Late-stage assessment

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

Final Protocol

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

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1 Decision problem

This late stage assessment (LSA) aims to determine if the value added by incremental innovation in drug-eluting coronary stents for treating coronary artery disease justifies variation in price to the NHS.

Table 1 summarises the decision problem to be addressed in this assessment. Further detail on each element can be found in the published scope for the assessment.

Table 1. Summary table of the decision problem

Population	People having PCI (including primary PCI) and for whom drug-eluting stent is indicated for treating coronary artery disease (including stable angina, STEMI, unstable angina or NSTEMI) Where data permits, the following subgroups may be considered: • Women • Ethnicity (important subgroups are discussed in section 3.1) • People with left main stem lesions • People with bifurcation lesions • People with high bleeding risk • People with diabetes
Interventions	Drug-eluting coronary stents: • XIENCE PRO 48 • XIENCE PRO S • Skypoint • XIENCE Skypoint 48 • Xience Skypoint LV • Coroflex ISAR NEO • BioFreedom • BioMatrix Alpha • BioFreedom Ultra • Orsiro Mission • Synsiro Pro • Promus ELITE • Synergy MEGATRON • Synergy XD • XLIMUS • ihtDEStiny BD • Angiolite

	• Onyx Frontier • BioMime • BioMime Branch • BioMime Morph • EverMine 50 • Firehawk • Firehawk Liberty • MAGMA • Supraflex • Supraflex Cruz • Ultimaster Nagomi • Ultimaster Tansei
Comparator(s)	A drug-eluting stent or stents or a type or types of drug-eluting stent that is considered the current standard of care in the NHS (for example the drug-eluting stent is widely being used as the comparator in non-inferiority trials on drug-eluting stents). The comparator may differ between subgroups.
Healthcare setting	Secondary care, tertiary care
Outcomes	Outcome measures for consideration may include but are not limited to: Intermediate outcomes: • Accurate stent positioning (related to visibility under fluoroscopy) • Ability to deliver the stent • Acute procedural success • Procedure and fluoroscopy time • Amount of contrast used Patient reported outcomes: • Health-related quality of life • Symptom relief (for example angina relief) Costs and resource use: • Cost of technologies • Cost of staff training • Cost of further diagnostic tests (for example pressure wire and IVUS or OCT guided PCI) • Cost of treatment (including costs of any adverse events, retreatment and for example lesion modifying therapy such as rotational and orbital atherectomy or intravascular lithotripsy) Clinical outcomes: • Intervention related adverse events • Major Adverse Cardiac Events (MACE)

	• Bleeding • Target lesion or vessel failure • Acute and chronic stent failure • Target lesion and target vessel revascularisation • Restenosis • Stent thrombosis • Myocardial infarction • Patient orientated cardiovascular events (POCE, a composite of ischemic and bleeding events, see Academic Research Consortium for definition) • All-cause mortality • Cardiac mortality Outcomes and criteria that users consider important when making decisions on which technology to use will be based on the principles of multi-criteria decision analysis if considered appropriate for the assessment.
Economic analysis	A health economic model will be developed, where possible, comprising a cost-comparison or cost utility analysis. Costs will be considered from an NHS and Personal Social Services perspective. Sensitivity and scenario analysis should be done to address the relative effect of parameter or structural uncertainty on results. The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared.
Existing UK registries	• A registry that is potentially relevant and may help inform this assessment is the National Institute for Cardiovascular Outcomes Research (NICOR) collects data and produces analysis to enable hospitals and healthcare improvement bodies to monitor and improve the quality of care and outcomes of cardiovascular patients. • BCIS collects and analyses annual survey data from PCI centres in the UK. • Registry data may not capture all the population or lesion characteristics that are important for consideration of clinical effectiveness, these may be more fully recorded in trial data. • Some drug-eluting coronary stent manufacturers may have large registries or cohorts in the UK. These would include only the manufacturer's stents.
Other considerations	• Key evidence on the included technologies may be on their previous versions (not included in the scope if they are no longer available through the NHS Supply Chain framework), this evidence should be considered where clinical equivalence between versions is claimed.

	• Where no evidence is available on a technology comparing it to another drug-eluting stent, key evidence that includes another comparator could be considered.

