based on net monetary benefit and ranking tables 24 and 25 be removed from the executive summary and economic modelling section** as the relative effects from the NMA are unreliable, as outlined by the EAG, and the uncertainty in the economic findings "*prevented a firm conclusion to be drawn*". We agree with the EAG conclusions on the severe limitations and substantial uncertainty of the NMA and economic findings in that *"the relative effect was too uncertain to establish any conclusions"; "insufficient prior information to enable NMA model to*	Not factual inaccuracy. The EAG acknowledged the limited analysis on subgroups in the scope, due to data availability. However, the study characteristics of included studies are broadly in line with that of the NICOR data, except the proportion of STEMI. This was reported in the EAG report. The EAG encourage the discussion of the uncertainty in NMA estimates at committee.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				estimate reliably"; "NMA using long-term data is highly dependent on the prior distribution, meaning the reliability of the estimate is a concern" and *"the economic findings are impacted by the underlying issue in the NMA and this key source of uncertainty prevented a firm conclusion to be drawn".* In addition, sensitivity analysis shows that the *"95%CI NMB for all devices are overlapping which reflects the considerable uncertainty associated with the model inputs"* We therefore suggest that it is inappropriate and potentially misleading to produce ranking tables on net monetary benefit based on these unreliable estimates. In addition, only a proportion of the DES population are covered by the studies included in the NMA therefore ranking is potentially misleading as the evidence in the high-risk population has not been assessed.	
74.	Medtronic	13, 15 103-126	Executive summary 10. Economic modelling results	We believe it is inappropriate to rank devices based on cost alone as the assumption on clinical equivalence has not been demonstrated due to the acknowledged limitations of the NMA. As there has been no assessment of high-risk patients, it is entirely inappropriate to assume clinical equivalence in these groups. Furthermore, simple ranking based on cost alone was available before this process started and assumed insufficient for NHS decision making hence the development of the LSA programme.	Not factual inaccuracy. No changes made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				On a similar basis, we believe it is inappropriate to "call out" in the executive summary, devices that yield "*the highest NMB*" or "*cheapest option*" as this could be misleading as the EAG highlighted that there is *"Insufficient prior information to enable NMA model to estimate reliably"* and *"NMA using long-term data is highly dependent on the prior distribution, meaning the reliability of the estimate is a concern".* In addition, the EAG highlighted that *"Economic findings are impacted by the underlying issue in the NMA, and this key source of uncertainty prevented a firm conclusion to be drawn".* **We ask the EAG to update the executive summary and the economic evidence section to address these limitations.**	
75.	Medtronic	52	5.2 NMA Methods	**Exploration of potential effect modifiers to satisfy the transitivity and consistency assumption was not well documented.** We understand all NMAs should identify a priori possible effect modifiers and compare their distributions across comparisons, which should not differ across trials. While this was acknowledged in the methods (as stated on page 34 of the report): "*A valid NMA relies on the assumption of transitivity, where covariates that act as effect modifiers across trials must be similar".* The EAG identification of possible effect modifiers was not further discussed.	Table 8 summarises key study characteristics across all included studies. In addition, the EAG acknowledged a meta-regression might be helpful in exploring the impact of effect modifiers on the treatment effect. However, given the insufficient studies (minimum 10 studies per pairwise comparison as recommended by Cochrane Handbook), it is not feasible to undertake this analysis. No changes made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				While we acknowledge the EAG explored the transitivity assumptions using the 'global approach' (pg. 37) and also presented the results of this approach showing '*Model fit statistics suggest that there are no significant differences between the FE and RE model'* The EAG also concluded on pg. 74*: "The variation in study characteristics indicates that the effect modifiers are not well-balanced across trials, hence the EAG preference in fitting a RE NMA model, despite the challenges in estimating the between-study SD from the trial data".* **We request that the EAG provide additional information on the effect modifiers defined a priori and how the imbalance of these affected the transitivity and consistency assumptions overall.**	
76.	Medtronic	65	5.2.4 NMA results	**Reporting of the NMA was inadequate - insufficient information provided and inconsistent results reporting** Valid reporting guidelines for NMA such as the PRISMA NMA checklist (Hutton et al. 2015)[1] should have been utilised to ensure sufficient information on the methods, results and conclusions of the NMA	For the purpose of the assessment report, the EAG believe the information reported in the report is sufficient. Adding the suggested information would not change the overall NMA results, therefore may not be helpful in the decision making.

