EEPRU

Economic Evaluation of Health and Social Care Interventions Policy Research Unit

RESEARCH REPORT

Supporting the routine collection of patient reported outcome measures in the National Clinical Audits for assessing cost-effectiveness

Work Package 1

What patient reported outcome measures should be used in the 13 health conditions specified in the 2013/14 National Clinical Audit programme?

APPENDIX K, CARDIOVASCULAR DISEASE

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The Department of Health's Policy Research Unit in Economic Evaluation of Health and Care Interventions is a 7 year programme of work that started in January 2011. The unit is led by Professor John Brazier (Director, University of Sheffield) and Professor Mark Sculpher (Deputy Director, University of York) with the aim of assisting policy makers in the Department of Health to improve the allocation of resources in health and social care.

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An erratum has been posted online relating to the collection of the EQ-5D variable in the cardiac arrythmia audit (http://bit.ly/1V3aQjC).

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TABLES

Acronym	Definition
ACS	Acute coronary syndrome
AE	Adverse events
AF	Atrial Fibrillation
AFTEQ	Atrial Fibrillation Effect on Quality Of Life questionnaire
AIC	Academic in confidence
AVB	Atrioventricular block
BI	Barthel Index
BP	Blood pressure
CABG	Coronary artery bypass graft
CCAD	Central Cardiac Audit Database
CCSC	Canadian Cardiovascular Society grading scale
CES-D	Center for Epidemiological Studies depression scale
CHD	Coronary heart disease
CHF	Congestive heart failure
CRM	Cardiac rhythm management
CRT	Cardiac resynchronisation therapy
CRT-D	Cardiac resynchronisation therapy defibrillator
CRT-P	Cardiac resynchronisation therapy pacemaker
CVD	Cardiovascular disease
DES	Discrete event simulation model
DH	Department of Health
ECG	Electrocardiogram
EQ-5D	EuroQol 5 dimensions
EQ-5D-5L	EuroQol 5 dimensions 5 Levels
ES	Effect size(s)
FR	Future research
GMC	General Medical Council
GP	General practitioner
GRACE	Global Registry of Acute Cardiac Events
IC	Intra-cranial
ICC	Intraclass correlation
ICD	Implantable cardioverter defibrillators
HRQoL	Health related quality of life
HR	Hazard Rate
HS	Health states
HTA(s)	Health technology assessment(s)
HUI2	Health Utility Index mark 2
HUI3	Health Utility Index mark 3
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left ventricular ejection force
LVSD	Left ventricular systolic dysfunction
MA	Meta-analysis
MCS	Mental component summary
MCT	Mixed treatment comparison
MLHF	Minnesota Living with Heart Failure questionnaire

MRS	Modified Rankin scale
MTA	Multiple technology assessment
MI	Myocardial infarction
MINAP	Myocardial ischaemia national audit project
NACRM	National audit of cardiac rhythm management
NACSA	National adult cardiac surgery audit
NAPCI	National Audit of Percutaneous Coronary Interventional Procedures
NCA	National Clinical Audit
NHFA	National Heart Failure Audit
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NSTEMI	Non- ST elevation myocardial infarction
NVAF	Non-Valvular Atrial Fibrillation
NYHA	New York Heart Association classification
ONS	Office of National Statistics
OPT	Optimal pharmacologic therapy
OR	Odds ratio
PCI	Percutaneous coronary intervention
PCS	Physical component summary
PCT	Primary care trust
PR	Potential recommendations
PROM(s)	Patient reported outcome measure(s)
QALY(s)	Quality adjusted life year(s)
QLMI	Quality of life after myocardial infarction
R&D	Research and development
RCT	Randomised controlled trial
SCD	Sudden cardiac death
SF-36	Short form 36 Health Survey
SF-6D	Short form 6 dimensions
SF-12D	Short form 12 dimensions
SG	Standard gamble
SR	Systematic review
SRM	Standardised response mean(s)
SSS	Sick sinus syndrome
STEMI	ST elevation myocardial infarction
STA	Single technology assessment
TA(s)	Technology Appraisal(s)
TAG	Technology Assessment group
TIA	Transient ischaemic attack
TIMI	Thrombolysis in Myocardial Infarction
TLR	Target lesion revascularisation
TVR	Target vessel revascularisation
TTO	Time trade off
UK	United Kingdom
US	United States
VAS	Visual analogue scale

WP	Work package

1. BACKGROUND

EEPRU was approached by Jason Cox (R&D Division) to prepare a programme of research to support the appropriateness of, and use of, patient reported outcome measures (PROMs) collected for the National Clinical Audit (NCA). The EEPRU programme was informed by a R&D template prepared by Simon Bennett, Steve Fairman and Keith Willett at NHS England.

The purpose of introducing PROMs into the NCA programme is to be able to 1) compare performance between providers and commissioners in the National Health Service (NHS), 2) compare the cost-effectiveness of alternative providers in delivering the specific services (i.e. linking outcomes and resource use), and 3) assess the cost-effectiveness of alternative interventions and other changes in the NHS. The intention is to introduce PROMs across a range of conditions over the next 3 years commencing with 13 conditions in the 2014/15 NCA programme.

The agreed research programme consists of 3 concurrent work packages (WP) as described in the document submitted to the DH (8th November 2013). The current document provides details on the objectives, methodology and results for Work Package 1 (WP1): to determine what PROMS should be used in the 13 health conditions specified in the 2014/15 NCA programme.

2. OVERVIEW

WP1 is split into three separate components consisting of:

- WP1.1 To examine whether the EQ-5D is appropriate in the 13 health conditions specified in the 2013/14 NCA programme.
- WP1.2 To identify what measure could be used when the EQ-5D is not appropriate in the 13 health conditions, taking into account that the proposed measure would be used to generate preference-based utility measures (either directly through existing preference-based weights, or indirectly through existing mapping functions suitable for the proposed measure).
- WP1.3 To identify the evidence required to address questions of cost-effectiveness using the NCA data.

