NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA152 drug-eluting stents for the treatment of coronary artery disease (part review of TA71) – this guidance was originally reviewed in April 2009. Reference will be made in this paper to information that is still relevant.

This guidance was issued in July, 2008
The review date for this guidance is June, 2010

Recommendation

- The decision to review the guidance should be deferred until June 2012. That we consult on the proposal.

Consideration of options for recommendation:

Options	**Comment**
A review of the guidance should be planned into the appraisal work programme.	Since the systematic review was conducted in 2005 there have been numerous studies published for the stents included in TA152 that have longer follow-ups and more head to head trials of drug eluting stents. However this new evidence would not change the original recommendations in TA152. There are also now several new stents available although data on these may be limited; these have been considered as topics for the evaluation pathway programme.
The decision to review the guidance should be deferred until June 2012 as a number of ongoing trials will have reported their results by that date.	**If chosen, this would allow for further evidence to emerge**
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	No related technology appraisal
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No new technology appraisals
A review of the guidance should be	No relevant clinical guideline

updated into an on-going clinical guideline.*[1]	
A review of the guidance should be transferred to the 'static guidance list'.	The technology in this area is rapidly developing and given the amount of trials that have been conducted since the last appraisal the guidance should not be transferred to the static list.

Original remit(s)

To update current NICE guidance on the clinical and cost effectiveness of drug eluting coronary artery stents for the primary prevention of restenosis following percutaneous coronary intervention (PCI) in ischaemic heart disease and to provide guidance to the NHS in England and Wales.

Current guidance

Sections 1.1 and 1.5 of technology appraisal guidance 71 recommend when to use a stent. This part review recommends under what circumstances a drug-eluting stent should be used.

1.1 Drug-eluting stents are recommended for use in percutaneous coronary intervention for the treatment of coronary artery disease, within their instructions for use, only if:
• the target artery to be treated has less than a 3-mm calibre or the lesion is longer than 15 mm, and
• the price difference between drug-eluting stents and bare-metal stents is no more than £300.

Relevant Institute work

TA71 Ischaemic heart disease - coronary artery stents. October 2003, with sections 1.2-1.4 of this guidance replaced by TA152.

Unstable angina and NSTEMI: the early management of unstable angina and non-ST-segment-elevation myocardial infarction Clinical guidelines CG94 Issued: March 2010. Expected review date: TBC

[redacted]

[1] See Appendix A on page 4

Details of new products

As mentioned in the review carried out in April 2009, there are a number of new stents now available that have been CE marked since the guidance was published:

- Xience V / Promus (Abbott Vascular / Boston Scientific) - polymeric, everolimus eluting
- Coroflex Please (B Braun) - polymeric, paclitaxel eluting Biomatrix (Biosensors) - polymeric, biolimus eluting
- Nobori (Terumo) - polymeric, biolimus A9 eluting
- Monarch (Insitu Technologies) - polymeric, paclitaxel eluting
- Infinnium (Sahajanand) - polymeric, paclitaxel eluting
- Endeavor Resolute (Medtronic) - zotarolimus eluting

On-going trials

Trial	Details
NCT00811772 Comparison of the Long-Term Effects on Mortality and Cardiovascular Morbidity of Percutaneous Coronary Intervention With Drug-Eluting Stent Versus Bare-Metal Stent. Randomized, Five-Year Prospective, Multicenter Clinical Trial	Phase IV. Currently recruiting. Estimated study completion date June 2015.
NCT00823212 PLATINUM: A Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System (PROMUS Element™) for the Treatment of up to Two De Novo Coronary Artery Lesions	Phase III. Currently recruiting. Estimated study completion date November 2014.
NCT00496938 XIENCE V™ SPIRIT Women: A Clinical Evaluation of the XIENCE™ V Everolimus Eluting Coronary Stent System in the Treatment of Women With de Novo Coronary Artery Lesions	Phase IV. Currently recruiting. Estimated study completion date December 2015.
NCT00852215 Do Cobalt Chrome Stent and Paclitaxel-Eluting Stent Have Equivalent Clinical Result in Non-Complex Lesion? (COPE Study): Long-Term Follow-up Study	Phase IV. Currently recruiting. Estimated study completion date July 2010.
NCT00792753 A Randomized, Single Blind, Consecutive Enrollment Evaluation of The Elixir Novolimus-Eluting Coronary Stent System With	Phase II / III. Currently recruiting. Estimated study completion date July 2014.

