NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

HEALTHTECH PROGRAMME

Draft guidance

Drug-eluting stents for treating coronary artery disease

Guidance development process

Late-stage assessment (LSA) guidance evaluates categories of technologies that are already in widespread use within the NHS. It assesses whether price variations between technologies in a category are justified by differences in innovation, clinical effectiveness and patient benefits. This will support NHS commissioners, procurement teams and healthcare professionals to choose technologies that maximise clinical effectiveness and value for money.

Find out more on the NICE webpage on late-stage assessment (LSA) for medtech.

NICE is producing this late-stage assessment guidance on drug-eluting stents in the NHS in England. The medical technologies advisory committee has considered the evidence and the views of experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence.

The committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

After consultation:

- Based on the consultation comments received, the committee may meet again.
- If committee meet again it will consider the evidence, this evaluation consultation document and comments from stakeholders.
- The committee will then prepare the final draft guidance, which will go through a resolution process before the final guidance is agreed.

Note that this document is not NICE's final late-stage assessment guidance on drug-eluting stents. The recommendations in section 1 may change after consultation.

More details are available in NICE's health technology evaluations: the manual and NICE's late-stage assessment interim process and methods statement.

Key dates for this late-stage assessment:

- **Closing date for comments**: 20 January 2025
- **Second committee meeting**: 27 February 2025

1 Recommendations

1.1 NHS trusts should provide access to a range of drug-eluting stents, so that a clinically appropriate stent is available for everyone with coronary artery disease.

1.2 Evidence shows that stents are comparable in terms of clinical and cost effectiveness, and that there is no justification for price variation.

1.3 If more than one drug-eluting stent is clinically appropriate, choose the least expensive stent.

What information is needed

More information is needed to justify price variation between different drug-eluting stents. This can be from primary studies or secondary analyses of real-world data.

Key outcomes and information that should be captured include:

- intervention-related adverse events
- major adverse cardiac events (MACE)
- target lesion or vessel failure
- acute and chronic stent failure
- target lesion and target vessel revascularisation
- restenosis and stent thrombosis
- the drug-eluting stent used.

All studies and analyses of real-world data should adjust for a range of confounding factors, including:

- the impact of anatomical characteristics of the target vessel and lesion
- the person's age, sex, ethnicity and medical history.

What this means in practice

Procurement and commissioning considerations

- Although alternative treatments (such as drug-eluting balloons) are in use, clinical experts predict that stents will remain the main treatment for coronary artery disease. So, it is important that the NHS continues to ensure the best value for money when buying drug-eluting stents.
- If a company introduces a new drug-eluting stent with new features to the market, evidence of clinical superiority should be provided to show additional value. This evidence would ideally be from a randomised controlled trial.
- If a company introduces a new drug-eluting stent or a new generation of the technology with minor improvements, evidence of clinical non-inferiority is sufficient.

Healthcare professional considerations

- When choosing a clinically appropriate drug-eluting stent, healthcare professionals should consider the patient, vessel and lesion characteristics, comorbidities and other factors that can make a stent more suitable.
- Healthcare professionals should work with commissioners and procurement specialists in their NHS trust to ensure access to a range of stents.

Why the committee made these recommendations

Drug-eluting stents are the main treatment to restore blood flow after a heart attack and to reduce the symptoms of coronary artery disease. NHS trusts have access to a range of drug-eluting stents to ensure that a clinically appropriate stent is always available, and this should continue.

Clinical trial evidence shows that different stents had similar clinical outcomes for people with coronary artery disease. There is no concern about the overall

cost-effectiveness of stents. But because there is uncertainty about the cost effectiveness estimates, it is not possible to determine whether some drug-eluting stents are more cost-effective than others. To show any additional value for new stents, more evidence comparing different drug-eluting stents would be needed.

2 The technology

2.1 A build-up of fatty substances in the coronary arteries may reduce blood supply to the heart, causing coronary artery disease. To restore blood flow, a drug-eluting stent can be inserted into a coronary artery during percutaneous coronary intervention (PCI).

2.2 Drug-eluting stents are made from metal and coated with an antiproliferative drug. These vary between stents. In some stents the drug is applied on a durable or absorbable polymer, whereas others are polymer free. Each drug-eluting stent has an instructions for use (IFU) document that includes the indications for which the device can be used. The indications for use vary and may specify subpopulations or lesion types. They often specify the size of vessels the stent can be used for. Some stents can be purchased for use in specific cases because they are indicated for a particular subpopulation or lesion type, or because they have certain design features.

