NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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

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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.

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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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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.

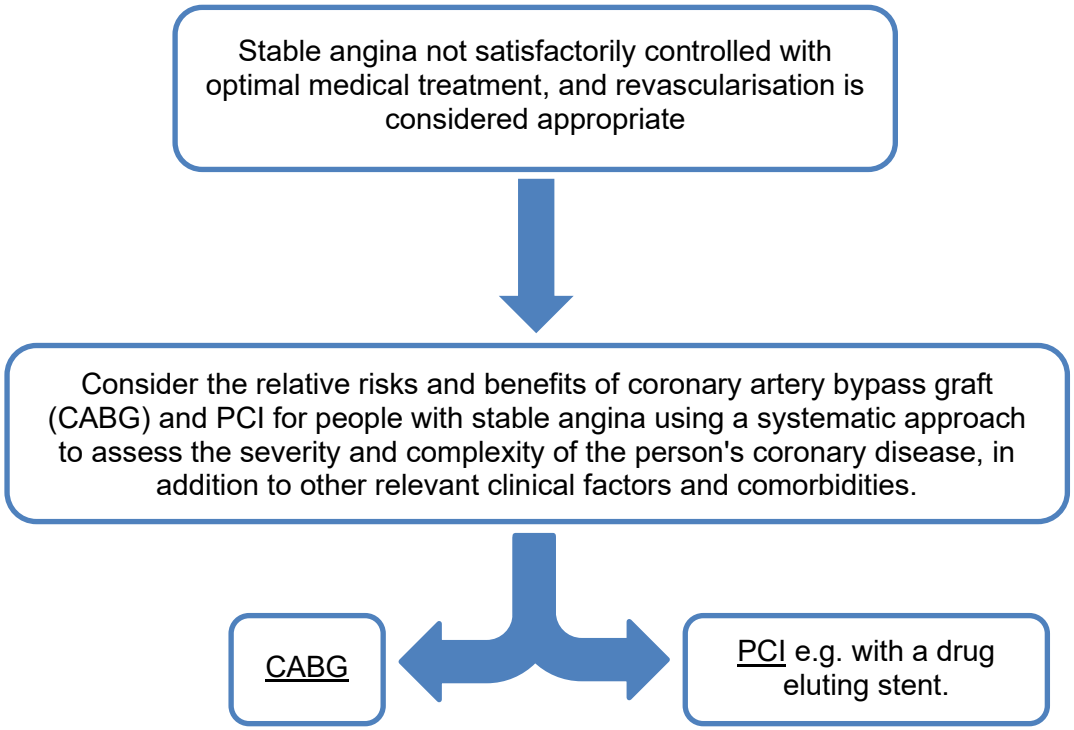


Figure 1: Simplified stable angina clinical pathway.

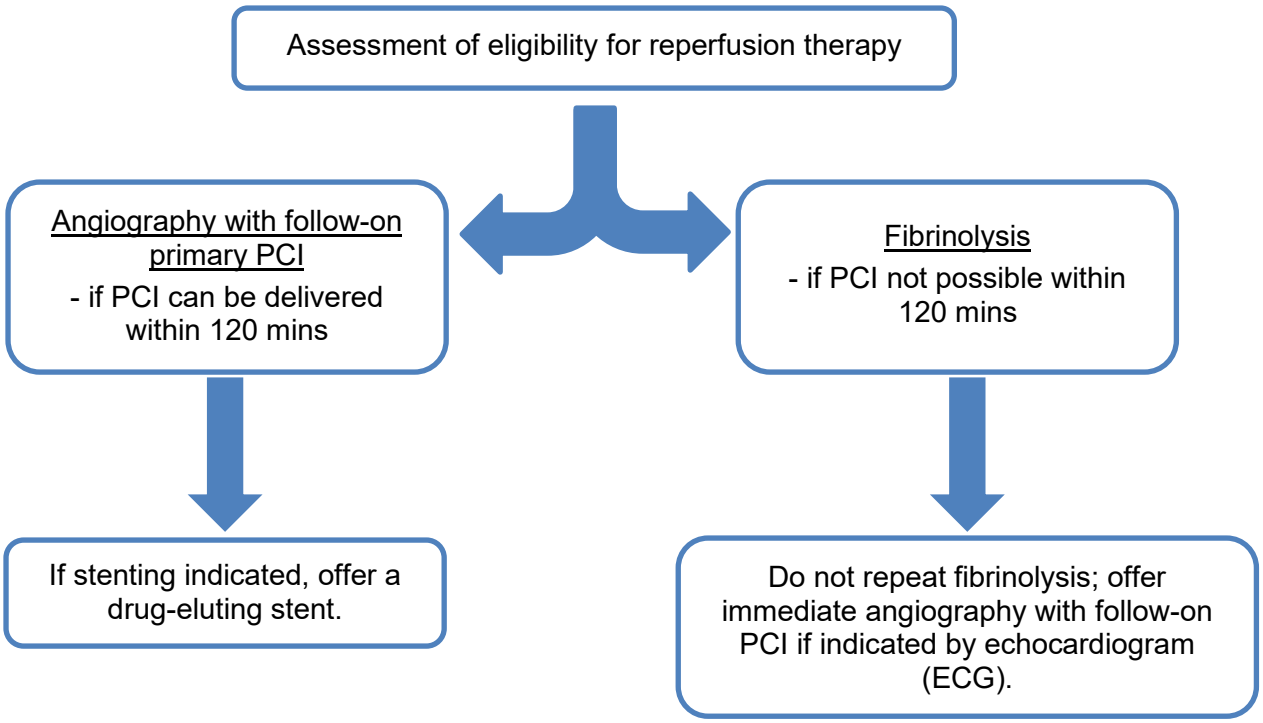


Figure 2: Simplified STEMI clinical pathway.