Durable Polymer Compared to the Medtronic Endeavor Zotarolimus-Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions and a Non-Randomized, Consecutive Enrollment Evaluation of the Elixir Novolimus-Eluting Coronary Stent System With Bioabsorbable Polymer Compared to Contemporary Controls in the Treatment of Patients With De Novo Native Coronary Artery Lesions	
NCT00598637 Prospective Randomized Trial of Everolimus- and Zotarolimus-Eluting Stents for Treatment of Unprotected Left Main Coronary Artery Disease: ISAR-LEFT-MAIN-2	Phase IV. Currently recruiting. Estimated study completion date January 2010.
NCT00819923 Comparison of Bio-Active-Stent to the Everolimus-Eluting Stent in Acute Coronary Syndrome (A Prospective, Randomized and a Multicenter Clinical Study)	Phase III. Currently recruiting. Estimated study completion date December 2010.
NCT00752362 PercutAneous INTervention With Biodegradable-Polymer Based Paclitaxel-Eluting, Sirolimus-Eluting, or Bare Stents for the Treatment of de Novo Coronary Lesions (PAINT).	Phase IV. Ongoing, not recruiting. Estimated study completion date May 2012.
NCT00699543 The Efficacies of The New Paclitaxel-Eluting CoroflexTM Please Stent in Percutaneous Coronary Intervention: Comparison or Efficacy Between COroflex PLEASe ANd TaxusTM Stent	Phase III. Not yet recruiting. Estimated study completion date December 2013.
NCT00768846 Randomized Comparison of Zotarolimus- and Everolimus-Eluting Stents for Coronary Treatment (ZEPPELIN)	Phase IV. Currently recruiting. Estimated study completion date June 2011.
NCT00322569 A Randomized, Multi-Center Study of the Pimecrolimus-Eluting (Corio™) and Pimecrolimus/Paclitaxel-Eluting Coronary Stent System (SymBio™) in Patients With De Novo Lesions of the Native Coronary Arteries	Phase III. Ongoing, not recruiting. Estimated study completion date April 2012.
NCT00617084 RESOLUTE-III All-Comers Trial: A Randomized	Phase IV. Ongoing, not recruiting. Estimated study completion date

Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention	December 2013.
NCT00698607 Comparison of the Efficacy of Everolimus-Eluting Versus Sirolimus-Eluting Stent for Coronary Lesions (EXCELLENT)	Phase IV. Not yet recruiting. Estimated study completion date June 2014.
NCT00307047 SPIRIT IV Clinical Trial: Clinical Evaluation of the XIENCE™ V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions	Phase III. Ongoing, not recruiting. Estimated study completion date September 2013.
NCT00492908 Randomized Clinical Trial Comparing A Titanium-Nitride-Oxide Coated Stent With A Zotarolimus-Eluting Stent in Patients With Coronary Artery Disease	Phase IV. Currently recruiting. Estimated study completion date June 2012.
NCT00428454 A Randomized Comparison of Sirolimus-Eluting Stent Implantation With Zotarolimus-Eluting Stent Implantation for the Treatment of Chronic Total Coronary Occlusions. The PRISON III Trial	Phase III. Currently recruiting. Estimated study completion date December 2013.
NCT00148356 A Randomized, Controlled Trial to Evaluate the Safety and Efficacy of the ZoMaxx Drug Eluting Coronary Stent System Compared to the TAXUS™ Express2 Paclitaxel-Eluting Coronary Stent System in de Novo Coronary Artery Lesions	Phase II / III. Ongoing, not recruiting. Estimated study completion date July 2010.