Each component consists of a series of reviews of the literature.

This Appendix provides the detailed results for the cardiovascular disease (CVD), which include cardiac arrhythmia, heart failure (HF), coronary angioplasty, cardiac surgery and acute coronary

syndrome (ACS), and should be read in conjunction with both the main report and the methods/search strategy appendices.

3. METHOD

The full detailed methodology used is provided in Appendix A, including the search strategy, selection criteria for studies included, and data extraction etc. In summary, for each included cardiovascular condition a review of the literature was undertaken to assess the appropriateness of the EQ-5D in terms of classic psychometric criteria (WP1.1); where the EQ-5D was not considered appropriate, additional searches were undertaken to identify alternative measures (WP1.2); and finally, existing health technology appraisals were reviewed and data requirements were compared with variables currently collected in the CVD audits (WP1.3).

3.1 Psychometric properties (WP1.1)

Assessments reported in the included studies were categorised according to the following definitions:

Acceptability

Data relating to how acceptable the measure was to the person completing it, expressed as the proportion of completed surveys, or the proportion of missing data.

Reliability

There are two main definitions for reliability, a) the degree to which a measure reproduces the same results in an unchanged population and b) the degree to which a measure reproduces the same results when completed by different assessors (e.g. patient and proxy report). In both cases, reliability can be assessed by re-testing, and calculating the correlations or difference between tests. In case a) the comparison may be between the same populations separated by time, where no change in health state was observed (as compared to using an alternative condition specific or generic measure). In case b) the measure may be completed by multiple people (proxies) on the patient's behalf and their responses compared with those of the patient. Where the outcome measure is specifically designed for self-report by patients, this test of reliability may be expected to produce less agreement.

Construct validity

This is an assessment of how well an instrument measures what it intends to measure. Two main definitions are used in this review.

a) Known group validity, where estimates for groups that are known to differ in a concept of interest are compared either qualitatively or statistically. The known groups may be defined using other measures, according to clinical categorisation.

b) Convergent validity assesses the extent to which a measure correlates with other measures of the same or similar concepts. Correlation coefficients were considered low if <0.3, moderate if between 0.3 and 0.5, and strong when >0.5.

Responsiveness

a) Change over time. This is an assessment of whether measurements using the instrument can detect a change over time, where a change is expected. This may be before and after an intervention, or through progression of a disease. Evidence was considered to be good where a t-test was significant, though weaker evidence to support responsiveness was considered where there was a change in the expected direction, but was not statistically significant or not tested. Effect size and standardised response mean were also acceptable assessments of responsiveness.

b) Ceiling and floor effects were also considered to be indicators of responsiveness. Assessments of ceiling effects include the proportion of patients who score full health within a group of patients with known health detriments. A ceiling or floor effect can affect the sensitivity of the measure in detecting changes over time in patients at the extremes of the measure (for example those with severe disease activity and those with just minor symptoms of the condition).

3.2 **Alternative measures** (WP1.2)

As the EQ-5D was found to be acceptable for CVD conditions, no additional searches for alternative measures were conducted.

3.3 **Evidence required for economic evaluations** (WP1.3)

The existing Health technology assessments (HTAs) were reviewed by CVD condition alongside the variables currently collected for each relevant NCA to determine if clinical or PROM data routinely collected in the NCAs would suffice to address questions of cost-effectiveness, and to identify any gaps in the evidence that would be required to compare providers, or the cost-effectiveness of interventions or policies.

4. RESULTS FOR CARDIAC ARRHYTHMIA

4.1 Evidence of appropriateness of EQ-5D in cardiac arrhythmia (WP1.1)

Evidence of the appropriateness of the EQ-5D is presented jointly for all CVD conditions considered in this Appendix. This was considered to be an appropriate way to present results, given i) the paucity of evidence available for each individual cardiovascular condition, and ii) the existence of some overlap of the study populations as defined by the CVD conditions (e.g. acute coronary syndrome (ACS)) patients can be treated with coronary angioplasty or cardiac surgery, such as coronary artery bypass graft (CABG). Evidence relevant to each individual cardiovascular condition is discussed in Section 4.1.5.

4.1.1 Selection of systematic review for CVD conditions

Two systematic reviews were identified through expert sources (1;2), and one (3) from the Longworth et al. review.(4) The process of selection of the most appropriate review is documented in Table 1.

Table 1: Selection of most appropriate review for cardiovascular conditions

Review	Search date	Relevance of review	Quality of search	Quality of review	Selection
Oxford (2009)(1)	August 2008	Question relevant, but too little data provided	Reliance on pre-existing database, with additional searches, but full strategy not provided (available on request).	No QA; search numbers provided; unclear reviewers SS, and DE; synthesis unclear	Exclude – less recent than Dyer; less psychometric detail than Dyer
Oxford (2010)(2)	July 2009	Question relevant, some detail provided	Reliance on pre-existing database, with additional searches. Full strategy provided in appendix.	No QA; details of search numbers provided; unclear reviewers SS, and DE, but at least 2 reviewers; synthesis unclear	Exclude –less psychometric detail than Dyer
Dyer et al(2010)(3)	October 2008	Question relevant, some detail provided	EMBASE, MEDLINE, And EuroQoL site searched, reference lists also searched. Search strategy described briefly (full search strategy NR) but available from authors.	No QA; details of search numbers provided; unclear SS and DE by reviewers, limited reporting of results and discrepant results not explained.	Include

QA, quality assessment; DE, data extraction; SS, study selection; NR, Not reported

4.1.2 Structured abstract for Dyer et al 2010 (3)

Purpose of review

Amongst other aims that are not relevant to WP1.1, the review aimed to synthesise the evidence on the validity and reliability of the EQ-5D in studies in CVD. The considerations in this abstract focus on the sections of the review that relate to WP1.1 only.(3)