NSTEMI/unstable angina

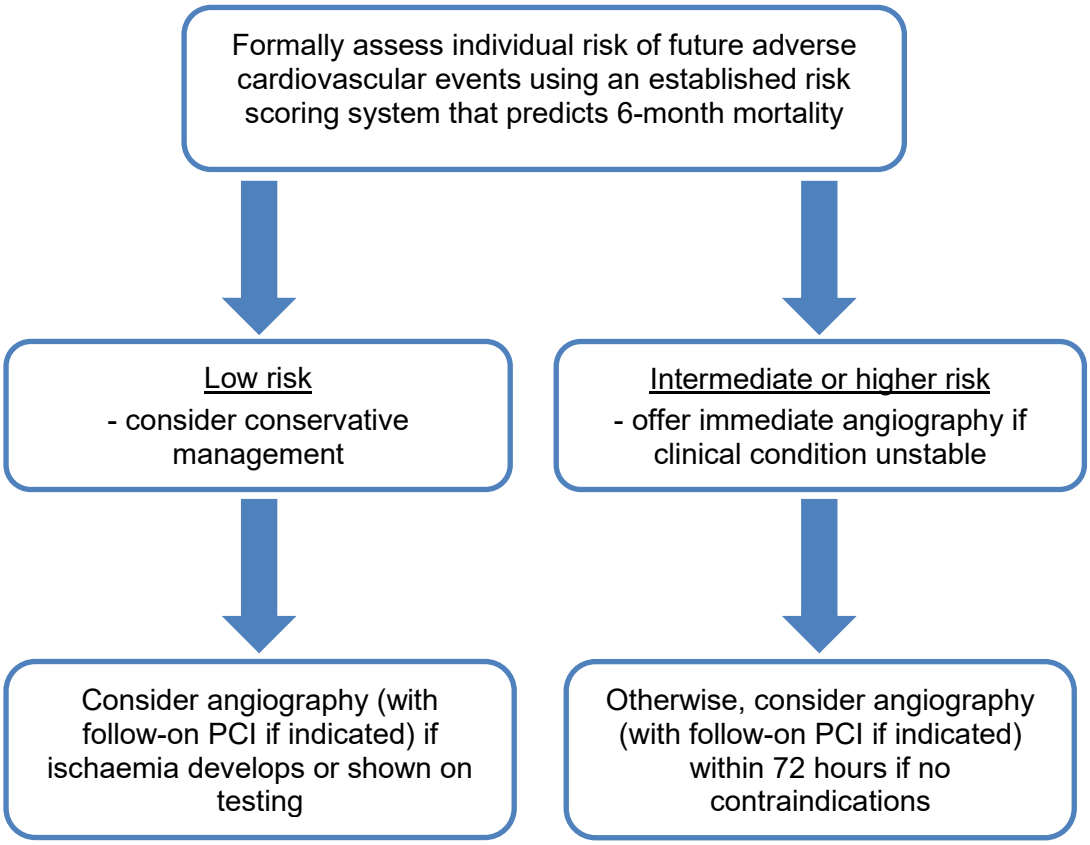


Figure 3: Simplified NSTEMI/unstable angina clinical pathway.

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.*

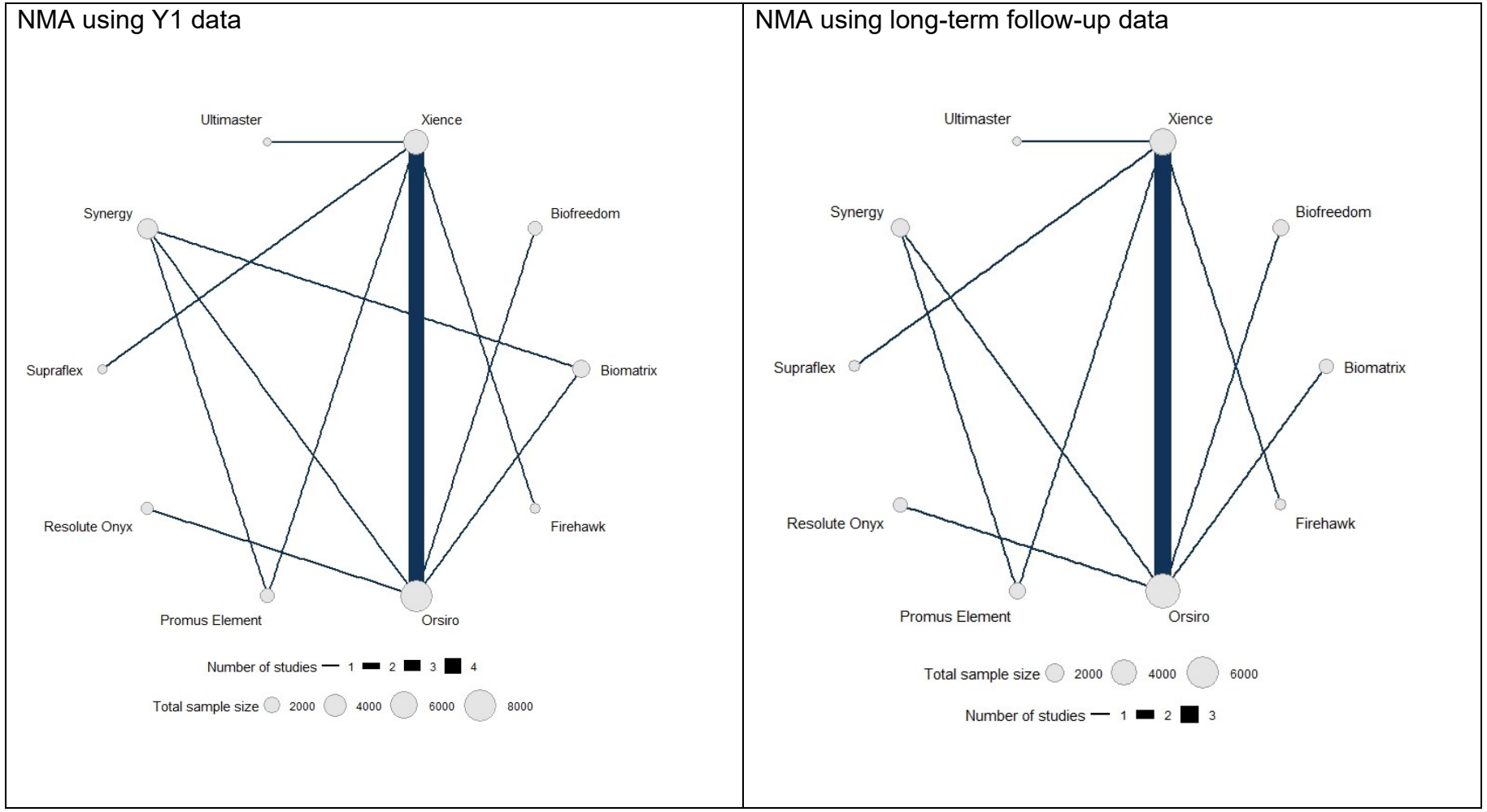


Figure 4: Network meta-analysis plot.