1.1 Objectives

The objective of this assessment is to identify and analyse evidence that will inform guidance on use of drug-eluting stents in the NHS. The overall research question the assessment will aim to answer is:

- Is there any value added by incremental innovation in drug-eluting coronary stents for treating coronary artery disease that could justify variation in price to the NHS?

The following broad objectives are proposed to address the research question:

Clinical Effectiveness:

- Identify and assess relevant evidence, focusing on inputs for the economic model
- Highlight any equalities issues not described in the scope
- Briefly outline the limitations of all evidence identified

Cost Effectiveness:

- Identify and assess relevant economic models
- Develop or adapt an economic model to determine value for money of each of the stents or using appropriate groupings of stents where sufficient evidence is available
- Report available model parameters and any key limitations

2 Evidence review

An independent search for relevant evidence will be conducted by the EAG. Evidence relevant to the scope will be identified using a combination of databases of published evidence, evidence provided by device manufacturers, and real-world evidence e.g. registry data.

Depending on the volume of evidence identified, certain pragmatic approaches may be used for the evidence review, in line with the NICE LSA interim process and methods statement. This may include prioritising only the most relevant and high-quality studies for appraisal and/or inclusion in the review and streamlining review processes such as single reviewer-screening of evidence. Meta-analysis or network meta-analysis may be considered to pool effect size of devices or to estimate the relative effects using data from published literature. However, the EAG acknowledges that the evidence may not be suitable for meta-analysis or network meta-analysis due to differences in patient population and lesion characteristics. Checks on heterogeneity or consistency will be performed to determine if meta-analysis or network meta-analysis will be appropriate and credible.

2.1 Inclusion criteria

Table 2 outlines the inclusion and exclusion criteria for the evidence review.

Table 2: Inclusion and exclusion criteria

Item	Inclusion Criteria	Exclusion Criteria
Population	• People having primary PCI or PCI and for whom drug-eluting stent is indicated for treating coronary artery disease.	• Children and young people aged <18 years.
Intervention	• Only devices named in the scope.	• Any intervention outside of scope, including drug coated balloons.
Comparators	• A drug-eluting stent or stents or a type or types of drug-eluting stent that is considered the current standard of care in the NHS **OR** • Any/no comparator (single arm studies), where good quality evidence with a comparator as described above is not available.	
Outcomes	• Only those included in the scope.	• Evidence will be excluded if no relevant outcomes are reported. If a subsection of outcomes are relevant to the scope, these alone will be reported.

Study design	• Systematic reviews, meta analyses and network meta analyses. • RCTs e.g. equivalence and non-inferiority trials. • Observational studies, including those reporting registry data. • Abstracts, conference presentations/posters (where there is insufficient evidence available in the form of other publications).	• Case reports. • Narrative reviews.

2.2 Search strategy

Searches will be developed in Medline ALL (Ovid) by an experienced Information Specialist. Search terms will include free-text terms and controlled terms from databases (e.g. MeSH). Searches will be structured around population and device names as detailed in the inclusion criteria (Section 2.1). The decision for searches to focus on device names has been made for pragmatic reasons given the number of devices within scope and to ensure that the screening stage is feasible within the agreed timeframe. The search strategy will be peer-reviewed by a second Information Specialist. A draft search strategy is available in Appendix A. The search strategy will be translated to each database.

The following bibliographic databases will be searched:

- Medline ALL (Ovid)
- Embase (Ovid)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- International HTA database (INAHTA)
- Epistemonikos
- Database of Abstracts of Reviews (DARE, via CRD)

If necessary, additional searches may be conducted to identify evidence relating to features that are considered to be important by clinical experts, to understand if such

features are associated with clinically meaningful differences in outcomes. Any planned additional searches and potential approaches will be discussed in advance with the NICE team.

Supplementary searches will also be conducted for economic studies. These searches will be focused and aim to retrieve studies that are relevant to the UK context where evidence is available. The following bibliographic databases may be searched for economic literature:

- Medline ALL (Ovid)
- Embase (Ovid)
- CEA Registry
- NHS Economic Evaluation Database (NHS EED, via CRD)

The following clinical trials registries will be searched for ongoing trials:

- ClinicalTrials.gov
- International Clinical Trials Registry Platform (ICTRP)

Where possible, the EAG will identify additional studies from the information provided by companies to NICE. To identify studies that have not been retrieved by the database searches, company websites will be searched for relevant publications.