Methods of review

Search and study selection: EMBASE and MEDLINE (database host platform used was unclear), the EuroQoL website. Electronic searches were conducted from January 1988 to October 2008, and combined, exploded or used medical subject headings relating to the CVD field and the EQ-5D as

follows: ('cardiovascular'/exp OR 'cardiovascular') OR ('cardiac'/exp OR 'cardiac') OR ('cardiology'/exp OR 'cardiology') AND 'euroqol' OR 'EQ 5D' OR 'EQ5D'. However, the full search strategies were not reported and exact terms used in the research database searches were not provided. The EuroQol website was also used to identify unique references, including working papers and conference proceedings that may not have been captured in the initial literature search. The review included studies that presented original research and reported EQ-5D scores specific to cardiovascular disease or reported psychometric properties of the EQ-5D in a population with cardiovascular disease. Studies presented as abstracts only were excluded. The psychometric properties of EQ-5D examined in the review were validity (construct, convergent and discriminative), reliability and responsiveness. Studies that only reported EQ-5D (index or visual analogue scale (VAS)) scores graphically in terms of change over time were explicitly excluded from the review. In terms of disease area, all CVDs were included in the review.(3)

Data extraction and synthesis: Data was extracted (unclear whether double data extraction or data checking performed) using a standard data abstraction form developed for the review. The psychometric properties were summarised according to the type of property assessed (namely validity, reliability and responsiveness), the comparison performed, the statistical test result, and included in tabular form in the Appendix. A narrative synthesis was performed according to the psychometric qualities mentioned above. The authors did not provide a conceptual description of each psychometric property, other than indicating that construct validity included convergent and discriminative validity.

Results of the review

Dyer et al. (2010)(3) included 10 articles which reported evidence on the measurement properties of the EQ-5D in CVD and included the following disease subgroups: ischaemic heart diseases (three studies), cerebrovascular diseases (three studies), HF (two studies), arterial embolism and thrombosis (one study) and peripheral vascular disease (one study). The review results were presented according to psychometric properties of the EQ-5D instrument, rather than by disease subgroup. In the included studies the EQ-5D index and VAS scores and dimensions were compared against generic health related quality of life (HRQoL) measures, namely the Health Utility Index mark 2 (HUI2), Health Utility Index mark 3 (HUI3), Short form 36 Health Survey (SF-36), Short form 12 dimensions (SF-12) and Short form 12 dimensions preference-measure (SF-6D) (Appendix). The EQ-5D was also compared against disease specific HRQoL measures, such as the MacNew quality of life questionnaire, Kansas City Cardiomyopathy Questionnaire (KCCQ) and VascuQol. In addition, the

studies also included the following clinical measurements of disease severity: the Barthel Index (BI), modified Rankin scale (MRS), the Center for Epidemiological Studies depression scale (CES-D), the New York Heart Association classification (NYHA) and the Canadian Cardiovascular Society grading scale (CCSC).

The narrative synthesis was brief, and the level of detail of tabulated study results was limited. The authors report that three studies found moderate to strong agreement between the EQ-5D index and VAS and other generic HRQoL measures, demonstrating construct (convergent) validity of the EQ-5D.(5-7) For discriminative validity, the EQ-5D was reported to be less sensitive to the detection of clinical change than disease specific measures, namely the KCCQ and NYHA, and to perform better at detecting larger compared to smaller clinical changes, based on the findings of one study.(8) The review also indicated that there was evidence of strong ceiling effects for EQ-5D domains and index values, based on two studies.(5;9) Finally, it was reported that the EQ-5D showed good reliability and responsiveness compared to other generic measures, namely the SF-12, but was less responsive than disease specific measures such as the KCCQ, according to two studies.(10;11)

Review authors' conclusions

The authors of the review concluded that the assessment of the validity and reliability of the EQ-5D suggested fairly strong convergent validity with other HRQoL measures and good discriminative abilities in detecting patients whose health status changed by a given clinical magnitude. They also concluded that there was evidence of strong ceiling effects across each health dimension and for the index values. Finally, they concluded that EQ-5D could be used by clinicians to evaluate the impact of cardiovascular disease on patients and to inform decision making and resource allocation.

4.1.3 Assessment of review in relation to objectives of WP1.1

Relevance of review question: One of the aims of Dyer et al, namely to synthesise the evidence on the validity and reliability of EQ-5D in studies in CVD, is consistent with the aims of WP1.1.(3) However, CVD is a wider disease group than the individual CVD conditions considered within this work package, and Dyer et al's categories were not always compatible with those of WP1.1. ACS would be included within the ischaemic diseases subgroup and there was direct correspondence in the case of HF. However, it was unclear whether coronary angioplasty and adult cardiac surgery were captured within the ischaemic heart disease subgroup. The remaining subgroups in the review (cerebrovascular diseases, arterial embolism and thrombosis, and peripheral vascular disease) did not correspond to any of the CVD conditions in WP 1.1.

Assessment of review quality: Dyer et al. (2010)(3) scored poorly against the relevant AMSTAR criteria. It was unclear whether an a priori design was used, as no reference was made to it within the review. The studies included in the review do not appear to have been subjected to quality assessment, and therefore, this was not taken into account when formulating conclusions. Furthermore, it was not stated how data extraction and data checking were conducted, and the number of reviewers involved in the process.

Acceptability of the search: Overall, the reported approach, combination of cardiovascular keywords with EQ-5D, and sources searched by the review authors was considered appropriate for the purpose of the review. It was not possible to comment on the database search strategy given that full strategies were not provided in the review.

Acceptability of study selection: The selection criteria were well described and were in accordance with the aims of WP1.1. In a small deviation from the selection criteria of WP1.1, studies published as abstracts only were excluded, as were studies that only presented data graphically. However, overall, the included studies were in accordance with the inclusion criteria of WP1.1, and there is only a small risk of having missed studies.