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.

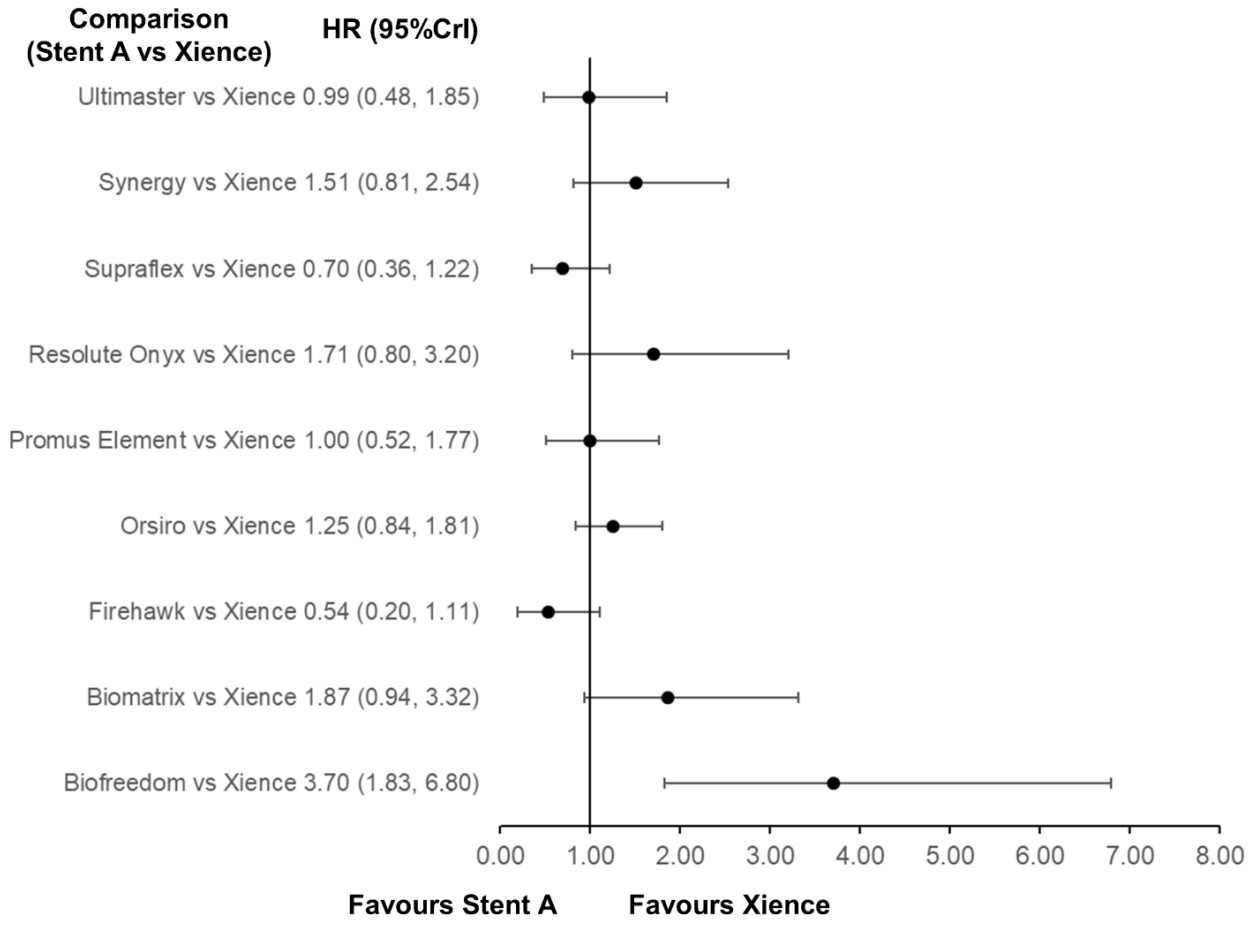
While both the uncertainty around the relative effects and between-study SD are higher with the use of a higher prior heterogeneity distribution, the overall conclusions on their relative effect remain the same.

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):