2.3 This assessment included 29 drug-eluting stents (table 1) available through the NHS Supply Chain. Each stent had valid CE certification as a class 3 implantable device.

Table 1 Drug-eluting stents for treating coronary artery disease

Manufacturer	Technology	Scaffold material	Polymer type	Drug
Abbott Medical	XIENCE PRO 48	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE PRO S	Cobalt chromium	Durable	Everolimus
Abbott Medical	Skypoint	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE Skypoint 48	Cobalt chromium	Durable	Everolimus
Abbott Medical	XIENCE Skypoint LV	Cobalt chromium	Durable	Everolimus
B. Braun Medical	Coroflex ISAR NEO	Cobalt chromium	Polymer free	Sirolimus

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

Terumo	Ultimaster Tansei	Cobalt chromium	Biodegradable	Sirolimus

3 Committee discussion

The medical technologies advisory committee considered evidence on drug-eluting stents for treating coronary artery disease from several sources. This included company submissions, targeted reviews of published literature, and stakeholder comments on the assessment reports. Full details are available in the project documents for this guidance.

The condition

3.0 Around 2.3 million people in the UK have coronary artery disease. The condition is caused by a build-up of fatty substances in the coronary arteries, at locations known as lesions. This can reduce blood supply to the heart. A typical symptom is angina. This is chest pain that can be exacerbated by exertion (stable angina) or is unpredictable (unstable angina). A critical reduction in blood supply to the heart may result in myocardial infarction (heart attack) or death.

Current practice

3.1 To restore blood flow in coronary artery disease, a drug-eluting stent can be inserted into a coronary artery during percutaneous coronary intervention (PCI). PCI and stents are used to treat both stable angina and acute coronary syndromes.

3.2 In 2023, around 65% of the spend on drug-eluting stents within the NHS was directed through the NHS Supply Chain. The clinical experts explained that contracts for stents at NHS trusts typically include 2 or 3 drug-eluting stents that can be used across various types of lesions. A small proportion (for example, 10%) of the contract is reserved for purchasing stents for use in specific cases.

Clinical effectiveness

RCTs are the most suitable source of evidence

3.3 To compare the clinical effectiveness between stents, the EAG did targeted literature searches to identify relevant published clinical evidence. The review focused on randomised clinical trials (RCTs) comparing outcomes between the stents in the scope of this assessment. For 8 of the 29 stents there was no randomised evidence that compared one stent with another in scope. The committee agreed that RCTs were the most suitable source of evidence for this assessment. But it acknowledged that there was a large volume of other types of evidence (14 non-randomised or observational comparative studies and 54 single-arm studies) related to the stents in the scope.

Clinical equivalence between stent versions

3.4 If evidence was not available for a stent in the scope, the EAG looked for evidence on clinically equivalent predecessors. Manufacturers provided information on whether evidence for a predecessor stent could be generalisable to a stent in the scope, but this information was not available for all stents. The manufacturers clarified that where equivalence was stated, the changes between stent generations were usually related to the deliverability of the stent, rather than the polymer or drug.

Most RCTs comparing stents showed similar clinical outcomes

3.5 The EAG identified 22 key RCTs comparing 1 or more stents with another in scope. Of the 22 studies, 21 were non-inferiority studies that determined whether a stent works as well as its comparator. The committee noted that most of the 22 studies showed similar clinical outcomes (target lesion failure, major adverse cardiac events, stent thrombosis, repeat revascularisation and death from cardiac causes) between the different stents.

3.6 The EAG examined whether any of the 22 key RCTs provided outcome data for the subgroups in the scope. Some data on subgroups was available for women and for people with left main-stem lesions, bifurcation lesions, high risk of bleeding or diabetes. Some of the studies reported subgroup results, and some reported whether the subgroup characteristic had an effect on the clinical outcomes. 3 studies had 1 of these populations as the main population. The subgroup results were similar to the overall study results. None of the subgroup characteristics had a significant effect on the clinical outcomes. The committee heard from clinical experts that this was reflective of their experience.

3.7 The committee noted that none of the 22 key studies reported results by ethnicity or the effect of ethnicity on clinical outcomes, or included any information about the ethnicity of study participants.