Adequacy of available data and synthesis: The data reported in the review was insufficient to adequately inform W.P1.1, as not all relevant results from the included studies were reported or discussed in the review. Moreover, the main text of the review referred mostly to favourable evidence on the performance of the EQ-5D. The authors did not discuss seemingly discrepant results or the reasons why results might be in disagreement. The review authors did not comment on the amount of evidence available to assess each of the psychometric properties of EQ-5D under analysis, other than to state that most studies assessed convergent validity. As the number of patients in each study was not reported in the review, it was not possible to make strong statements regarding the amount of evidence available. Nevertheless, based on the number of studies used it would appear that less evidence was available to assess the reliability and responsiveness of EQ-5D, which may limit the robustness of conclusions regarding these characteristics. Another limitation of this review, given the wider objective of work package 1.1, is that the available evidence was not examined in terms of the individual cardiovascular conditions. Examining the results across the CVD subgroups in the review, and with the caveat that the number of patients in each study was unknown, the amount of evidence seems to differ considerably. There were no studies examining convergent

validity in HF, with only discriminative validity and responsiveness being assessed for this condition. Ischaemic heart diseases and cerebrovascular diseases were the disease subgroups with more psychometric properties of EQ-5D assessed, and also with more included studies. One of the cardiovascular conditions for WP 1.1, cardiac arrhythmia was not covered by the studies included in the review. This appeared to be due to a lack of available evidence on psychometric properties of EQ-5D in cardiac arrhythmia, given that studies in this condition were included for the other objectives of the review. Other conditions, such as adult cardiac surgery and coronary angioplasty may have been included and grouped under the ischaemic heart diseases subgroup, but the information in the review was too limited to be sure of their inclusion within wider disease subgroups (e.g. ischaemic diseases). Similarly to cardiac arrhythmias, studies on adult cardiac surgery and coronary angioplasty were included for the other objectives of the review, thus it was anticipated that the potential non-inclusion of studies on the psychometric properties of EQ-5D in these conditions was due to lack of available evidence. The studies on cerebrovascular diseases, arterial embolism and thrombosis, and peripheral vascular diseases would not have been included according to the WP1.1 inclusion criteria, as they did not correspond to any of the CVD conditions of interest. Thus, the number of included studies would have been reduced to five, which reduced considerably the amount of evidence that was available for the purposes of WP1.1. Finally, the review did not aim to assess the acceptability of the EQ-5D in patients with CVD, which was a psychometric property of interest for WP 1.1.

The above mentioned limitations of the review in terms of data reporting, formulation of conclusions and lack of absolute correspondence between included CVD conditions determined the need for remedial action. Thus, all studies were re-considered for inclusion, and a search was conducted for the period between 2008 to March 2013, so as to update the review with any other primary studies that might provide relevant data to the review. A detailed data extraction and synthesis of all studies was also performed. All related tables are provided in the Appendix.

4.1.4 Reanalysis and update of Dyer et al. 2010(3)

Of the 10 studies initially included in the review, 5 met the inclusion criteria of WP1.1.(5;6;8-10) The updated search identified 18 studies of potential relevance to the review for which the full text was obtained. Only 7 of these studies met the criteria for inclusion in this review.(12-18) As such, a total of twelve studies were included in this reanalysis and update. The excluded articles are listed in Appendix B with reasons for exclusion.

Given the paucity of evidence available for each individual CVD condition, as well as the existence of some overlap of the study populations as defined by the CVD conditions (e.g. ACS patients can be treated with coronary angioplasty or cardiac surgery, such as CABG), the results were presented for CVD, and the overall evidence was discussed. Notwithstanding, the available evidence by each individual conditions is also discussed in Section 4.1.5.

Five of the studies assessed the psychometric properties of the EQ-5D in ACS.(5;6;13;18;19) The studies were conducted in Germany,(5) United States (US),(6) several European countries(18;19), and Turkey.(13) Different tariffs were applied to estimate the EQ-5D index score across the studies. Schweikert et al (2006) applied the Greiner et al (2003) European tariff,(20) Nowels et al (2005), De Smedt et al (2013) and De Smedt et al (2014) applied the UK standard tariff,(21) and it was not reported which tariff was applied in Sut et al. (2011). The European tariff is not comparable to UK tariff as the former has values in a considerably different range (0-100).(20) Therefore, only results referring to the health dimensions of EQ-5D, and not to the index were reported for Schweikert et al (2006) in this review.

Five of the studies assessed the psychometric properties of the EQ-5D in HF.(8;10;14-16) The studies were conducted in the US and Canada,(8;10;14;16) and Greece.(15) Most of these studies(8;10;15) applied the UK standard tariff(21) to estimate the EQ-5D utility score, whereas one study(16) applied the US specific tariff(22) and another did not report which tariff was applied.(14)

One of the studies examined the acceptability of EuroQol 5 dimensions 5 Levels (EQ-5D-5L) in cardiac arrhythmia.(17) The study was conducted in the UK, and the EuroQoL EQ-5D-5L crosswalk was used to estimate the utility score (but it was unclear which country tariff was applied).

Four of the studies assessed the psychometric properties of the EQ-5D in a patient population that included more than one CVD condition in WP1.1. There were three studies that included ACS, coronary angioplasty and cardiac surgery, and one study that included coronary angioplasty and cardiac surgery.(9) The van Stel et al (2006) was conducted in the Netherlands, and applied the UK tariff to estimate EQ-5D index scores.(21)

The results for analyses conducted on the EQ-5D health dimensions and EQ-5D index scores are reported below by psychometric property assessed, with considerations regarding individual

conditions presented in Section 4.1.5. Study characteristics and results are tabulated in the Appendix.

Acceptability: One study assessed the acceptability of EQ-5D(5) by estimating the proportion of missing and invalid responses, which ranged between 0.6 to 2.9% within the study follow-up (up to three months after discharge from the hospital), and performed slightly better on this property than SF-36 (missing range 1.5 to 6.5%) (Appendix). Withers et al,(17) assessed the acceptability of a PROM tool that included the EQ-5D-5L questionnaire, as well as two other disease-specific HRQoL questionnaires. The initial return rate of complete responses for the PROM tool ranged from 45 to 50%, across centers in the study. Following reminders to non-responders, the response rate went up to 71.2% for the full sample.(17) In another study,(9) acceptability was not formally assessed, but the percentage of missing data by instrument was reported (Appendix), with EQ-5D having less missing data than SF-6D at both time points (baseline 9.1% vs. 15.9%; post-intervention 15.9% vs. 22.6%). Acceptability could not be assessed from the data reported in the remaining studies, as analyses were mostly based on patients that completed the different questionnaires.