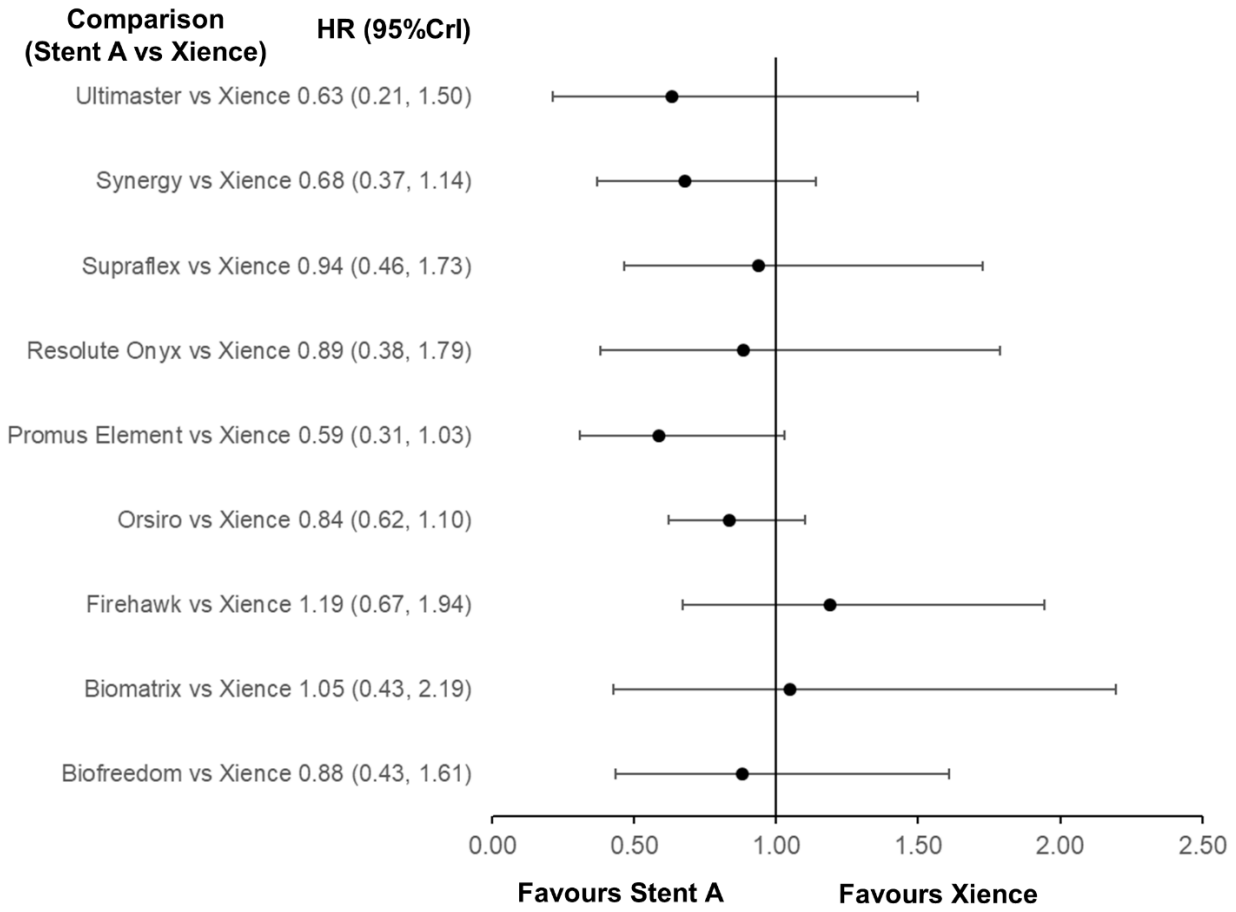


Figure 5: Forest plots: First-year follow-up (HR with CrI)

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

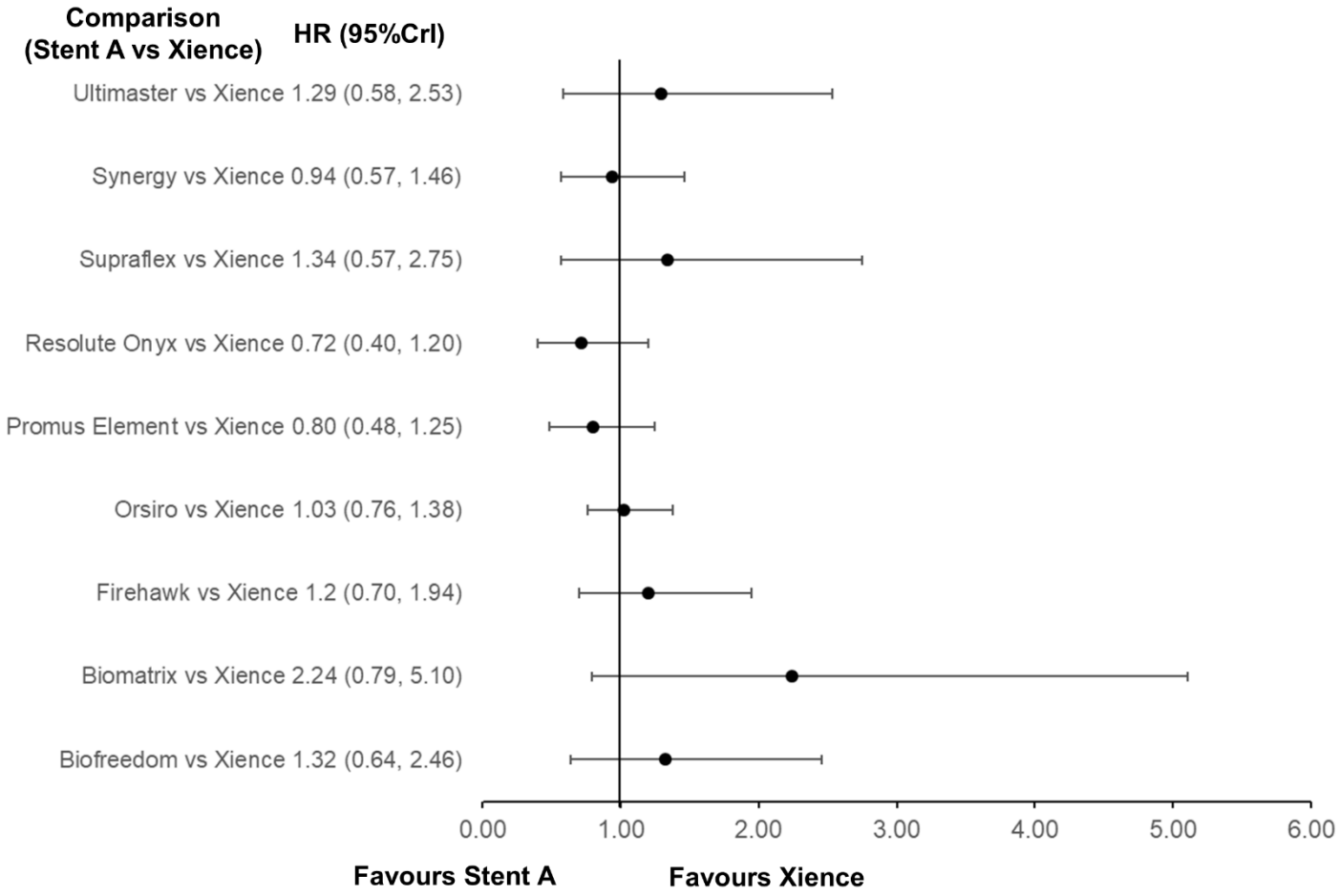
single comparison (Orsiro vs Xience) was explored in 4 studies, and one fewer trial reported outcomes at longer follow-up than in Y1. Thus, HRs from longer-term follow-up NMAs had wider CrIs than for Y1 NMA because the sparse data from very few studies were insufficient to estimate between-study posterior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