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from 2009 onwards were reviewed. The results of the literature search are discussed in the 'Appraisals comment' section below.

Implementation

A submission from Implementation is attached at the end of this paper.

Equality and diversity issues
No relevant equality and diversity issues have been identified.

Appraisals comment:

Since the review in February 2009, there have been no new RCTs evaluating drug-eluting stents. No RCTs were identified which evaluated the stent models which received CE marking after the original appraisal.

There are 5 Cochrane systematic reviews which are due to be published in 2010 on the efficacy and safety of drug eluting stents.

In TA152, safety issues arose about the relationship between drug eluting stents and late stent thromboses. There have been no new published studies which assess this outcome since the review in 2009.

Third generation bioabsorbable / biodegradable stents were developed to overcome the problem of permanent stents causing blood clots. A case study of 30 patients given a bioabsorbable everolimus-eluting coronary artery stent has been published since the appraisal, but no RCTs have been published. Biodegradable stents have been considered as topics for the evaluation pathway programme.

A large scale meta-analysis (over 24,000 patients) of data from observational studies carried out between 1996 and 2009 has been published since the publication of TA152. This study found there was a significantly higher risk of repeat revascularization in the DES-PCI group than in the CABG group (HR=4.06; 95% CI=2.64-6.24; p<0.001). In addition, the overall major adverse cardiac and cerebrovascular events rate was higher in the DES-PCI than in the CABG group (HR=1.86; 95% CI=1.36-2.54; p<0.001). However, CABG was not a comparator in TA152.

A Cochrane systematic review and network meta-analysis spanning the period 1986 to April 2006 has been published since the publication of TA 152. Sixty three RCTs were included and the median follow-up period was 12 months. This study evaluated the effectiveness of percutaneous transluminal balloon coronary angioplasty (PTCA), bare metal stents and drug eluting stents for the treatment of non-acute coronary artery disease. The study did not identify any statistically significant differences between groups in terms of mortality or MI. A statistically significant a reduction in CABG with drug eluting stents compared with bare metal stents was identified (RR 0.56, 95% CI: 0.36, 0.88)

A second systematic review, published since the publication of TA152, found that sirolimus-eluting stents were associated with a lower rate of major adverse cardiac events than bare-metal stents in the management of patients with ST-segment elevation myocardial infarction over one year of follow-up. An observational study (ARTS-11) published since the appraisal found that at 5 years, siromolinus eluting stents had a safety record comparable to CABG and superior to bare metal stents.

A 5-year observational study of adverse cardiac events in people receiving drug eluting stents (Infinnium-Core and Paclitaxel-Eluting Coronary Stent) is

due to be completed for the primary outcome, - major adverse cardiac events, in July 2010.

Manufacturers expressed the view that there were no changes to their CE marking and insufficient new evidence at this time to warrant a departure from the original decision to recommend drug eluting stents. Boston Scientific provided details of two ongoing RCTs, both of which evaluate products which were available before TA152 was published.

Key issues [to be completed by AD]

New evidence has become available since the guidance in TA152 was published, although it does not appear that the evidence would change the Committee's original decision to recommend drug-eluting stents for use in percutaneous coronary intervention for the treatment of coronary artery disease, within their instructions for use. In addition, there is a lack of substantial evidence on the newer stents which received their C.E marking. In conclusion no real substantial evidence that would affect the recommendation made in TA152 has been identified and that a NICE appraisal at this time would not add value to the NHS.

GE paper sign off: Elisabeth George, 25 May 2010
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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

IMPLEMENTATION DIRECTORATE

Guidance Executive Review

Technology appraisal 152: Drug eluting stents for the treatment of coronary artery disease

1. National data

The NICE implementation directorate has not looked at any routinely collected data in order to determine the uptake of this technology appraisal (TA).