Reliability: One study reported results for test/retest reliability for patients who reported no change in health status by estimating the proportion of agreement and kappa statistics within two time periods (period 1 from admission to discharge, and period 2 from discharge to three months afterwards). Patients were identified as not having experienced change within periods according to a 'transition question' in the questionnaire used at discharge and three months post-discharge which explicitly asked whether patients felt better, worse, or unchanged compared with their previous situation. The mean duration of period 1 was not reported in the study. The proportion of agreement in patients who reported no change in period 1 (n=11/106) ranged from 55% for the health dimension usual care (kappa=0.17, p-value not reported) to 100% for the health dimension self-care (kappa=1.0), and for period 2 (n=32 to 34/106) ranged from 65% for the health dimension anxiety/depression (kappa=0.24, p-value not reported) to 88% for the health dimension self-care (kappa=0.53) (Appendix).(5)

Construct validity (Convergent): Seven studies reported results that provided some support for the convergent validity of the EQ-5D. One study compared the proportion of patients citing no problems in each EQ-5D health dimension in two subgroups (Myocardial infarction (MI) vs. CABG patients) for which quality of life was expected to be higher for MI patients.(5) With the exception of the health

dimension anxiety/depression (p=0.822), the percentage of patients indicating 'no problems' for the EQ-5D health dimensions was significantly higher for MI than for CABG patients (p<0.05) (Appendix). Another study assessed the construct validity of the Turkish version of the EQ-5D by estimating the Spearman rank correlations of EQ-5D index with the MacNew questionnaire subscales (r: 0.557-0.721, p<0.001) and global score (r=0.688, p<0.001) and considered the strong and significant correlations to be evidence of the validity of the instrument (Appendix).(13) van Stel et al (2006) estimated Spearman rank correlations between dimensions of the SF-6D and EQ-5D, and found moderate to strong correlations in related domains (r=0.31-0.47, p<0.0001) (Appendix).(9) De Smedt et al (2014) also found moderate to strong correlations in related health dimensions of EQ-5D and SF-6D (r=0.390-0.630, p<0.0001), as well as a strong correlation and moderate agreement between utility scores of both instruments (r=0.695, p<0.01; intraclass correlation (ICC)=0.536, p<0.01) (Appendix)(19). Nowels et al (1995) estimated the Spearman rank correlations between health dimensions of EQ-5D and the domains of two instruments, the SF-36 and the disease specific Quality of Life after Myocardial Infarction (QLMI). The correlations between similar health dimensions of the EQ-5D and SF-36 were strong (r=0.5-0.75), but significance was not reported. The correlations between EQ-5D and QLMI ranged from weak to strong (r= 0.01-0.64) across the comparison (Appendix), but were in general high for related dimensions with some exceptions (e.g. restriction and self-care; r=0.07).(6) The studies also assessed the convergence of the EQ-5D index with overall scores of other measures. Van Stel et al. (2006) reported the ICC between the EQ-5D and SF-6D utility scores (ICC=0.45) which was considered poor by the authors.(9) Kontodimopoulos et al (2011) found a similar ICC (0.484, p<0.0001), but a strong correlation between the two scores as estimated by the Pearson correlation coefficient (r=0.647, p<0.001).(15) In the Nowels et al (2005) study, the correlation between the EQ-5D index and the QLMI total score was strong (r=0.57), although significance was not reported.(6) The correlation between the EQ-5D index and SF-12 summary scores was also found to be strong (Physical component summary (PCS): r=0.64; Mental component summary (MCS): r=0.47; p<0.05) (Appendix)(18). Garster et al (2009) examined the partial correlation (partial on age, race, and sex) between the EQ-5D utility scores and the CVD proxy scores described above for the coronary heart disease (CHD) subsample of the study. The correlation was negative (the CVD score decreased with increased HRQoL as expected) and strong (r=-0.65), but significance was not reported.(14) One study examined the association between EQ-5D health dimensions response level (no problems, moderate problems, severe problems) and median SF-36 and McNew subscales at admission, i.e. by estimating median scores of comparable subscales by response levels of corresponding EQ-5D health dimensions.(5) The authors found that for all EQ-5D

dimension levels the median SF-36 and McNew subscales were ranked as expected and significantly different between groups ($p<0.001$, Kruskal-Wallis H test).(5)

Construct validity (known group): One study examined known-group validity by assessing the relationship of EQ-5D with age, gender and education, using the Kruskall-Wallis test. EQ-5D mean scores were found to be significantly different ($p<0.001$) for each category within age, gender and education level, and it confirmed the hypothesis that quality of life decreased with age, and lower education, and was lower for females (Appendix).(18) Known-group validity was also assessed as discriminative ability by comparing subgroups of patients of different clinical severity. Nowels et al (2005) compared differences in EQ-5D index scores between two groups based on their CCSC scores (I vs. II, III, or IV), using Mann-Whitney rank-sum testing, which showed evidence of excellent discriminative ability between the two groups ($p<0.001$). The difference in means for the subgroups categorised as CCSC I or CCSC II were also compared, and statistical difference was found using the Mann-Whitney rank-sum testing ($p<0.05$), but not with a t-test ($p=0.1$).(6) Garster et al (2009) examined the ability of EQ-5D to differentiate between subgroups classified by disease severity (no CHD, CHD no chest pain medication, and CHD plus chest pain medication).(14) The corresponding effect sizes (ES) were compared to a CVD proxy score derived from the Minnesota Living with Heart Failure questionnaire (MLHF). Significant differences in unadjusted mean EQ-5D scores ($p<0.001$, F-test) were found for 'No CHD' vs. 'CHD no medication' (difference =-0.055) and 'No CHD' vs. 'CHD plus medication' (difference=-0.14). Similar results were found for mean scores adjusted by baseline characteristics. ES for EQ-5D scores were lower (moderate to large ES: 0.32-0.84) than for the CVD proxy score (large ES: 0.51-1.13) across subgroup comparisons. The comparison between 'CHD no medication' vs. 'CHD plus medication' yielded large ES for the CVD proxy score (0.62) and for EQ-5D (0.52). The authors considered that ES were in general of the same magnitude as for the CVD proxy score, and that generic indexes (which included other HRQoL instruments besides EQ-5D) could capture differences in HRQoL between populations with and without CHD.(14)