Results of the NMA are uncertain but suggest no difference in clinical outcomes

3.8 To present the comparative effectiveness of multiple stents in a single analysis, the EAG did a network meta-analysis (NMA). There was sufficient evidence to include 18 of the 29 stents in the NMA. Of the 22 key studies, 14 studies contributed to the 1-year analysis and 12 studies to the long-term analysis of 2 clinical outcomes that were reported in all the included studies: target lesion revascularisation and target vessel-related myocardial infarction. The wide 95% confidence intervals around the effect estimates from the analyses indicated that the estimates were uncertain. But, as with the results of the individual primary studies, most of the NMA results suggested that the 2 clinical outcomes were similar between stents. The EAG explained that having only limited data for each comparison in the analysis, even less so for the long-term analysis, was a key reason for the uncertainty. The committee recalled the assumptions around clinical equivalence (see section

3.4). Using evidence from predecessor stents may have added uncertainty to the results.

The clinical evidence is generalisable to the NHS

3.9 Only 2 studies in the NMA were done partly in the UK. The clinical experts explained that there are some differences in clinical practice between countries. For example, intravascular imaging during PCI is more common in the UK than in some other countries. But this difference would mean that better clinical outcomes could be expected from the trials if they were done in the UK. Distributions of populations with stable angina and acute coronary syndrome are the same across the world. The committee had no concerns about the generalisability of evidence to the NHS.

Cost effectiveness

The model structure was appropriate

3.10 The EAG developed a multi-state Markov model to estimate and compare the cost-effectiveness of the drug-eluting stents. The model included 2 clinical events: target vessel revascularisation and target vessel-related myocardial infarction. The committee agreed that, for the purpose of comparing different stents, the model was an appropriate representation of clinical practice in the NHS.

The clinical parameters in the model were uncertain

3.11 To calculate the probabilities of the 2 clinical events in the model (target vessel revascularisation and target vessel-related myocardial infarction), the EAG used the relative clinical effect estimates from the NMA. The economic model reported results for 18 stents because only 18 of the 29 stents were included in the NMA. The committee recalled that the amount of randomised evidence comparing effectiveness between the stents in the NMA

was limited, so the treatment effects were uncertain (see section 3.8).

3.12 The model's base case estimated outcomes with a 1-year time horizon following the index (first) PCI. In the alternative scenario estimating 5-year outcomes, the clinical event rate after 1 year was assumed constant. The clinical experts noted that it is not correct to assume that the long-term outcome rate would stay the same, but added that the evidence did not suggest a difference in clinical outcomes. The EAG explained that this assumption about long-term outcomes was made because of the limited data available. It cautioned that the long-term cost-effectiveness analysis should be considered exploratory. The committee recalled that there was considerable uncertainty, especially around the long-term effectiveness estimates from the NMA (see section 3.8).

Stent costs are a small part of the total procedure cost

3.13 The model included the cost of the stents using NHS Supply Chain weighted average of 2023 purchase costs or framework price, other PCI procedure costs, treatment and care costs after PCI and repeat revascularisation and myocardial infarction-related costs. The committee concluded that the cost of the stents is a small part of the total procedure cost, and the price differences between most stents are generally relatively small. The committee noted that stents aimed for use in specific cases cost more, and these should be used only when they are clinically appropriate.

It is uncertain whether some stents are more cost effective than others

3.14 There was a limited amount of evidence comparing effectiveness between the stents, and subsequent uncertainty in the treatment effects from the NMA. So, there was considerable uncertainty in the model results. The EAG presented the results of the economic evaluation in terms of net monetary benefit, including the central

value and the 95% confidence intervals. The 95% confidence intervals around the net monetary benefit average estimates for all 18 stents in the model were wide and largely overlapped. At the £20,000 threshold, there was a low (less than 30%) probability of any of the stents being the most cost-effective. The committee had no concerns about the overall cost-effectiveness of stents. It noted that for the 11 stents not included in the economic model, there was no evidence available to suggest significant differences in cost effectiveness. But it concluded that, based on the model, it is uncertain whether some drug-eluting stents are more cost effective than others.

Resource impact

3.15 The committee discussed 2 hypothetical scenarios that estimated the financial impact of shifting towards stents with a lower price. In 1 scenario the shift was between the same manufacturer's brands. In the other scenario the shift was between different suppliers. The scenarios did not consider potential clinical differences or volume-based pricing. The committee recalled that the cost of the stents is a small part of the total procedure cost, and the price differences between stents are generally relatively small (see section 3.13). It was uncertain whether, in the context of the total spend on stents, these shifts would result in substantial savings.