[1] Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, Straus S, Thorlund K, Jansen JP, Mulrow C, Catalá-López F, Gøtzsche PC, Dickersin K, Boutron I, Altman DG, Moher D. The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations. Ann Intern Med. 2015;162(11):777-784.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				were included in the report for reviewers to perform a thorough critical appraisal. • Some notable omissions include: o Detailed study characteristics (tabulated for ease of comparison): in particular, detailed definitions of the PICOs used in each study should have been included. o Differences in 'all comers' vs other populations (such as high-risk) were not included in sufficient detail to allow assessment of reasons for study inclusion/exclusion. o Detailed definitions on all outcomes included in the NMA (and also primary outcomes of each study) were not clearly outlined or tabulated for ease of comparison. o Reasons behind scoring of risk of bias in Table 9 JBI Critical Appraisal checklist **We request that the EAG provide this additional information to ensure that the committee has sufficient information for decision making.**	
77.	Medtronic	10-15 65	Executive summary	**We ask the EAG to provide clarity and consistency in reporting the NMA results, and uncertainty surrounding the results, in the executive summary and the clinical evidence section.**	See EAG response to comment #15.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			5.2.4 NMA results	We note missing clarity and inconsistency in reporting of NMA results, including interpretation of results as *"some evidence"*, "*clear evidence*" or *"weak evidence*", which make interpretation difficult and potentially misleading. **We ask that a systematic and consistent approach to reporting is applied by the EAG.** For example, a result from the appendix was omitted in the main body of the report: *"There is clear evidence that BioFreedom resulted in higher TLR rate than Xience (HR 3.70, 95%CrI 1.83 to 6.80)".* This seems incomplete as from Appendix G (NMA league table: Y1 TLR) we can also conclude that Resolute Onyx (and other stents) have lower TLR than Biofreedom at 1 year follow-up.	
78.	Medtronic	10-12	Executive summary, Clinical evidence	In line with the request for complete and consistent reporting in the main clinical evidence section, **we ask that the EAG review the clinical evidence summary and provide consistent reporting of NMA results and uncertainty surrounding results**. For consistency, we request that the NMA results reported at 1 year be complemented by relevant results from the appendix on TLR rates that were lower e.g. for Resolute Onyx than Biofreedom. **We also request that the general limitations of the NMA be more consistently noted throughout the results reporting.** For example, we note an interpretation of a CrI indicating non-significance (crossing 1) as "*some evidence*" of "*meaningful*	Not factual accuracy. No changes made. Given that the NMA findings were used to inform the economic model with Xience Pro S as the comparator, the relative effect vs Xience was the primary focus in the EAG report (Section 5.2.4). However, if any strong/clear evidence between devices (95%CrI does not contain 1) was noted, this was reported as well.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				beneficial effect" for Promus Elite: "*At 1 year, results from the NMA suggest there is some evidence that Promus Elite has meaningful beneficial effect on TVMI rate when compared to Xience (HR 0.59, 95%CrI 0.31 to 1.03).*"	
79.	Medtronic		General	The protocol states a "pragmatic review" approach was chosen for the literature review. In this case, where a full systematic literature review was not undertaken, another validated methodology (e.g. Cochrane rapid review of effectiveness etc) should have been sought. Not performing a robust systematic review for this type of technology evaluation has implications on the findings of this report and its overall use in decision making.	The pragmatic approach taken by the EAG is permitted under the NICE LSA interim methods and processes. The EAG has prioritised the evidence it believes to be most relevant to the decision problem.
80.	Medtronic	51	5.2.1 Studies included in NMA	The NMA did not follow the final scoping PICO[3] accurately. As outlined in the scope of the review the included population was very broad, as follows: "*People having PCI (including primary PCI) and for whom drug eluting stent is indicated for treating coronary artery disease (including stable angina, STEMI, unstable angina or NSTEMI). Where data permits, the following subgroups may be considered: Women, Ethnicity (important subgroups are discussed in section 3.1), People with left main stem lesions, People with bifurcation lesions, People with high bleeding risk, People with diabetes".*	There is no sufficient comparative data to include subgroup analysis in the NMA. No changes made.