2.3 Study selection

Retrieved references will be imported into EndNote and deduplicated. EndNote will also be used to record reviewers' screening decisions. Titles and abstracts of identified studies will be screened by one reviewer and a minimum of 20% of excludes will be checked by a second reviewer against the pre-specified inclusion and exclusion criteria. Full-text articles of eligible studies will be obtained and screened by one reviewer with final inclusions and a random 20% of exclusions checked by a second reviewer. A list of studies excluded at the full text stage, with reasons for their exclusion, will be presented in an appendix in the report.

Where a large volume of evidence is identified, a pragmatic approach to study selection may be taken, in line with the NICE LSA interim process and methods

statement. Clinical evidence will be prioritised for inclusion based on its relevance to populating the economic model. Prioritisation of studies to be included may be based on factors such as type of study design, sample size and extent of generalisability to a UK population. Any decisions made and approaches taken by the EAG will be flagged with the NICE team for discussion.

2.4 Data extraction strategy

Where available, the following data will be extracted from studies: study information (i.e., author, year) study design, intervention characteristics (i.e., stent name), comparator, participant characteristics (i.e., demographics, indication), patient outcomes relevant to the economic model, cost and resource data if relevant to a UK setting. Data will be extracted into a standardised table and will be conducted by a single reviewer and checked by a second.

2.5 NICOR PCI registry

The UK NICOR PCI registry records PCI procedures carried out in NHS hospitals and a number of private hospitals in the UK. Data from time of admission to hospital discharge is collected, including patient baseline demographics, risk factors, procedural details and outcomes. Currently, the registry captures approximately 95% of all PCI cases in the UK. Data quality assurance is in place through a number of checks and assessments, to ensure the completeness, accuracy and consistency of the records (Rashid et al. 2019). The EAG consider that the NICOR PCI registry is a potentially useful data source that is representative of NHS setting, and linkage to administrative datasets – Hospital Episode Statistics (HES) and Office of National Statistics (ONS) would enable the assessment of long-term outcomes if feasible within the given timeframe.

However, a number of limitations with the use of NICOR registry or real-world data have been noted. Given the wide patient variation captured in NICOR registry, generalisation of the results across broad clinical groups may be inappropriate. Some data on patient or lesion characteristics are not captured in the registry that may be important considerations in the analysis. At the scoping workshop, an expert flagged the limited role of NICOR registry as it may be less complete where it captures in-hospital data and some meaningful outcomes are not collected. Although linking NICOR data to HES/ONS would allow long-term outcomes and mortality to be

estimated, it may not be possible for these to be directly attributed to the devices. Additionally, the EAG note that the NICOR registry may not include all of the devices listed in the scope. The length of follow up data is limited by the time that the device has been available in the NHS and recorded in NICOR data. The EAG will explore and consider the suitability and feasibility of using NICOR data in the analyses, with the assistance of NICOR PCI registry clinical lead. Where applicable, any results and key limitations will be discussed in the final EAG report.

2.6 Quality assessment strategy

Critical appraisal of key studies will be conducted using the JBI Critical Appraisal Tools as a guide, in accordance with NICE's health technology evaluations manual. A narrative summary of the key strengths and limitations of the evidence will be presented in the final report. This summary will highlight potential biases in individual studies for example, relevance to scope, potential confounding, and will discuss how these impact on the certainty of the results.

In line with NICE's real-world evidence framework, an assessment of the suitability and quality of real-world evidence (registry data and/or HES data) will be conducted using the Data Suitability Assessment Tool (DataSAT).