Responsiveness (change over time): Spertus et al. (2005) examined groups with different degrees of clinical change over a 6 week period (mean 6.7 weeks, standard deviation 2.6) as assessed by a cardiologist (large (n=5), moderate (n=13), or small deterioration (n=35), no change (n=320), small (n=65), moderate (n=34), or large improvement (n=4)). The differences in mean changes in EQ-5D scores for subgroups of patients whose condition had changed were compared to stable patients using t-tests. The results were presented graphically for all measures (KCCQ, 6-minute walk test, EQ-5D index, EQ-5D VAS, NYHA, SF-12 PCS and MCS, figure weight change, and B-type natriuretic

peptide), and level of significance was indicated. Mean changes in EQ-5D scores for all change categories, except large deterioration, were small (absolute change smaller than 0.1) and not significant. The mean change score for the large deterioration category was significant ($p<0.001$) between minus 0.4 and minus 0.3 (graphical depiction). In the same study, responsiveness to clinical change was also compared between the measures by estimating c-statistics, which represent the percentage of times that the measure correctly identified patients with clinical change for all possible pairs of patients, one experiencing clinical change and one not. This was estimated for four categories (moderate to large deterioration, small deterioration, small improvement, moderate to large improvement), and results were presented graphically with only estimates for KCCQ and 6-minute walk text being mentioned in the main text. From the graph, c-statistics for the EQ-5D index appeared to range from approximately 0.56 (for small clinical improvements) to approximately 0.69 (for moderate to large clinical deterioration). The authors concluded that KCCQ and NYHA have better discriminative abilities than the EQ-5D index.(8) It is worth noting that it would have been more appropriate to estimate ES or standardised response means (SRM) for each of the change groups (and provide more comparable evidence) to assess responsiveness to clinical change than the methods used by the authors. Furthermore, the data is presented in a way that hinders comparison between measurements. Eurich et al (2006) assessed EQ-5D's responsiveness to clinical change over a period of six weeks as defined by three separate criteria (change in NYHA classification, validated global rating of change assessment, and change in distance travelled in the 6-minute walk test), by estimating mean change scores in ES and SRM, amongst other statistics, for each degree of clinical change considered.(10) In this study, the same statistics were also estimated for KCCQ, EQ-5D VAS and RAND-12. The mean changes (statistical significance was not reported) in EQ-5D index over time across measures for individuals who had suffered clinical deterioration appeared to be smaller in general, when compared to those who improved their clinical status (Appendix). However, differences in change scores for EQ-5D were small for all degrees of clinical change and across all clinical change criteria, and corresponding standard deviations were relatively large. The EQ-5D appeared to be more responsive to higher degrees of clinical improvement, than to smaller clinical changes (both improvement and deterioration), according to NYHA and global rating of change, but this was less evident for the 6-minute walk test (Appendix). Nevertheless, the number of patients for the categories of larger improvement were very small (NYHA criteria, n=2; global rating of change criteria, n=7; 6-minute walk test, n=7) (Appendix), so results should be interpreted cautiously. The SRM estimated for the "no changes" categories according to the NYHA criteria (SRM: 0.25, n=206) and the global rating of change criteria (SRM: 0.21, n=206) were all higher than for the corresponding estimates for moderate improvement (NHYA SRM: 0.11, n=50; global rating of change

SRM: 0.15, n=53), which seems counterintuitive (Appendix). The authors concluded that the HRQoL measures were more responsive to improvement than to deterioration in clinical status, and that responsiveness varied for the same generic HRQoL depending on which responsiveness indices and external criterion were used to identify clinical change.(10)

Responsiveness of EQ-5D was also assessed in one study by comparing the degree of agreement in classifying patients' changes in HRQoL as a clinically significant improvement, deterioration or stability over a time period of 6 months compared with the MLHF.(16) The percentage of overall agreement was low (19%), and the k statistics also indicated lack of agreement (k=-0.25; weighted k=-0.3; n=86; $p<0.05$) (Appendix). The authors also compared the number of patients identified through EQ-5D as experiencing each type of change (improvement, no change, deterioration) in HRQoL by each type of change according to MLHF. The agreement was found to be low across similar categories (deterioration: n=11 (EQ-5D) vs. n=46 (MHLF); stable: n=2 (EQ-5D) vs. n=13 (MHLF); improvement: n=3 (EQ-5D) vs. n=27 (MHLF)), and there was also considerable disagreement in classifying changes in HRQoL with 16 patients experiencing a deterioration in HRQoL according to EQ-5D out of 27 patients being classified as showing improvement (Appendix).(16) Although this comparison can be considered methodologically naïve, and some of the sample sizes were extremely small, it provided some evidence against the responsiveness of EQ-5D that should not be ignored.