[3] https://www.nice.org.uk/guidance/gid-hte10039/documents/final-scope

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				As such, the removal of four RCTs (BIOFLOW-DAPT, BIOSTEMI, IDEAL-LM and Onyx ONE) that included 'high-risk' patients was not in-line with the final scope and PICO criteria. While it is understood that these studies were removed from the main NMA to ensure transitivity was observed, the studies should have been subject to further analysis within the evaluation as they met the population inclusion criteria. Further analysis of high-risk patients and other included subgroups as potential effect modifiers should have been explored further. As it stands, the evidence review and its conclusions do not adequately address key subgroups of interest. **If inclusion in NMA was not possible, we request that the evidence for the subgroups be discussed qualitatively, and conclusions included in the evidence summary.**	
81.	Medtronic	62	5.2.4 NMA results	In the line of limited scope of NMA, the EAG states that "*Although a number of different clinical outcomes were reported in the identified RCTs, only TLR and TVMI were analysed using NMA*". Given that EAG's NMA and review only addressed two clinical outcomes, **we ask that this is listed as another key limitation of the NMA and listed in key points for decision makers.**	This limitation was acknowledged in the EAG report (Section 12 Discussion). This has now been added in the key points for decision makers in the executive summary.
82.	Medtronic	82	6.3 Procedural outcome	**Given that procedural success was reported as one of the important criteria in user preference report, where the data is available, we ask that the EAG assess the procedural success rates in high-risk patient groups**.	Procedural outcomes reported in section 6.3 are reported for all included RCTs, including those conducted in high-risk patient groups. No changes made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			s; Table 16	In line with our view on the limitations of the EAG report, the key studies in high-risk patients are excluded from the EAG scope, resulting in missing the reported technical and procedural success rates in these population groups.	
83.	Medtronic	74 12-14	Limitations Executive summary	As acknowledged in several places throughout the EAG report, **there is considerable uncertainty regarding the effect of each device upon the key outcomes included in the economic model** (TLR, TVMI): - Page 12 states: "*At long-term follow-up, the NMA results using 12 trials with long-term data found no evidence for meaningful differences in TLR and TVMI rates between devices*." - With regard to prior heterogeneity, page 12 states: "*the relative effect was too uncertain to establish any conclusions*". - Page 13 states: "*The economic analyses demonstrate that there is a lot of uncertainty surrounding the NMB findings, which outweigh small NMB difference between devices*" - Also on page 13: *"...probabilistic sensitivity analysis results suggested that there was substantial uncertainty in relative treatment effect between devices*." - Page 74: "*Given the caveats and uncertainties associated with meta-analyses of sparse data, the EAG would advise that the*	Not factual inaccuracy. No changes made. The EAG encourage the discussion of these limitations at committee.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				NMA results should be interpreted with great caution." As further noted in the "Key points for decision makers" section, the EAG states that "*the economic findings are impacted by the underlying issue in the NMA, and this key source of uncertainty prevented a firm conclusion to be drawn*". This supports our view that the model results (especially the way in which the interventions are ranked) are not a useful decision-making tool. Given these uncertainties in the clinical outcomes, **it is inappropriate to use them in an economic analysis which ranks devices according to net monetary benefit. Using such unreliable estimates of treatment effect renders the model results unsuitable for decision-making purposes.**	
84.	Medtronic	91	9. Economic modelling methods	A 1-year time horizon was used in the base case analysis, guided by the EAG NMA findings, with a sensitivity analysis performed using a 5-year horizon. The project scope states that "*the time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies*". **The use of a 1-year time horizon is therefore inconsistent with the scope, given the existence of longer-term data demonstrating differences in outcomes** up to 5 years for Resolute Onyx vs. Orsiro in BIONYX trial. For example, van Vliet et al (2024) showed a significant reduction in TLR between 3 and 5 years (HR=0.47; p=0.026), and	The significant uncertainty with long-term NMA prevented the use of longer-term time horizon in the base case. This was justified in the EAG report. No changes made.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				a significant reduction in rate of TVF amongst patients aged over 75 years (HR=0.60; p=0.023). Ploumen et al (2021) reported that all-cause mortality was significantly lower with Resolute Onyx at 3 years (HR=0.67; p=0.034). As the EAG note on page 14 of their report: "*The scenario analysis showed that the results were sensitive to long-term treatment effect, where there was significant change in the NMB profile for most devices when the time horizon increased to 5 years*". This indicates that a more extensive analysis of long-term data is justified.	
85.	Medtronic	99	9. Economic modelling methods	We note that the main driver of the cost-effectiveness results (apart from device price) appears to be the disutility associated with TVMI (0.24 which is to be applied for a full cycle). By comparison, the disutility associated with repeat PCI is effectively zero. These points, combined with the exclusion of other clinical outcomes, places too much weight on the incidence of TVMI, especially when the associated disutility is assumed to apply for the full duration of the model horizon. **We therefore suggest that the duration of the disutility is adjusted to a more appropriate time period.**	The EAG agree that higher disutility would favour stents that reduce TVMI. A sensitivity analysis by reducing TVMI disutility to 0.12 was performed, however this did not change the overall NMB ranking.
86.	Medtronic	99-104	9. Economic modelling methods;	The cost-effectiveness results are almost impossible to interpret due to the high level of redaction in the EAG report. **We would request that the NMB column of Table 24 ('base-case results') be unredacted to allow the scale of the differences between devices to be formally assessed**. Similarly, we are unclear about why the unit costs of	This is subject to NICE discretion. No changes made by EAG.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
			Table 22-24	PCI and TVMI, as well as the costs of PCI follow-up care and DAPT have been redacted – **we would ask that these be unredacted to allow proper interpretation of the inputs**.	
87.	Medtronic	97	9.4 Resource use and cost parameters	**We ask that the transacted price of the DES is explored in the base-case of the cost effectiveness analysis. For scenario analysis, we ask that the quantification of all rebates is verified by NHS supply chain for all DES.** Stent costs in the economic model have been provided by NHS Supply Chain and are calculated as a weighted average of the purchase costs for all stents purchased through NHS Supply chain in 2023. These prices do not reflect the transacted prices as the commercial models and rebate structures differ substantially between companies and are not comparable e.g. differences in deals, rebates and Medpoints are not reflected in the average NHS cost.	See EAG response to comment #1.
88.	Medtronic	25	4.1.1 Assessment of clinical equivalence	Equivalence of evidence for previous generations does not seem to have been assessed based on objective criteria, and was only based on company information, with possibly different definitions of "equivalency". For example, The EAG has decided to consider Firehawk and Firehawk Liberty to be standalone devices, "*as the relationship between devices has not been confirmed*" (page 29 Table 3). This was also commented by the EAG "*There may be inconsistency in views between companies on what constitutes clinical equivalence so it is important to*	Not factual inaccuracy. The EAG encourage discussion of the limitations of the analysis at committee.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				note that any acceptance of clinical equivalence of predecessor devices to current devices in scope may be subjective." "*The acceptance of evidence for predecessor devices for the devices in scope may be considered a limitation of the EAG analysis*." **We ask the committee to acknowledge that the lack of objectivity and consistency in the assessment of equivalency potentially limits the NMA and its conclusions.**	
89.	Medtronic	10-15	Executive Summary	Given that we have made several comments asking for additions or changes to the Executive Summary, we have also summarised them here for convenience. • **Comment 2**: Given the serious limitations of the clinical and economic evaluations highlighted by the EAG, we ask that these limitations are strongly stated in the executive summary and that the EAG considers the addition of a conclusion highlighting that the level of uncertainty means that the NMA and resulting economic model are unreliable for LSA committee decision making. • **Comment 3**: We request that the EAG assess the evidence in high-risk population to enable the committee to make recommendations specifically for high-risk subgroups and identify which DES are supported with evidence. • **Comment 4:** We would like to remind the EAG the key studies in high-risk patient	See above responses to individual points.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				groups, and given this was a relevant subgroup identified in the LSA scope, we kindly ask the EAG to review and summarise this evidence in the clinical evidence section as well as the evidence summary and in the executive summary. • **Comment 6:** We ask the EAG to add a section in the executive summary outlining the indication and evidence available for DES approved in high-risk subgroups to ensure clarity in the report that not all the DES in scope have CE approval or specific evidence in high-risk patients. • **Comment 8:** For clarity and consistency, we ask the EAG to add a missing sentence from the executive summary and the clinical and economic evidence section "*Therefore, the EAG is unable to comment on any differences in outcomes between these devices and any comparator devices from a controlled setting"* for those technologies where no RCTs were identified. • **Comment 10**: We ask that statements relating to ranking of devices based on net monetary benefit and ranking tables 24 and 25 be removed from the executive summary and economic modelling section as the relative effects from the NMA are unreliable, as outlined by the EAG and the uncertainty in the economic findings "prevented a firm conclusion to be drawn".	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				• **Comment 11**: We ask the EAG to update the executive summary and the economic evidence section to address limitations. • **Comment 14 & 15**: We ask the EAG to provide clarity and consistency in reporting the NMA results and uncertainty surrounding the results in the executive summary and the clinical evidence section.	

Section B: User Preference Report – Comments collated table:

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
1.	Boston Scientific	4, 8, 12	N/A	**Sample size** We welcome the inclusion of the user preference analysis in this assessment, and the recognition of the importance of DES value that span beyond clinical outcomes and price. We understand that it may be difficult to recruit a sample of users (interventional cardiologists) completely free of direct financial interests. However, we do note that the study was rather small (N= 7) given that there are hundreds of operators in the UK and that a larger study would have provided a more complete picture of the range of drivers of user preferences, and heterogeneity in these preferences.	Thank you for this comment. The variation in ranking mostly depended on the participants' approach to the question 'what is important when choosing a stent?'. Some participants did not rank an item so high if they considered that the item did not differentiate between different stents (for example if they considered all currently used stents to perform well in terms of stent failure). Others ranked an item high regardless of whether they thought the item was a differentiating factor. Suitability of 1-month DAPT may have been tricky to rank because the importance may depend on individual clinical need (discussion on pages 12-13 notes assessing user preferences on a subgroup level is suggested as something future assessments