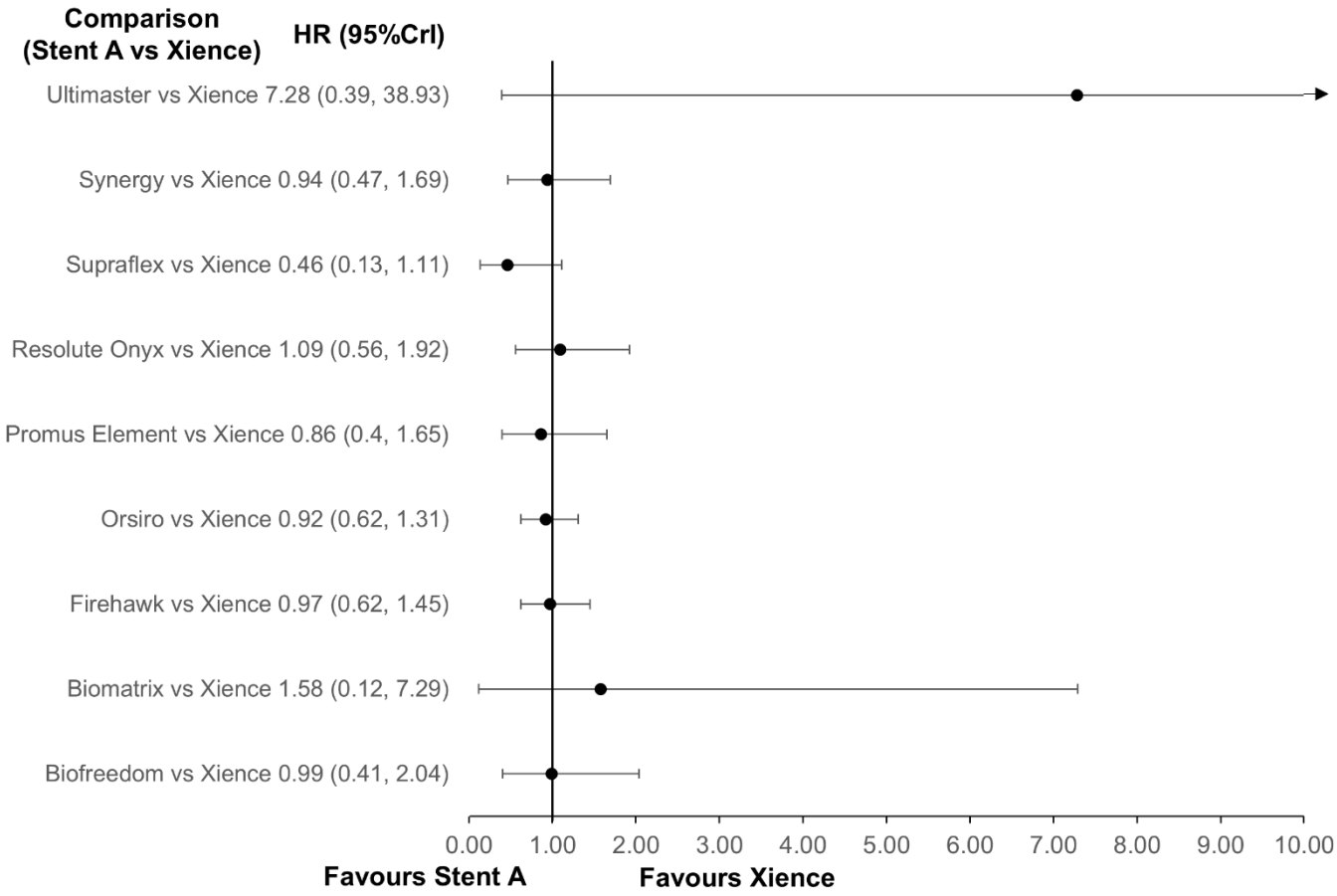


Figure 6: Forest plots: Long-term follow-up (HR with 95% CrI)