Responsiveness (ceiling effects): van Stel et al (2006) examined the existence of potential ceiling effects in the health dimensions and index scores for the EQ-5D and SF-6D at baseline.(9) Despite the considerable percentage of patients replying 'no problems' to individual EQ-5D health dimensions (ranging between 30.5% in usual activities to 93.1% in self-care), only 13.5% of patients scored full health on the EQ-5D compared to 0.4% on the SF-6D (Appendix). The authors considered that there was evidence of a ceiling effect for EQ-5D.(9) Another study, also found evidence of ceiling effects for EQ-5D, with 28.8% of patients reporting full health with this instrument compared to 4.2% with SF-6D (Appendix).(19)

4.1.5 Conclusion of appropriateness of EQ-5D in CVD conditions

Overall, the evidence base assessing the performance of the EQ-5D in CVD conditions is mostly positive, although relatively small with only twelve studies complying with the inclusion criteria for this review. The acceptability of EQ-5D was fair to good in the three studies that assessed this property. Evidence regarding reliability was very limited and indicated poor performance. Nevertheless, reliability was examined in one study alone and only at health dimension level.

Construct validity (convergent) between EQ-5D was generally good, and more evident at the index than at the health dimension level. This was the psychometric property for which there was more robust evidence, given the amount of evidence available and its general concordance. The available evidence in terms of construct validity also reinforced that the EQ-5D can distinguish between subgroups of patients of varying HRQoL, namely between MI and CABG patients. There was considerable positive evidence of known-group validity across groups defined by age, gender and educational level, provided by a large European study that included more than 8,000 patients from 22 countries.(18) The ability of EQ-5D to distinguish between groups of different disease severity (according to cardiologist assessment or based on self-report) was found to be good. Finally, evidence on responsiveness as change over time was poor across the three studies that assessed it, but it should be noted that the methodology used to assess it, and in one case the reporting of results, was not the most adequate. It was concluded that the evidence on responsiveness is mostly uncertain, but studies so far suggest that EQ-5D may perform poorly in this characteristic. Importantly, the studies that assessed responsiveness as change over time were all conducted in a single disease condition, HF, so there is also a question of whether the poor performance in this condition is likely to extend to other CVD conditions. One study detected a ceiling effect, i.e. a tendency towards single level response, that was considerably more pronounced for individual health domains of EQ-5D (especially for self-care), than for the utility score.(9) Evidence of ceiling effects for EQ-5D utility scores was also found in a large European study.(19) This may translate into less discriminative ability of EQ-5D for patients at lower levels of disease severity.

Six studies included in the review assessed the psychometric properties of EQ-5D in HF, and provided evidence of construct (both convergent and known-group) validity, but poor responsiveness. No other psychometric properties of EQ-5D were examined in HF. For ACS and cardiac surgery there was some evidence of the majority of all reported psychometric properties (with the exception of responsiveness), taken from five and four studies respectively. EQ-5D performed well in terms of acceptability and validity, but showed poor reliability. In the five studies in coronary angioplasty, EQ-5D performed similarly to what was found for ACS and cardiac surgery in the same properties. The only evidence found for cardiac arrhythmia refered to acceptability of EQ-5D, which was considered good. The number of studies available and conclusions on evidence by condition and psychometric property assessed are summarised below in Tables 2 and 3.

Table 2: Number of studies reporting psychometric properties of EQ-5D in CVD

Condition	Acceptability	Reliability	Construct validity (Convergent)	Construct validity (Known group)	Responsiveness (Change over time)	Responsiveness (Ceiling effects)
Cardiac arrhythmia	1(17)	0	0	0	0	0
Heart failure	0	0	3(13-15)	1(14)	3(8;10;16)	0
Coronary angioplasty	1(9)	0	3 (23) (12;18)	1(18)	0	2 (19;23)
Cardiac surgery	2(5;9)	1(5)	4 (18;19;23;24)	1(18)	0	2 (19;23)
Acute coronary syndrome	1(5)	1(5)	5 (13;18;19;24;25)	2(18;25)	0	2(19;23)

Table 3: Conclusions on evidence on psychometric properties of EQ-5D in CVD

Condition	Acceptability	Reliability	Construct validity (Convergent)	Construct validity (Known group validity)	Responsiveness (Change over time)	Responsiveness (Ceiling effects)
Cardiac arrhythmia	Good	NE	NE	NE	NE	NE
Heart failure	NE	NE	Good	Good	Poor	NE
Coronary angioplasty	Fair	NE	Fair/Good	Good	NE	Potential ceiling effects
Adult cardiac surgery	Fair/Good	Poor	Fair/Good	Good	NE	Potential ceiling effects
Acute coronary syndrome	Good	Poor	Good	Good	NE	Potential ceiling effects

NE, No evidence.

4.2 **Routinely collected proxy measures in cardiac arrhythmia** (WP1.2)

As the EQ-5D was found to be acceptable for CVD conditions, no additional searches for alternative measures were conducted.

4.3 **Evidence for economic evaluations in cardiac arrhythmia** (WP1.3)

4.3.1 Cost-effectiveness modelling approach used in recent HTAs in cardiac arrhythmia

Eight Technology appraisals (TAs) relating to cardiac arrhythmia were identified from the searches. One of the TAs was withdrawn,(26), and one of them is currently in development with anticipated issue date of June 2014.(27) Four of the TAs examined the clinical and cost-effectiveness of a pharmaceutical intervention in atrial fibrillation (AF),(28-31) while the other three assessed devices to manage cardiac arrhythmia.(27;32;33) Three of TAs compared anti-coagulant drugs in the prevention of stroke and systemic embolism in atrial fibrillation (AF) patients,(28-30) and one compared anti-arrhythmic drugs for the treatment of AF and atrial flutter. One of the TAs examined the clinical and cost-effectiveness of implantable cardioverter defibrillators (ICD) or cardiac resynchronisation therapy (CRT), in addition to optimal pharmacologic therapy (OPT) compared to OPT alone for the treatment of three patient populations: i) people with an increased risk of sudden cardiac death (SCD) as a result of ventricular arrhythmias: ii) people with HF (due to left ventricular systolic dysfunction (LVSD) and cardiac dyssynchrony); and iii) people with both conditions.(27) Another TA examined the clinical and cost-effectiveness of CRT for people with HF and evidence of dyssynchrony by comparing CRT pacemaker (CRT-P) and CRT defibrillator (CRT-D) devices each with OPT, and with each other.(32) TA88 examined the clinical and cost-effectiveness of dual-chamber pacemakers compared to single chamber pacemakers for bradycardia due to atrioventricular block (AVB) or sick sinus syndrome (SSS).(33)