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				Page 8 of the report recognizes that variations in individual responses (ranking and weighting) might be due to individual practice differences, which are amplified by the small sample. Please explicitly acknowledge the potential limitation of possible impact of small sample size on the results' variability and generalizability on page 12.	could consider doing) and on a contract level on the expected prevalence. Because of this, the variation may not have been solved by having a larger sample size. A clarification about the different approaches to ranking has been added to discussion section on page 12.
2.	Boston Scientific	8	N/A	**Compliant selling practices** We have concerns around the way stent bundling and fellowship sponsorships are discussed in the 'stent cost' section. Boston Scientific does not provide direct funding for Cardiology Fellowships as a benefit or reward for product usage as this is contrary to the compliance framework on which medical devices companies should operate. Further, we question whether the 'bundle' offerings discussed in this section are around Commitment Agreements instead, as such commitment deals may have additional benefits incorporated as part of the consumables offering which should be taken into account when assessing product costs. We ask that the terminology queried above be reconsidered due to the potential compliance concerns and certainty of scope regarding benefits.	The notes on bundling and fellowship sponsorships on page 8 have been removed.
3.	Abbott Medical			Nothing to add to this User Preference report as we believe it has been very well conducted.	No changes needed.
4.	TERUMO	8	Results - Identifying and	"*The group unanimously concluded that it would be important for the cost to be the lowest cost (if they are considered to have equal performance). But they also*	The notes on bundling and fellowship sponsorships on page 8 have been removed.

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
			defining criteria - Stent cost	*discussed that the cost may include considerations of other benefits that may be part of the contract such as bundling stents with other devices or sponsoring interventional cardiologist fellowship in the trust*." The assumption that all companies are conducting bundling approach as part of the contract with the Trusts or sponsoring fellowships in the Trusts and factoring those in the overall costs bring a major bias assumption in the calculation. The bundling nor the training provided by the manufacturer is part of the LSA scope and does not lie in the NICE mandate for this LSA.	
5.	Medtronic	User preference report	Tables 2 & 3	**We ask that NICE remove ranking and weightings from Tables 2 and 3 and provide them as an unranked list of criteria with a comment that consensus on ranking could not be reached.** Given that the MCDA was unable to gain consensus from participants on the ranking of the identified criteria, we suggest it is inappropriate to present raking tables with weightings as this is unreliable for committee decision making.	The report describes the variation in responses to allow for interpretation of the results in context. No changes needed.
6.	Medtronic	User preference report	Methods	NICE LSA Interim methods and Process (April 2024) section 4.27 outlines the purpose of user preference report as "s*o, users of these technologies can comment on the importance of characteristics or features of these technologies* ***that may not be captured elsewhere in the evidence base***." Whilst this LSA user preference report provides valuable information about criteria users consider important, the authors note that *"most of the criteria*	No changes needed.

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE Response
				that are important to interventional cardiologists are among the clinical or intermediate outcomes in the scope of the external assessment group's clinical and cost effectiveness assessment". **We suggest that this user preference does not provide sufficient information to support the committee's decision making as intended.**	

Section C Economic model - Comments collated table:

Comment	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
1.	Abbott Medical	Introduction tab – key assumptions states on the last bullet point: all TV-Mis are related to in-stent restenosis and stent thrombosis. It is unclear how these 2 parameters were factored into the calculated costs. Furthermore it is unclear which reference was used for each.	Suggest splitting restenosis from thrombosis. This is because both complications have different frequencies and different treatment pathways and related costs vary	Treating thrombosis has a high cost-implication. With Xience having consistently the lowest rate of stent thrombosis the net monetary value should be in favour of Xience	See EAG response to comment #34.

Comment	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
2.	Abbott Medical	Parameter tab – Clinical inputs Why are the probability variables for TLR lower than TMVI	Sharing the rationale behind the EAG calculation	Not able to predict yet	Trial data has been used to calculate these probabilities. No changes made.
3.	Abbott Medical	Parameter tab - Costs We have missing references for cMI, cRevasc, cPostRevasc, cFollow-up, cDAPT, cCardiac Rehab	Sharing the reference source used of the respective values into the model.	Not able to predict yet	This is subject to NICE discretion. No changes made by the EAG.
4.	Boston Scientific	Markov model structure: the current CEA markov model was developed with a yearly cycle length including seven health states: no further event, TLR, TVMI, TVMI-repeat revascularisation, post-revascularisation, post-MI and death. This is a non-conventional definition of health states in the markov model with a mixture of state/event (e.g., TVMI, post-MI, death, no further event) and procedure (TLR, TVMI-repeat	We suggest better defining the 'health state' and 'transition paths' as well as rate parameters for transitions.	Comparing results (total costs, QALY and NMB) from current model and a simplified Markov model structure with clearer health states as transition paths will make the findings more robust.	Thank you for the comment. The inclusion of health states in the EAG model are guided by the EAG review of 19 peer-reviewed models. The EAG acknowledge that events have been included in the model, however this enables a more transparent and clear costs and QALYs calculation in the model. No changes made.

Comment	Stakeholder	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)	EAG response
		revascularisaztion, post-revascularisation).			

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Late-stage assessment

GID-HTE10039 Drug-eluting coronary stents for treating coronary artery disease

User preference report

November 2024

Contents

Introduction

Alongside the assessment of a technology's value based on costs and effectiveness, the late-stage assessment on drug-eluting coronary stents includes an assessment of user preferences that influence decision making when selecting which technology to use (NICE's Interim methods and process statement for late-stage assessment). This report presents the key findings from the user preference assessment that was done to understand:

- which criteria are important to consider for technology selection
- how important the criteria are
- how the criteria can be measured.

The user preference report should be read alongside the final scope and the external assessment report.

Background

In coronary artery disease, the heart's blood supply may become reduced by a build-up of fatty substances in the coronary arteries. A typical symptom of coronary artery disease is angina (chest pain that is exacerbated by exertion). A critical reduction of the blood supply to the heart may result in myocardial infarction (heart attack) or death. To restore the blood flow, a stent may be inserted in coronary arteries during percutaneous coronary intervention (PCI).

There are 29 technologies from 17 manufacturers included in this evaluation. These are drug-eluting coronary stents available on the NHS Supply Chain framework for interventional cardiology (Lot 1 of NHS Supply Chain framework for Interventional Cardiology, Interventional Radiology and Interventional Neuroradiology, Cardiac Rhythm Management and Electrophysiology). Appendix A lists the included stents (for more information, see table 1 on pages 7 to 9 of the final scope).