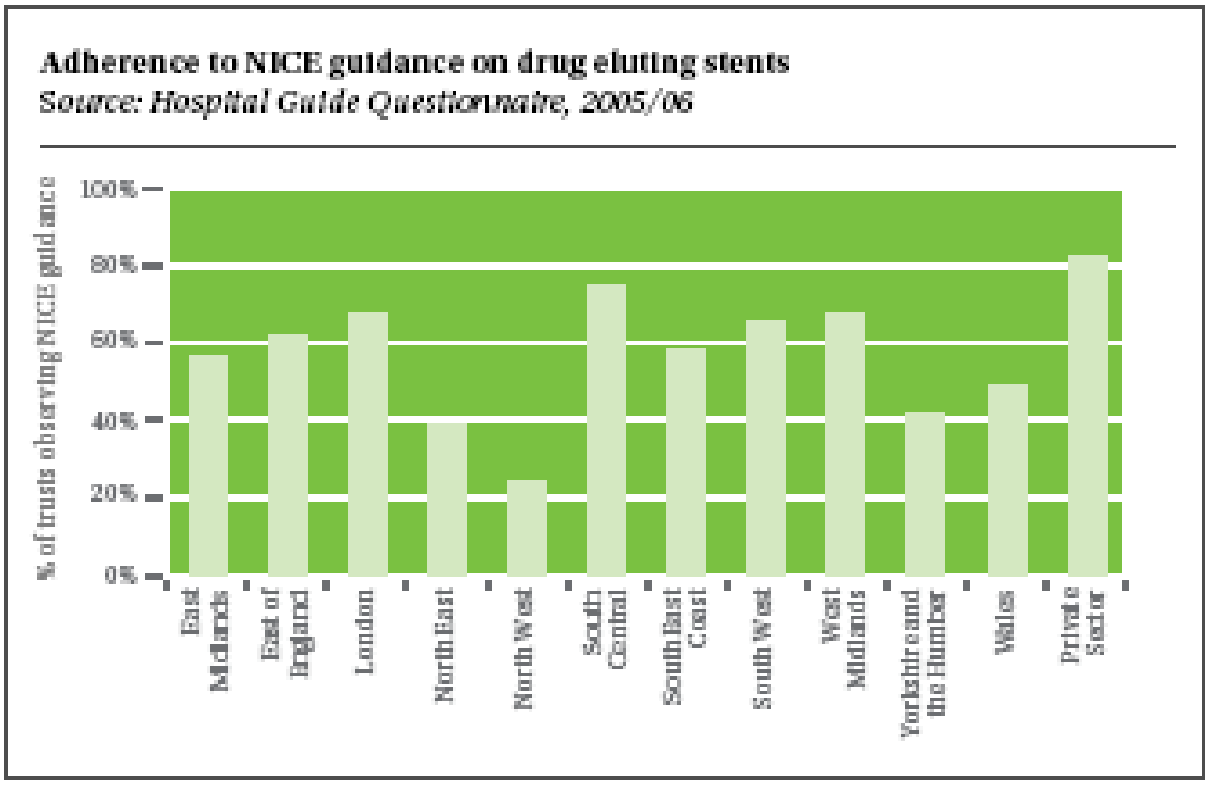
2. External literature

2.1 ERNIE

2.1.1 Dr Foster Intelligence (2007) Dr Foster Hospital Report: How healthy is your hospital?

Dr Foster Intelligence (2007) carried out a hospital survey which included a section on NICE guidance. The results showed 54% of trusts reported adherence to NICE guidance on stents. The survey showed considerable regional variation, for example only 24% of hospitals in the North West were likely to adhere to the NICE guidelines about the use of drug eluting stents compared to 75% in South Central. Compliance with this measure remains high in the private sector. Of the 17 private hospitals that carried out angioplasty, 82 per cent reported following NICE guidance on the use of drug eluting stents.

Commercial in confidence information is highlighted in black



3. Qualitative Data

3.1 Feedback from Field Implementation Team suggests that a non-permissive decision against stents would be controversial