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

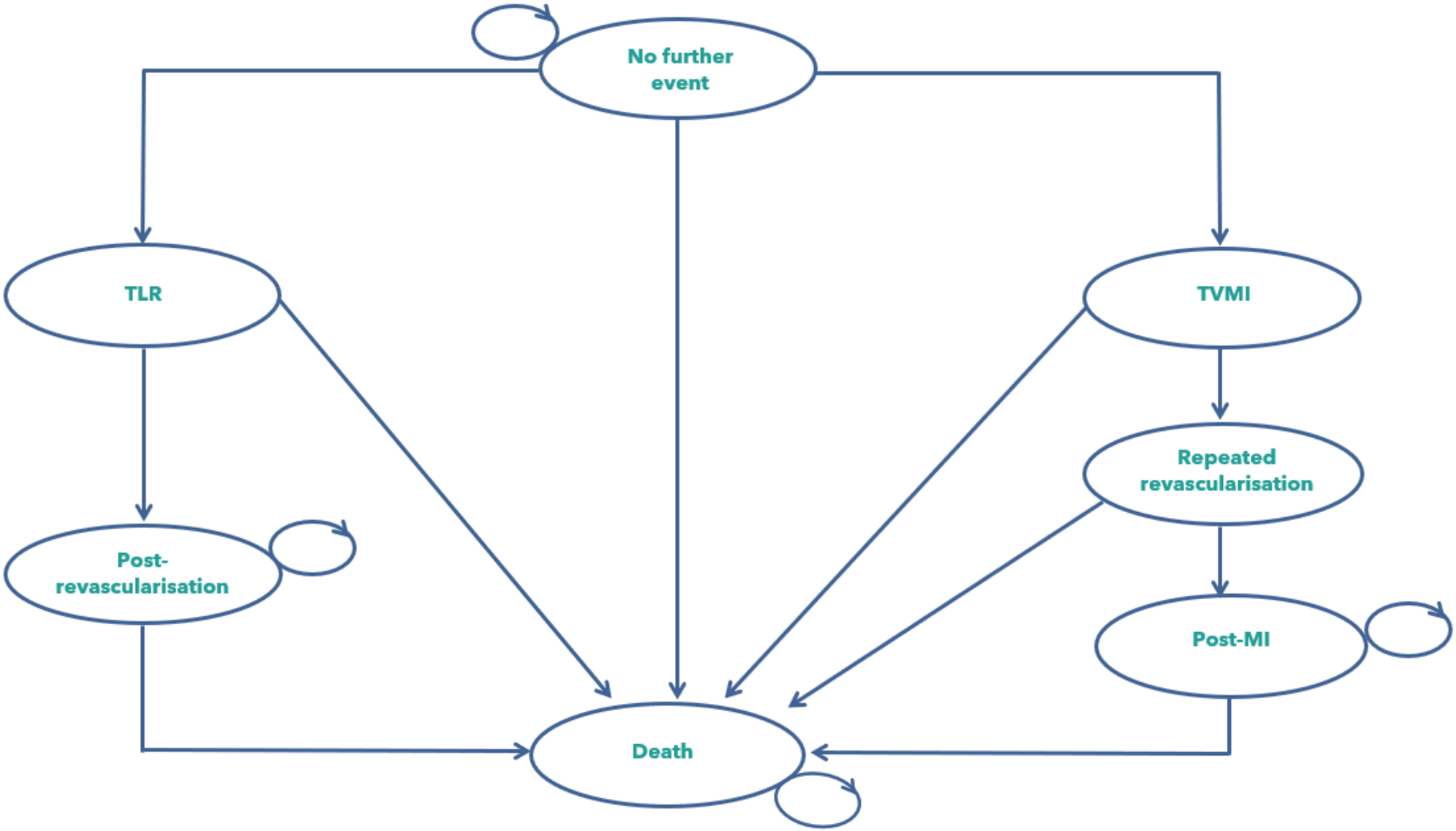


Figure 7: Schematic representation of the EAG economic model

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.*

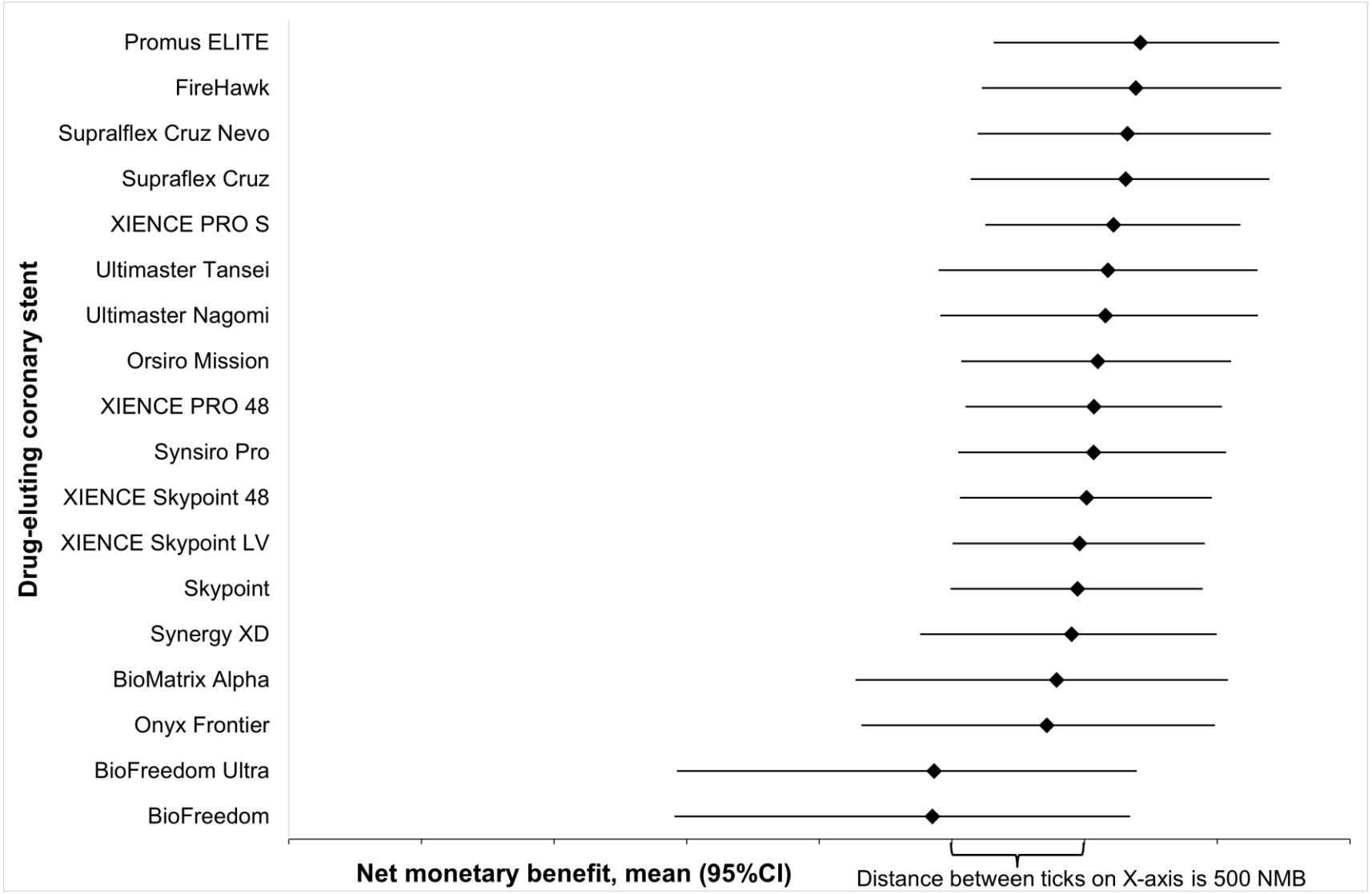


Figure 8: Net monetary benefit of each device at WTP £20,000, mean and (95%CI) [the figure has been partly redacted]