In 2023, around 65% of the drug-eluting stents spend within NHS went through the NHS Supply Chain. NHS trusts or groups of trusts joined for procurement purposes, either independently or supported by NHS Supply

Chain or by external contract management organisations, may negotiate further contracts with stent suppliers. These contracts may include pricing based on for example the expected market share within the trust (centralising suppliers) or bundling of stents with different types of PCI devices or larger capital equipment. These contracts typically include 2 to 3 drug-eluting stents that can be used across various types of lesions. Some room, for example 10% of the contract, may be left for more specialised stents. Interventional cardiologists are often involved in the purchasing decisions.

Methods

This user preference assessment was done in line with NICE's Interim methods and process statement for late-stage assessment. The aim of capturing user preferences is to transparently collect and present information to the committee on the criteria that users consider important when deciding which technology to choose. Users are defined as those who will use the technology and are directly involved in the decision to choose one technology over another.

Participants

For this assessment, users were identified as interventional cardiologists. A total of 7 interventional cardiologists participated the assessment. They were recruited in line with NICE's interim methods and process statement for late-stage assessment. NICE's policy on declaring and managing interests for NICE advisory committees was considered during the recruitment process. Interventional cardiologists directly employed by a company whose technologies are being evaluated were not eligible to participate. Register of interests is available on the NICE website.

The participants were from NHS trusts across the country (East of England, North East, North West, South East, West Midlands, Yorkshire and the Humber). Appendix B lists the participants. All participants had used a variety of different drug-eluting coronary stents in clinical practice. Of the 7 participants, 6 had experience with more than 10 (3 of these 6 with 15 or

more) of the 29 different drug-eluting coronary stents included in this late-stage assessment. Appendix A provides further details on stent use.

Assessment stages

The user preference assessment was done through participation in 1 online workshop and 2 email tasks. This was split into the following 3 stages:

- Stage 1: identifying and defining criteria (workshop)
- Stage 2: ranking criteria in order of importance (email task)
- Stage 3: weighting criteria (email task)

Of the 7 participants, 6 attended the workshop to identify and define the criteria, 5 individually ranked the set criteria and 6 assigned weights for the ranked criteria.

A second workshop was planned to explore how users would measure the performance of a technology against each criterion. But the performance rules were a natural part of the discussion already in the first workshop. They were captured for all criteria items either in the criteria definitions or the EAG's model. Therefore, a decision was made to not hold a second workshop. Notes on the performance rules are included in the results section of this report.

Stage 1: identifying and defining criteria

Interventional cardiologists were asked to identify key factors that are important when choosing a drug-eluting stent for treating coronary artery disease. This assessment focused on the overall population in scope. Two lists of criteria and definitions were identified and agreed on during an online workshop. This was to explore key factors related to both decisions at a patient-level and at the contract-level to cover most cases. Typical contracts include 2 to 3 drug-eluting stents that can be used across various types of lesions.

Stage 2: ranking criteria in order of importance

Interventional cardiologists were then asked to rank each of the 2 criteria in order of importance to them. This was done via email. Ranked lists from all respondents were collated, averaged and ordered from most important to least important, creating 2 final ranked lists of criteria and definitions (using the SMART ranking technique, see appendix C for a detailed definition). A tie between the last 2 factors in the averaged, ordered contract level criteria was resolved by putting the factor with a narrower standard deviation around the average rank above the factor with a wider standard deviation (more uncertainty) around the average rank in the final ranked list.

Stage 3: weighting criteria

Interventional cardiologists were asked to weight each of the 2 final ranked lists of criteria to show how much more important 1 criterion was compared with the criterion ranked below (using the swing weighted technique, see appendix C for a detailed definition). To weight the criteria, interventional cardiologists were asked to give each criterion a score from 0 to 100%. A score of 0% meant that there was no difference in importance between a criterion and the criterion ranked below, and a score of 100% meant that it was considered twice as important. Weighted lists for all respondents were collated, averaged and weights were calculated.

Results

Identifying and defining criteria

During the workshop, the participants identified 4 items that are important in choosing at the patient-level which technology to use. They also identified 6 items that are important in choosing stents to cover most or 90% of the cases (contract-level). The 2 sets of criteria with definitions are shown in table 2 and 3. Both lists had criteria related to the size of the stent. Both included also stent failure, procedural success and suitability for people having abbreviated 1-month DAPT. Additionally, the contract-level criteria included the stent cost.

Criteria related to stent size

The group noted that in addition to suitable length and diameter, suitability of the stent size is also determined by the stent's expansion capability. It was clear that on the patient-level, what size is suitable would depend on the clinical case. On the contract-level, the group explored the size range that would be suitable for most cases. They agreed that a diameter from 2.25 to 4mm that can be dilated to maximum 5.5mm and length from 8 to 38mm is likely to cover most lesions and vessels. But there was some disagreement over whether a 48mm (XL stent) was part of a usual selection of length, with some using this length in routine practice and others only needing it occasionally. The group noted that information on the most common vessel and lesion characteristics or stent sizes used would be needed to confirm the size matrix to cover most cases. Sources of this information could be for example NICOR data or data on purchasing. If this was not available, the size matrix of the most used stents could also give an idea. The group discussed that among the 2 to 3 stents to cover most cases, it would be good to have at least 1 stent that is available in more extreme (large or small) lengths.

Stent failure

The participants agreed that the key evidence indicating stent failure could include evidence on thrombosis, in-stent restenosis and target lesion failure.

Procedural success

The group felt it was important to consider evidence on procedural success and explored different stent characteristics that may be considered to contribute to the procedural success. They concluded that the key things may be radial strength, visibility under imaging and deliverability. They noted that many variables may affect visibility of the stent under imaging, for example the age of equipment being used and not everyone would think visibility as a key consideration about the stent. The participants noted that, overall, it's quite rare that a stent cannot be delivered. Procedural success may depend more on the lesion characteristics, delivery equipment and operator than the stent.