3 Methods of synthesis/analysis

Subject to the content of manufacturer submissions, or publicly available information, the EAG will aim to describe the following in relation to each device:

- information relating to intended use/purpose,
- stent scaffold material,
- polymer coating,
- antiproliferative drug used and eluting time,
- generation, or other grouping,
- additional properties that clinical experts describe as important,

- cost (any confidential information will be handled as described in Section 5),
- additional procurement information that experts describe as important,
- time period that they have been available, and relation to other devices in family,
- indication of available evidence types (RCT, observational study, registry)

Clinical effectiveness evidence synthesis

Meta-analysis or network meta-analysis of clinical effectiveness data will be considered if the data is suitable to be pooled, including whether the assumption of transitivity is met for network meta-analysis. Where meta-analysis or network meta-analysis is not considered appropriate, clinical outcome data identified will be presented in a suitable tabular format, accompanied by brief narrative synthesis highlighting any evidence of differences in clinical effectiveness that can credibly be attributed to the drug-eluting stent used. Where no evidence is available to demonstrate clinical effectiveness that can be directly attributed to the drug-eluting stent used, or certainty of the evidence is limited, the EAG will state this in the assessment report. Evidence for previous versions of technologies may be considered where clinical equivalence between versions is claimed. If there is more than one study that provides relevant outcome data for a single drug-eluting stent, the EAG will consider several methods to select the most appropriate input for the economic model, including setting prioritising criteria or pooling study estimates where appropriate.

Real-world data analysis

Depending on the suitability of registry data for the purpose of the assessment, the EAG will liaise with the NICOR PCI registry clinical lead to define the data request. Variables may include, for example, patient demographics, indication, confounding factors and outcomes. If feasible, NICOR registry data will then be linked to HES and ONS. Prior to data analyses, appropriate steps will be conducted including data cleaning, checks for data completeness and multiple imputation, if plausible.

Propensity score matching will be applied to balance covariates across treatment groups. To explore the correlation of outcomes for each device included in the dataset, analysis such as multivariate analysis or regression will be considered. All results will be discussed and confirmed with the NICOR PCI registry clinical lead. Findings from the analyses will be used to inform the economic model.

Alternatively, all of the data could be requested as an aggregate output if the linked data is not available. The type of aggregated data needed will be guided by the NICOR PCI registry clinical lead. The main consideration would be how to describe and group patient characteristics in the output. The second consideration would be careful definition of relevant follow up events.

4 Economic analysis

The economic analysis will be performed in line with the NICE reference case, where there is sufficient clinical evidence available. The perspective of NHS and Personal Social Services will be undertaken. Costs will be expressed in 2023 prices and where applicable, costs will be inflated using NHS Cost Inflation Index (NHSCII). Quality-adjusted life years (QALYs) will be calculated using utility values for each device or group of stents. All costs and outcomes will be discounted at 3.5% per annum. The cost-effectiveness of each device or appropriate group of devices will be estimated in terms of incremental cost per additional QALY gained. Using the willingness-to-pay threshold of £20,000 per QALY in base-case, the net monetary benefit will be calculated. The value for money of each device or group of devices will be determined by considering the price variation and incremental benefits, in comparison to the predetermined price range of the comparator.

Given the chronic nature of coronary heart disease, a sufficiently long time horizon will be used in the base case analysis where possible. In the EAG scoping search, the level of evidence of devices varies significantly, and short- and/or long-term data may not be available for some devices. Depending on the nature of available data, extrapolation of short-term outcomes to longer-term will be considered. If appropriate, extrapolation will be conducted in line with NICE DSU Technical Support Document 14. The time horizon used in the model will depend on the follow-

up duration of available evidence. Any changes in the EAG economic approach will be discussed with NICE team in advance.

In the EAG scoping searches, the economic models in the NICE guidance (CG126 for stable angina and TA71 for coronary heart disease) were identified. An executable version of the model was requested to evaluate for suitability. Quality assessment of any potentially suitable models will be conducted using the Drummond checklist (Drummond et al. 2015). If there is a suitable existing model, the EAG will rebuild and adapt the model in Microsoft Excel to represent the current clinical practice for stable angina and acute coronary syndrome (unstable angina, NSTEMI and STEMI). Where no suitable model is available, a *de novo* model will be developed in Microsoft Excel. Expert opinions will be sought to ensure the model reflects NHS practice. All assumptions applied in the economic model will be clearly stated, and all model inputs and data sources will be reported.

It is anticipated that there may be insufficient data for modelling for some devices. In these cases, the EAG will summarise the costs and technical features of the stents together with expert opinion on the impact of these features.

Economic evidence will be identified from guidance and literature. A pragmatic search for economic model papers will be undertaken to retrieve relevant UK-based papers, as outlined in Section 2.2. Data extracted may include, for example, health-related quality of life, resource use and costs of clinical events, complications and adverse events.