User preferences

3.16 The committee discussed evidence from the user preference assessment. This involved a group of 7 interventional cardiologists who explored the most important factors to consider when choosing a drug-eluting stent. They identified a set of 4 criteria most important at the patient level when a stent is decided upon as the most appropriate treatment. They also identified 6 criteria most important for cardiologists when choosing 2 or 3 stents that can be used in most cases (see section 3.2). High on both sets were stent

failure and suitable stent size. The group noted that it is important to provide a range of stent sizes, so that the a stent appropriate for each vessel diameter can be used. Clinical evidence was important for measuring performance. The experts noted that the evidence on the commonly reported clinical outcomes (target lesion revascularisation and target vessel-related myocardial infarction) in the key studies comparing stents provided information on stent failure. The committee recalled that most RCTs comparing drug-eluting stents showed that different stents had similar clinical outcomes (see section 3.5).

Equality considerations

3.17 The committee discussed any equality issues. These included stent failure being more common among people with type 2 diabetes, and worse PCI outcomes among women and people from Southeast Asian groups because they tend to have smaller vessel diameters. The committee recalled that some subgroup data was available for women and for people with diabetes, and that these subgroup characteristics had no significant effect on the clinical outcomes (see section 3.6).

3.18 The committee recalled that none of the key studies in the EAG's review reported results by ethnicity or the effect of ethnicity on clinical outcomes, or included any information about the ethnicity of study participants (see section 3.7). The clinical experts noted that, overall, ethnicity has not been widely or well recorded. For example, the National Institute for Cardiovascular Outcomes Research (NICOR) registry, which collects data on everyone having PCI in the UK, records ethnicity for only 70% of people. The committee agreed that trials and registries using drug-eluting stents should collect information about study participants and adjust analyses for ethnicity.

3.19 The clinical experts explained that some stent manufacturers have stent registries or cohorts located across various countries. Although these registries include only a single stent or stents from only 1 manufacturer, they do cover different ethnic groups. The experts were not aware of reports of concerning event rates from these registries.

Justification for price differences

3.20 The committee discussed the clinical and economic evidence overall. It concluded that it was not possible to determine whether the differences in cost between stents were justified by benefits derived from additional features. The committee recalled that NHS trusts currently have access to more than one drug-eluting stent (see section 3.2). It emphasised the importance of continuing to have access to a range of stents, so that a clinically appropriate stent is always available.

Evidence needed to show additional value

3.21 The committee concluded that to show additional value more evidence comparing clinical outcomes of different drug-eluting stents for people with coronary artery disease would be needed. This would ideally be from an RCT designed to show the clinical superiority of a stent. If a company introduces to the market a new drug-eluting stent or a new generation of the technology with minor improvements, it should show clinical non-inferiority. The committee noted that long-term data (up to 5 years) needs to be captured to help inform a cost-effectiveness analysis. But it recognised that other factors not related to the stent or target lesion may become more important after 1 year, and this could limit the validity of the conclusions from any long-term studies. The committee acknowledged that the lack of evidence for the additional value of a stent against its comparators in the evidence

review does not necessarily mean that there is no difference in cost-effectiveness.

4 Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE also recruited clinical experts and specialist committee members for this topic.

Specialist committee members

Ferrah Choudhary
Consultant interventional cardiologist and PFO service lead, Manchester University Hospitals NHS Foundation Trust

Joel Giblett
Cardiologist and honorary senior clinical lecturer, Liverpool Heart and Chest Hospital

Stephen Hoole
Affiliated associate professor, University of Cambridge, and consultant interventional cardiologist, Royal Papworth Hospital NHS Foundation Trust

Adnan Nadir
Consultant cardiologist coronary and structural heart interventions, Queen Elizabeth Hospital, Birmingham

Ian Purcell

Consultant interventional cardiologist, Freeman Hospital, Newcastle upon Tyne

Sudhir Rathore

Consultant interventional cardiologist, Frimley Health NHS Foundation Trust, and honorary reader, University of Surrey

Clinical experts

Dawn Adamson

Consultant cardiologist, University Hospitals Coventry & Warwickshire

Mamas Mamas

Professor of cardiology, Keele University, and honorary consultant interventional cardiologist, Royal Stoke Hospital

Abdul Mozid

Consultant cardiologist, Yorkshire Heart Centre, Leeds Teaching Hospitals NHS Trust

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