Suitability for people having abbreviated 1-month DAPT

The group discussed whether suitability for people having abbreviated 1-month DAPT could be considered a class effect for polymer-free stents but concluded that they would want to see clinical evidence as a measure of suitability. They also noted that the suitability is not limited to stents with a particular type of coating. The group further noted that the most evidence on this may currently be studies comparing different length antiplatelet regimes in people who have received a stent instead of studies comparing different stents.

Stent cost

The group unanimously concluded that it would be important for the cost to be the lowest cost (if stents are considered to have equal performance).

Ranking criteria in order of importance

After the workshop, the participants individually ranked the 2 sets of criteria in order of importance. The final averaged ranks for the 2 sets of criteria are shown in table 2 and table 3. Both on a patient- and contract level, stent failure and availability of suitable stent size or suitable stent size matrix to cover most cases were the top 2 criteria of the averaged list. Suitability for people having abbreviated 1-month DAPT was lowest or near the bottom in both averaged lists.

There was some variation in individual responses, somewhat more so on the contract-level and so some disagreement with how the averaged ranking looked like. Some participants noted that while the stent failure is the most important factor, it may not be viewed a major discriminator in choosing one platform against another. This because all currently used stents perform similarly and acceptable performance would be considered as a basic requirement for any stent. Similarly, it was noted that while the ability to deliver a stent is crucial, all stents that are currently used are excellent in terms of deliverability and procedural success will be achieved similarly in all stent platforms and so because it is less of an issue in practice, procedural success could be ranked lower. Some noted that if stents can be considered

equal in all other criteria, cost becomes central to the final decision, Some noted that they would have placed the suitability for 1-month dual antiplatelet therapy (DAPT) much higher in the list, higher for example than procedural success. Some noted that it is challenging to rank suitability for 1-month DAPT especially on a patient-level because it is not a blanket response to cover all patients. In cases where the risk of bleeding is an important issue and will override some other considerations, you would assign a higher value to this feature. But in others, bleeding is not an issue and therefore reduced DAPT has no relevance. During the workshop, some cardiologists estimated that around 10% patients they see would benefit from reduced DAPT. It was noted that published registry data suggests that this population overall may be as high as 40% to 50% of the patients. The anonymised individual responses from the ranking exercise are shown in appendix D (tables 4 and 5).

Weighting criteria

After ranking the criteria, the participants individually assigned weights to the 2 sets of ordered criteria. Table 2 and 3 show the final weights, averaged from the individual weightings. On the patient-level list, stent failure was unanimously twice as important as the next item down the list, the suitable size. Stent failure carried nearly 50% of the total weight of the list. On the contract level, stent failure shared the 50% weight of the total list weight with stent matrix to cover most cases. Some participants noted it was difficult to weigh the items without the possibility of changing the order of importance. The anonymised individual responses from the weighting exercise are shown in appendix E (tables 6 and 7).

Table 2: Patient-level criteria ranked in order of importance

Order of importance	Weight	Criteria	Definition	Performance rule
1	45%	Stent failure	Stent has evidence on thrombosis, in-stent restenosis, target lesion failure	Section 5.1 on pages 39 to 50 of the external assessment report (EAR) summarises clinical outcomes in the key RCTs identified for this late-stage assessment
2	23%	Suitable size (including expansion capability)	Availability in a suitable length and diameter, over expansion up to manufacturer limits	Suitable size depends on vessel and lesion characteristics
3	18%	Procedural success	Stent has evidence for procedural success. This may include radial strength, visibility under imaging (many variables affect this, for example age of equipment being used) and deliverability.	Section 6.3 on pages 83 to 86 of the EAR summarises procedural outcomes in the key RCTs identified for this late-stage assessment
4	14%	Suitability for people having abbreviated 1-month dual antiplatelet therapy (DAPT)	Stent has clinical evidence for safety in people (with high bleeding risk or not) having abbreviated 1-month DAPT	Section 6.2 on pages 81 and 82 of the EAR summarises evidence comparing different length DAPT regimens for people having PCI with a stent or stents in the scope of this late-stage assessment

Table 3: Contract-level criteria ranked in order of importance

Order of importance	Weight	Criteria	Definition	Performance rule
1	26%	Size matrix covers most cases (workhorse)	Available in diameters from 2.25 to 4mm that can be dilated to maximum 5.5mm and lengths from 8 to 38mm. Suitable size matrix to cover most lesions and vessels.	Size matrix that is likely to cover most lesions and vessels is noted in the definition. To confirm this is the case, data on the vessel and lesion characteristics or stent sizes used would be needed.
2	26%	Stent failure	Stent has evidence on thrombosis, in-stent restenosis, target lesion failure	Section 5.1 on pages 39 to 50 of the external assessment report (EAR) summarises clinical outcomes in the key RCTs identified for this late-stage assessment
3	16%	Procedural success	Stent has evidence on procedural success. This may include radial strength, visibility under imaging (many variables affect this, for example age of equipment being used) and deliverability	Section 6.3 on pages 83 to 86 of the EAR summarises procedural outcomes in the key RCTs identified for this late-stage assessment
4	12%	Cost	Lowest cost (may include consideration of for example bundling with other devices)	Criterion is captured in the external assessment group's evidence review and model
5	12%	Suitability for people having abbreviated 1-month dual antiplatelet therapy (DAPT)	Stent has clinical evidence for safety in people (with high bleeding risk or not) having abbreviated 1-month DAPT	Section 6.2 on pages 81 and 82 of the EAR summarises evidence comparing different length DAPT regimens for people having PCI with a stent or stents in the scope of this late-stage assessment
6	9%	Size matrix covers extreme cases	Extra-long stents (up to 48mm) or large diameter (up to 6.25mm) for minority of cases	Size matrix that is likely to be cover extreme cases is noted in the definition

Discussion

A group of interventional cardiologists participated in this user preference assessment to explore what is important when they consider which drug-eluting coronary stent to use. They identified a set of 4 criteria at the patient-level after the decision about the treatment with stents has been made. They also identified a set of 6 criteria that are important when choosing typically 2 to 3 different stents to have available to cover most cases they expect to treat. High on both lists were stent failure and suitable stent size. Suitability for people having abbreviated 1-month DAPT and procedural success also featured on both lists. Clinical evidence was key for measuring performance against most criteria.

This user preference assessment has several strengths. The assessment reflected current practice in that it assessed user preferences at both main points when choice about which stent to use is made. The participants were from NHS trusts across different regions of England and all had experience in using a variety of different drug-eluting coronary stents in clinical practice. The engagement level of the group was good throughout the assessment.