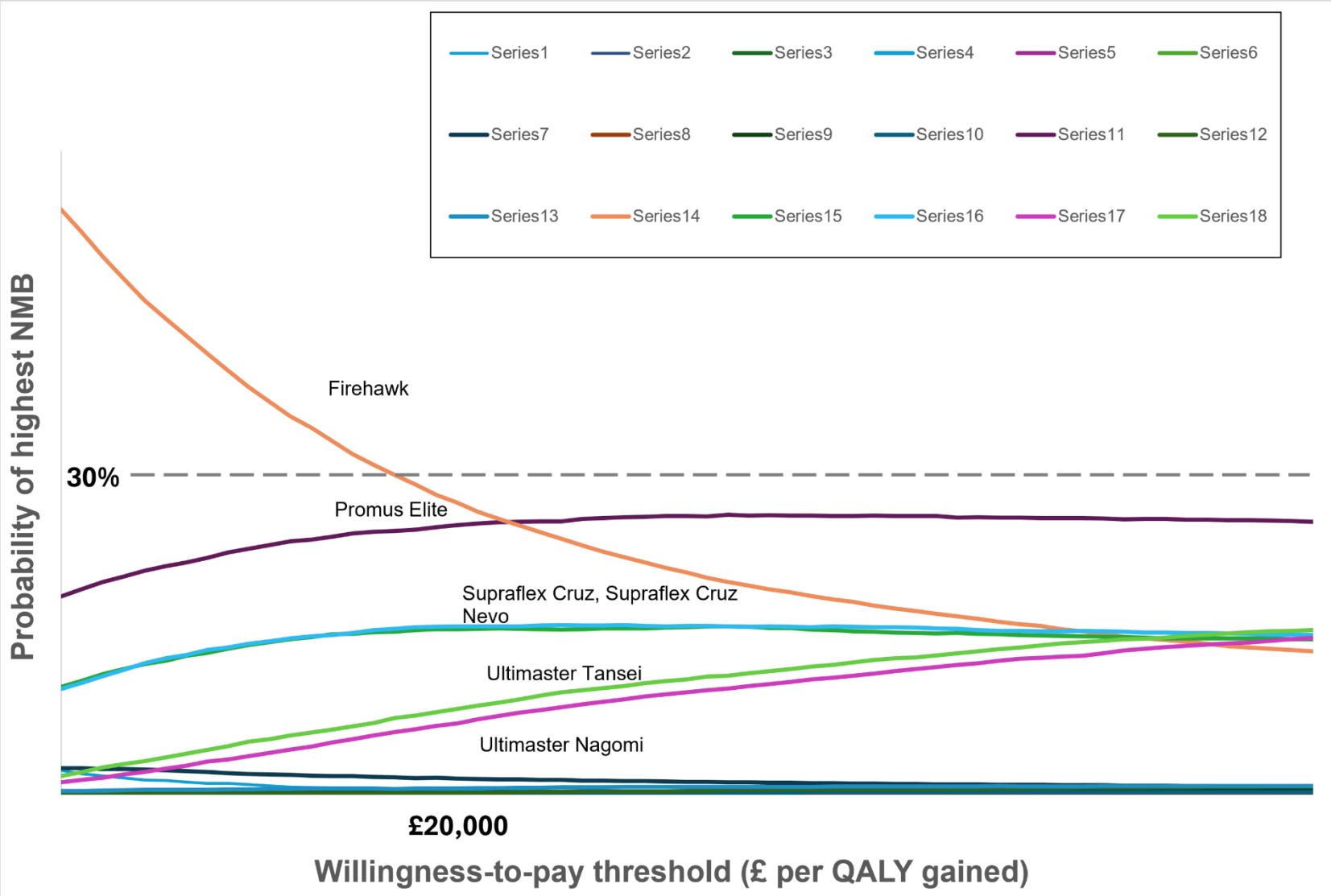


Figure 9: Cost-effectiveness acceptability curve [the figure has been partly redacted]

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.

13 References

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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

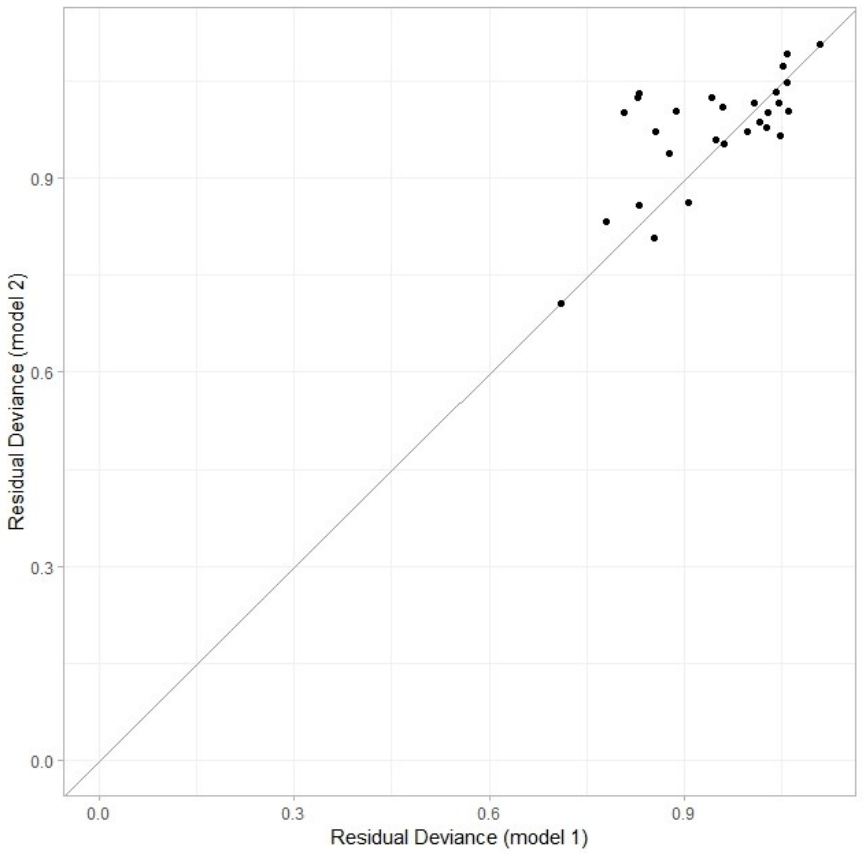
Notes:

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

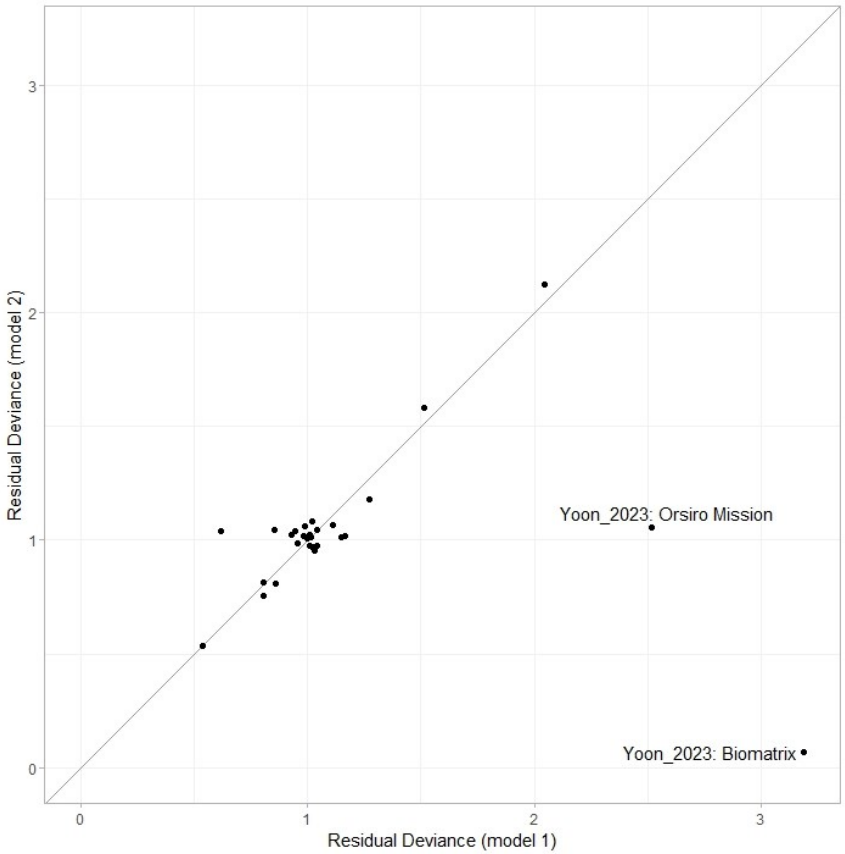
Abbreviations*: DIC: Deviance Information Criterion; FE: fixed effects; NMA: network meta-analysis; pD: effective number of parameters; RE: random effects; SD: standard deviation; TLR: target lesion revascularisation; TVMI: target vessel-related myocardial infarction; UME: unrelated mean effects.*

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

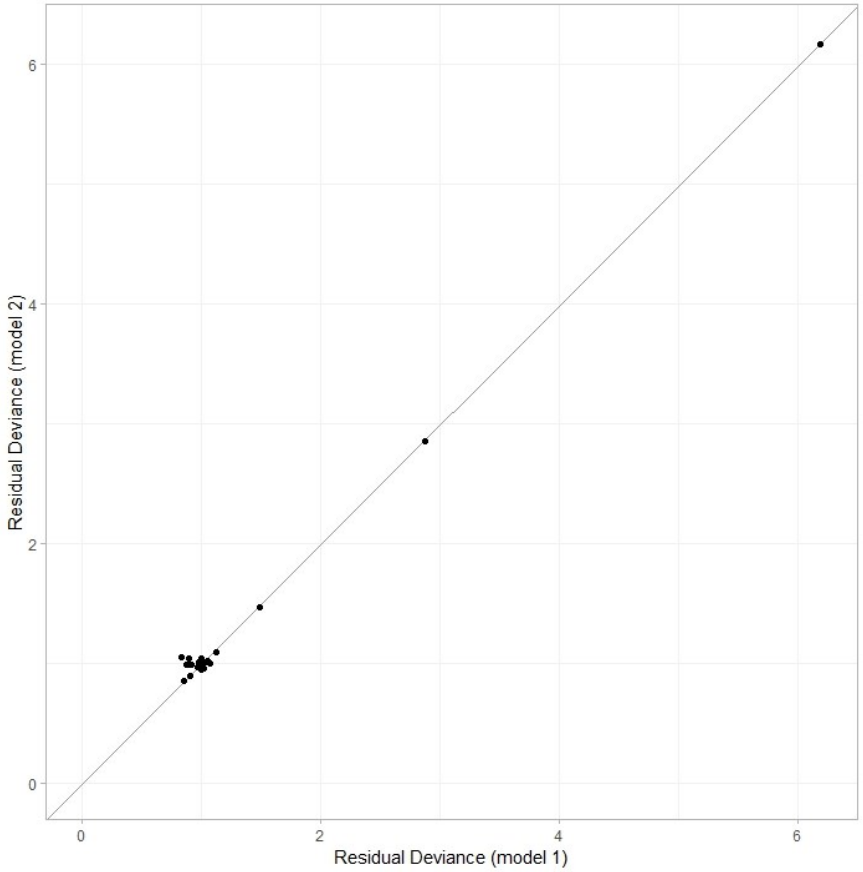
Y1 NMA: TLR



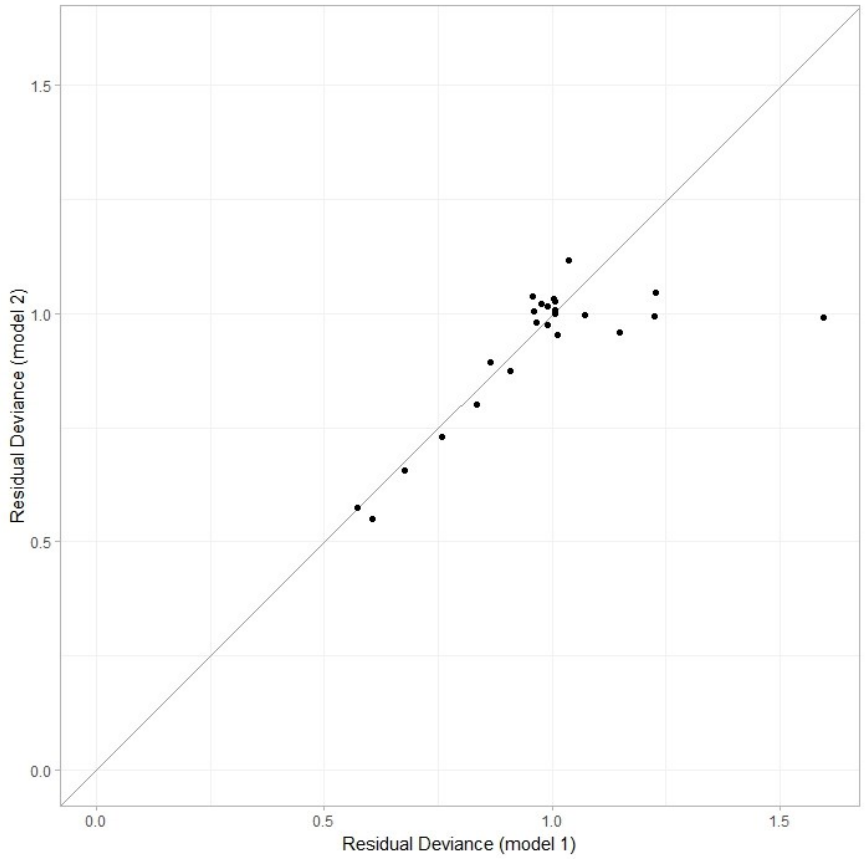
Y1 NMA: TVMI



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.

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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.*