4.1 Model development

A cost-effectiveness analysis comparing each stent or using appropriate grouping of stents against comparator will be undertaken if feasible. A cost-comparison analysis will be considered if the evidence identified for clinically meaningful outcomes suggests comparable effectiveness. Clinically meaningful outcomes may include, for example, revascularisation, complications (stent thrombosis, bleeding) and mortality. The selection of outcomes will be guided by clinical experts.

The EAG will develop and adapt the suitable model in Microsoft Excel by adding functionality to compare multiple devices and incorporate outcomes to reflect findings from Section 3. Structural changes and assumptions will be guided by

clinical experts, to ensure the structural changes and assumptions are valid and representative of the patient pathway in an NHS setting.

Costs will be considered from an NHS and Personal Social Services perspective, consistent with the methods and data sources recommended in NICE reference case. Costs in the model may include:

- Cost of the device
- Cost of training if applicable
- Cost of PCI and dual antiplatelet therapy
- Cost of follow-up appointments after the index procedure
- Cost of subsequent clinical events and adverse events such as MI, bleeding
- Cost of further diagnostic tests if applicable

For utility or disutility associated with health states in the economic model, the values will be identified from NICE guidance and literature search. If more than one value are reported, the EAG will select the most updated and appropriate value based on the primary data source using a set of pre-defined selection criteria. Criteria may include study population, sample size and elicitation method. Where appropriate, sensitivity analyses will be undertaken to examine the impact of different utility values.

Where possible, model inputs related to demographics such age, PCI indication will be obtained from the UK NICOR registry, either aggregated data or patient-level data. This is because of its representativeness of the patient population undergoing PCI in the UK.

Deterministic and probabilistic sensitivity analyses will be undertaken to identify the key cost drivers and to explore the impact of uncertainty, where possible. Deterministic sensitivity analyses may include one-way sensitivity analysis, varying time horizon, using £30,000 per QALY as the willingness-to-pay threshold and impact of model assumptions. Subgroup analyses may be performed for different patient subgroups if sufficient evidence is available to do so. Where applicable,

threshold analysis may be conducted to identify the price range where the device or group of devices is considered as value for money. In the probabilistic sensitivity analysis (PSA), 95% CI of the model input reported in the literature or calculated from the UK NICOR registry will be used. To assess the parameter uncertainty, a Monte Carlo simulation with 1,000 replicates of parameters sampled from the assigned distributions. Using PSA results, a cost-effectiveness scatterplot and cost-effectiveness acceptability curves will be presented.

To validate the EAG model, the model will be reviewed and checked by a second health economist independently. This will include checking model calculations used in calculating model inputs, patient transitioning in the model and results to give total and incremental costs and QALYs. All model inputs will be checked against their original source, and model inputs will be varied to check if the results are consistent with *a priori* expectations.

5 Handling information from the companies

All data submitted by the companies in Requests for Information (RFI) by NICE or other stakeholders will be considered by the EAG if received by 26th July 2024. Data received after this date will not be considered. If the data included in the information provided meets the inclusion criteria for the review they will be extracted, and quality assessed in accordance with the procedures outlined in this protocol.

All correspondence between the EAG and companies will occur through NICE. The EAG may seek clarification or additional information from companies where necessary. Any ‘commercial in confidence’ data provided by the company, and specified as such, will be highlighted in blue and underlined in the report, economic model and correspondence log. Any ‘academic in confidence’ data provided by the company, and specified as such, will be highlighted in yellow and underlined in the report, economic model and correspondence log. If confidential information is included in the economic model, the EAG will provide a copy of the model with ‘dummy variable values’ for the confidential values (using non-confidential values).

6 Additional information sources

Clinical experts identified by NICE will be consulted by the EAG during the assessment process to provide clarification and guidance on interpreting and prioritising evidence that has been identified as relevant to the assessment, where necessary. Additionally, clinical experts may be asked to contribute opinions on key points of uncertainty that arise from the clinical evidence review and economic modelling. This may involve consideration of user preference work or discussions conducted by NICE.

7 Competing interests of authors

None.