There are also some limitations to this work. While the consensus on the items on the criteria was pretty good, it did not hold when the participants ranked the items on each list in order of importance. This was mainly because some participants ranked the items they expected to differentiate between the stents higher than the items they expected to be similar between the stents (for example stent failure or procedural success). This meant that not everyone agreed with the final ranking that averaged the individual rankings. Because of this, some participants found it difficult to assign proportionate weights that were relative to a criterion higher up on the ranked list to criteria that in their view would have been more important than the item above.

The group noted, that at a patient-level, one of the criteria suitability for people having abbreviated 1-month DAPT, may not be important in all cases when choosing which stent to use. It would only be important if there was a prospect of 1-month DAPT. Future assessments could, in addition to overall criteria,

consider determining subgroup-specific criteria for example for the subgroups considered important in the scope.

In addition to interventional cardiologists, the contracts for which stents may be available to cover most cases are negotiated together with the purchasing partners. Future assessments looking at this contract-level criteria, could consider including other people who are involved in the purchasing to the user group assessment. Although they are not users of stents, they may bring in further factors that are important in the decision-making on which stents to have available.

This user preference assessment provides transparent insight into the types of user preference considerations there may be when choosing which stent to use. Based on this assessment, most of the criteria that are important to interventional cardiologists are among the clinical or intermediate outcomes in the scope of the external assessment group's clinical and cost-effectiveness assessment. This user preference assessment highlights that the users consider clinical evidence as an important measure of performance.

Appendix A: Participants' experience with the drug-eluting coronary stents in the assessment

Manufacturer	Technology	1	2	3	4	5	6	7	Total
Abbott Medical	XIENCE PRO 48	x	x	x	x	x	x	x	7
Abbott Medical	XIENCE PRO S	x		x	x	x	x	x	6
Abbott Medical	Skypoint	x		x	x	x	x	x	6
Abbott Medical	XIENCE Skypoint 48	x		x	x	x	x	x	6
Abbott Medical	XIENCE Skypoint LV	x		x	x	x		x	5
B. Braun Medical	Coroflex ISAR NEO								0
Biosensors International	BioFreedom		x	x	x	x	x	x	6
Biosensors International	BioMatrix Alpha			x		x	x	x	4
Biosensors International	BioFreedom Ultra			x		x	x	x	4
Biotronik	Orsiro Mission					x			1
Biotronik	Synsiro Pro							x	1
Boston Scientific	Promus ELITE	x	x	x	x	x	x	x	7
Boston Scientific	Synergy MEGATRON	x		x		x	x	x	5
Boston Scientific	Synergy XD	x	x	x	x	x	x	x	7
Cardionovum	XLIMUS								0
IHT	ihtDEStiny BD								0
iVascular	Angiolite								0
Medtronic	Onyx Frontier	x	x		x	x		x	6
Meril	BioMime			x					1
Meril	BioMime Branch								0
Meril	BioMime Morph								0
Meril	EverMine 50								0
Microport	Firehawk							x	1
Microport	Firehawk Liberty							x	1
QualiMed	MAGMA								1
Sahajanand Medical Technologies	Supraflex Cruz	x			x	x		x	4
Sahajanand Medical Technologies	Supraflex Cruz Nevo	x			x	x		x	4
Terumo	Ultimaster Nagomi	x		x		x			3
Terumo	Ultimaster Tansei	x		x		x			3

Appendix B: Participants

Joel Giblett, Cardiologist and Honorary Senior Clinical Lecturer, Liverpool Heart and Chest Hospital

Stephen Hoole, Affiliated Associate Professor, University of Cambridge and Consultant Interventional Cardiologist, Royal Papworth Hospital NHS Foundation Trust

Mamas Mamas, Professor of Cardiology, Keele University and Honorary Consultant Interventional Cardiologist, Royal Stoke Hospital

Abdul Mozid, Consultant Cardiologist, Yorkshire Heart Centre, Leeds Teaching Hospitals NHS Trust

Adnan Nadir, Consultant Cardiologist Coronary & Structural Heart Interventions, Queen Elizabeth Hospital, Birmingham

Ian Purcell, Consultant Interventional Cardiologist, Freeman Hospital, Newcastle upon Tyne

Sudhir Rathore, Consultant Interventional Cardiologist, Frimley Health NHS Foundation Trust, Camberley, Surrey and Honorary Reader, University of Surrey

Appendix C: Glossary

Term	Definition
SMART ranking technique	A multi-criteria decision-making technique that allows criteria to be ordered by importance. Individual responses from each member of a group are collated and averaged, ensuring equal say among the group (Von Winterfeldt D, Edwards W. (1993) Decision analysis and behavioural research. Cambridge: Cambridge University Press).
Swing weighting technique	A technique used for calculating and reporting the relative importance (weight) of each criterion from a ranked list. Each member of a group provides individual responses deciding how important each criterion is over the criterion below it (on a scale of 0-100%). Individual responses from each member of the sample are collated, averaged and weights are calculated (Von Winterfeldt D, Edwards W. (1993) Decision analysis and behavioral research. Cambridge: Cambridge University Press).
Performance rule	A rule (or rules) describing how users would measure the performance of a technology in relation to each criterion.
Performance matrix	A table reporting the criteria most important to users when choosing a technology and the associated performance rules.

Appendix D: Individual responses and variation in criteria ranking

Table 4: individual user responses for criteria ranking patient level

Criteria	1	2	3	4	5	Mean	SD	Final rank
Stent failure	1	1	1	2	3	1.60	0.89	1
Suitable size (including expansion capability)	3	2	2	1	1	1.80	0.84	2
Procedural success	2	4	4	4	2	3.20	1.10	3
Suitability for people having abbreviated 1-month DAPT	4	3	3	3	4	3.40	0.55	4

Table 5: individual user responses for criteria ranking contract level

Criteria	1	2	3	4	5	Mean	SD	Final rank
Size matrix covers most cases (workhorse)	4	2	2	1	1	2.00	1.22	1
Stent failure	1	6	1	3	3	2.80	2.05	2
Procedural success	2	5	5	5	2	3.80	1.64	3
Cost	3	1	6	4	6	4.00	2.12	4
Suitability for people having abbreviated 1-month DAPT	5	3	3	6	4	4.20	1.30	5
Size matrix covers extreme cases	6	4	4	2	5	4.20	1.48	6

The criteria ‘Suitability for people having abbreviated 1-month DAPT’ and ‘Size matrix covers extreme cases’ had the same average rank. Because the variation around the mean for ‘Suitability for people having abbreviated 1-month DAPT’ was slightly smaller than that for ‘Size matrix covers extreme cases’, it was given the higher final rank.

Appendix E: Individual responses and variation in criteria weighting

Table 6: Individual responses to criteria weighting patient level

Criteria	1	2	3	4	5	6	Mean importance	SD	Final weight
Stent failure	100	100	100	100	100	100	100.00	0.00	45%
Suitable size (including expansion capability)	25	0	50	50	25	0	25.00	22.36	23%
Procedural success	0	0	0	0	100	100	33.33	51.64	18%
Suitability for people having abbreviated 1-month DAPT									14%

Table 7: Individual responses to criteria weighting contract level

Criteria	1	2	3	4	5	6	Mean importance	SD	Final weight
Size matrix covers most cases (workhorse)	0	0	-75 (0)	0	0	0	0.00	0.00	26%
Stent failure	0	100	150 (100)	100	100	0	66.67	51.64	26%
Procedural success	0	0	-200 (0)	0	100	100	33.33	51.64	16%
Cost	0	0	-50 (0)	0	0	0	0.00	0.00	12%
Suitability for people having abbreviated 1-month DAPT	0	0	25	50	100	0	29.17	40.05	12%
Size matrix covers extreme cases	0	0	0	0	0	0	0.00	0.00	9%

Weights given outside the weighting range (0 to 100%) were normalised to the closest end of the range. The normalised scores that were used in the calculation of the final weight are shown in brackets.

NICE National Institute for Health and Care Excellence

Advisory Committee Interests Register

Topic: Drug-eluting coronary stents for treating coronary artery disease

NICE's declaration of interest policy can be accessed here

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comment
Adnan Nadir	Specialist Committee Member	Financial interest	Private Practice	29/06/2022	30/05/2024	Ongoing	No action other than open declaration
Ferrah Choudary	Specialist Committee Member	N/A	Nothing to declare	-	29/05/2024	-	No action other than open declaration
Helen Titu	Specialist Committee Member	N/A	Nothing to declare	-	27/05/2024	-	No action other than open declaration
Ian Purcell	Specialist Committee Member	Non-financial professional and personal interest	Member of British Cardiovascular Intervention Society clinical standards group	2020	24/05/2024	Ongoing	No action other than open declaration
Ian Purcell	Specialist Committee Member	Non-financial professional and personal interest	Clinical Lead for Cardiac Services in North East and Yorkshire Region	June 2024	24/05/2024	Ongoing	No action other than open declaration
Joel Giblett	Specialist Committee Member	Financial interest	I undertake a small private practice in cardiology seeing patients in the Rowan Suite at Liverpool Heart and Chest Hospital	01/04/2023	21/05/2024	Ongoing	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comment
Stephen Hoole	Specialist Committee Member	Financial interest	Director Radial Cradle Ltd	2016	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Medical advisor to Octiocor Ltd	2024	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Medical advisor to Plaquetec Ltd	2013	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Private/ Medicolegal Practice	2011	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Medical advisor to MHRA	2016	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Research grants Moulton Charity, EU Horizons 2020 and 2021, BHF, NNF	2018	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Research grants MRC DPFS	2016	03/05/2024	2024	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Financial interest	Research grants Abbott Vascular	2015	03/05/2024	2022	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comment
Stephen Hoole	Specialist Committee Member	Financial interest	Research grants AZ	2015	03/05/2024	2020	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Non-financial professional and personal interest	Chair NCG OA Guideline	2017	03/05/2024	2022	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Non-financial professional and personal interest	Member, NCG Chest pain Guideline	2016	03/05/2024	2017	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Indirect interest	Royal Papworth Hospital NHSFT	2011	03/05/2024	Ongoing	No action other than open declaration
Stephen Hoole	Specialist Committee Member	Indirect interest	NICE Committees		03/05/2024		No action other than open declaration
Sudhir Rathmore	Specialist Committee Member	N/A	Nothing to declare	-	03/05/2024	-	No action other than open declaration
Abdul Mozid	Expert	Financial interest	Received speaker fees from SMT and Abbott	2022	11/07/2024	Ongoing	No action other than open declaration
Abdul Mozid	Expert	Financial interest	Received proctoring fees from Boston Scientific	2021	11/07/2024	Ongoing	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comment
Dawn Adamson	Expert	Non-financial professional and personal interest	National speciality advisor for heart disease for NHS England	03/01/2023	23/08/2024	Ongoing	No action other than open declaration
Mamas Mamas	Expert	Financial interest	Abbott Vascular- unrestricted educational grant to support PhD student at keele university	2020	11/09/2024	Ongoing	No action other than open declaration
Mamas Mamas	Expert	Financial interest	Biosensors - speaker fees	2020	11/09/2024	Ongoing	Verbal declaration and remain for part 1
Mamas Mamas	Expert	Financial interest	Terumo- unrestricted educational grant to support PhD student at keele university and speaker fees	2020	11/09/2024	Ongoing	Verbal declaration and remain for part 1
Mamas Mamas	Expert	Financial interest	Boehringer Ingelheim- consulting, safety endpoint committee chair	2023	11/09/2024	Ongoing	No action other than open declaration
Mamas Mamas	Expert	Financial interest	Amgen speaker fees	2021	11/09/2024	Ongoing	No action other than open declaration
Mamas Mamas	Expert	Financial interest	Astra Zeneca- consulting	2022	11/09/2024	2023	No action other than open declaration
Mamas Mamas	Expert	Non-financial professional and person interest	BCIS National audit lead	2022	11/09/2024	Ongoing	No action other than open declaration

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comment
Mamas Mamas	Expert	Non-financial professional and person interest	AHA interventional council	2023	11/09/2024	Ongoing	No action other than open declaration
Mamas Mamas	Expert	Non-financial professional and person interest	Circulation Cardiovascular Interventions Associate Editor	2019	11/09/2024	Ongoing	No action other than open declaration