8 References

Drummond, M. F., Sculpher, M. J., Claxton, K., Stoddart, G. L., & Torrance, G. W. (2015). Methods for the economic evaluation of health care programmes. Oxford university press.

Guidance on the use of coronary artery stents (2003) NICE technology appraisal guidance TA71. Last updated: 18 November 2020

Joanna Briggs Institute (JBI). JBI Critical Appraisal Tools. (n.d.). Available from: JBI Critical Appraisal Tools [online; accessed 02/07/2024]

Latimer, N. NICE DSU Technical Support Document 14 (2013): Undertaking survival analysis for economic evaluations alongside clinical trials - extrapolation with patient-level data. [online; accessed 02/07/2024]

National Institute for Health and Care Excellence (NICE). (2024a). Drug eluting stents for treating coronary heart disease: Late Stage Assessment. [GID-HTE10039] Final scope. Available from: Project documents | Drug eluting stents for treating coronary heart disease: late stage assessment | Guidance | NICE

National Institute for Health and Care Excellence (NICE). (2024b) Interim methods and process statement for late-stage assessment. Available from: Late stage assessment (LSA) for medtech | What we do | About | NICE

National Institute for Health and Care Excellence (NICE). (2023). NICE health technology evaluations: the manual. Available from: Overview | NICE health technology evaluations: the manual | Guidance | NICE

National Institute for Health and Care Excellence (NICE). (2022) NICE real-world evidence framework. Available from: https://www.nice.org.uk/corporate/ecd9/chapter/overview

Rashid, M., Ludman, P.F. & Mamas, M.A. (2019). British Cardiovascular Intervention Society registry framework: a quality improvement initiative on behalf of the National Institute of Cardiovascular Outcomes Research (NICOR). Eur Heart J Qual Care Clin Outcomes. 5(4):292-297.

Stable angina: management (2011) NICE Guideline CG126. Last updated: 25 August 2016

Appendix A: Draft search strategy

Ovid MEDLINE(R) ALL <1946 to June 28, 2024>

1	xience*.tw.	569
2	skypoint*.tw.	1
3	xlimus*.tw.	4
4	cardionovum.tw.	8
5	coroflex*.tw.	34
6	(braun and "drug eluting stent*").tw.	16
7	biofreedom*.tw.	39
8	"biosensors international".tw.	12
9	("biomatrix alpha*" or "BMX alpha*" or "biomatrix neoflex*").tw.	7
10	"orsiro mission*".tw.	1
11	(biotronik* and (orsiro* or "drug eluting stent*")).tw.	55
12	synsiro*.tw.	0
13	("boston scientific" and (synergy or promus)).tw.	54
14	"Synergy XD".tw.	0
15	"promus elite*".tw.	1
16	angiolite*.tw.	5
17	ivascular*.tw.	7
18	(magma* and ("drug eluting stent*" or QualiMed)).tw.	25
19	(QualiMed and "drug eluting stent*").tw.	0
20	"onyx frontier*".tw.	2
21	(medtronic and (onyx* or "drug eluting stent*")).tw.	133
22	biomime.tw.	24
23	"meril life".tw.	35
24	evermine*.tw.	4

25 firehawk*.tw. 28

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

27 supraflex*.tw. 24

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

29 ultimaster*.tw. 70

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

31 ihtDEStiny.tw. 2

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

33 or/1-32 1020

34 ((coronary or isch?emi*) adj3 "heart disease").tw. 95235

35 ((IHD or CAD) and Heart).tw. 13550

36 Coronary artery disease.tw. 101099

37 Coronary Disease/ 133326

38 Coronary Artery Disease/ 79380

39 ((Myocardial or Coronary) adj isch?emi*).tw. 38836

40 Myocardial Ischemia/ 42575

41 (stemi or nstemi).tw. 17209

42 ST Elevation Myocardial Infarction/ 8340

43 Non-ST Elevated Myocardial Infarction/ 1846

44 ((stable or unstable) adj angina).tw. 21413

45 Angina, Stable/ 1680

46 exp Angina, Unstable/ 11397

47 "acute coronary condition*".tw.4

48 "heart attack*".tw. 6801

49 or/34-48 388247

50 33 and 49 595

51 exp animals/ not humans.sh. 5235946

52	50 not 51	589
53	limit 52 to english language	583