All TAs except one used Markov models to examine the cost-effectiveness of the interventions under appraisal; the exception was TA197, which used a discrete event simulation model (DES).(31) The Markov models used to assess anticoagulant therapy comprised of discrete health states representing the clinical pathway for AF patients at the point of intervention. The number of health states varied across models from 4 to 23 discrete health states, corresponding mostly to the occurrence of thromboembolic, ischaemic and bleeding events, as well as stable states and death.(28;29) One of the models defined the health states based on the level of disability (as measured by the MRS), with probabilities of future clinical events conditioned by disability level.(30) In three TAs transitions between states were modelled based on data from clinical trials (single trial data or estimates resulting from meta-analyses). All cause mortality was modelled based on UK

specific life tables, usually adjusted for $CHADS_2$ score, which is a predictor of stroke risk. Cardiovascular mortality was generally informed by clinical trial data (baseline and relative risks).(28-30)

The DES model had 4 discrete health states (normal sinus rhythm, permanent AF with uncontrolled symptoms, permanent AF with controlled symptoms, and death), and clinical events included AF recurrence, ACS, stroke, congestive HF and changes in AF symptoms. Occurrence of events within the model was informed by survival analysis from clinical trial data. Treatment effects and adverse events rates were estimated through evidence synthesis of trial data. All cause mortality was also based on UK life-tables, adjusted by $CHADS_2$ scores. (31)

Two of the models used to assess the cost-effectiveness of devices in cardiac rhythm management included discrete health states and key clinical events which represented the clinical pathway for people with HF (or with HF and increased risk of SCD) at the point of the intervention. The number of health states varied across models from 4 to 28 discrete health states, depending on if the occurrence of clinical events was modelled as individual health states or grouped within health states. Cardiovascular mortality (due to worsening of HF or SDC) was generally modelled using survival data from clinical trials (survival curves and hazard ratios). Other key clinical events encompassed hospitalisations, surgical complications, device related procedures (in TAs on CRT) and heart transplants, and their occurrence was generally modelled using trial data (relative risks). When trial data was not used, relative risks were estimated based on individual studies in the published literature or on evidence synthesis of trial estimates conducted within the TAs.(27;32) Another TA used two separate Markov models to examine the cost-effectiveness of dual-chamber pacemakers compared to single chamber pacemakers for bradycardia. The clinical pathway was considered to differ according to underlying aetiology (SSS or AVB), hence the need for two separate models. Each model included numerous discrete health states that reflect main outcomes in each pathway following pacemaker insertion, and comprised of complications of insertion, remaining well with the pacemaker, developing pacemaker syndrome (mild or severe), upgrade to dual chamber pacemaker, atrial fibrillation, HF, stroke generator expiry or death. The clinical event rates were sourced from clinical trial data (single trials and meta-analysis), and cardiovascular mortality was assumed to be constant in time and cause specific. (33)

All of the studies quality adjusted survival by assigning mean utility values to the discrete health states. In the models in HF populations the utilities were sourced from the published literature, and

differed according to the NYHA classification for HF severity.(27;32) The majority of TAs used EQ-5D data taken from the published literature as the main source of HRQoL estimates,(27-31) although one TA also used time trade-off and standard gamble elicited utility values to inform the model.(32) Another used mostly time trade-off elicited utilities from patients within a clinical trial.(33) Across the TAs, HRQoL in patients with cardiac arrhythmia has been assumed to depend mostly on underlying coronary disease and its severity, complications subsequent to surgical procedures, symptoms, and adverse effects of anticoagulant drugs.(27-33) Disability following stroke is another important aspect of HRQoL, especially in patients at increased risk of stroke, i.e. patients with AF, with assigned utility weights varying by level of disability. (28-30)

Table 4: Summary of existing models in cardiac arrhythmia

Model approach	Method used to model utilities
MTA (ID:481): Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure (review of TA95 and TA120); 2014(27)	
TAG de-novo Markov model 4 separate health states: stable, hospitalisation, transplanted and dead. Key clinical events: hospitalisation due to heart failure or arrhythmia, transplant, device failure, death, peri-operative complications of implant procedure, routine device replacements, lead displacement, infections, and device upgrades. Effectiveness: Survival curves for cardiac mortality (SCD and HF) RR risk for other key clinical events, treatment effects applied as RR reductions. Source: clinical RCTs , MA, published literature	Utility: EQ-5D; mean values assigned to health states according to NYHA classes. Source: published literature, observational analysis of RCT data, assumptions
STA (TA275): Apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation; 2012(28)	
Manufacturer's Markov model; 18 separate health states: NVAF, ischaemic stroke (mild/moderate/severe/fatal); haemorrhagic stroke (mild/moderate/severe/fatal); non-fatal or fatal other intracranial haemorrhage (i.e non-haemorrhagic stroke); non-fatal or fatal systemic embolism; non-fatal or fatal other major bleeds; clinically relevant non-major bleeds; non-fatal or fatal MI; other cardiovascular hospitalisations. Effectiveness: HR of events applied to baseline risk ($CHADS_2$ score adjusted); risk modified by HR of treatment effect; stroke severity distribution; type of bleed distribution. Source: Clinical RCT	Utility: Mean EQ-5D; TTO elicitation; SG elicitation; assumptions. Applied to separate health states. Source: Published literature.
STA (TA256): Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation; 2012 (29)	
Manufacturer's Markov model; 22 separate health states: stable AF; therapy initiation; off therapy stable, on therapy stable; systemic embolism; on therapy minor bleed; on therapy major bleed; on therapy minor stroke; on therapy major stroke; on therapy post-minor stroke; on therapy post-major stroke; on therapy minor bleed; on therapy major bleed; off therapy minor stroke; off therapy major stroke; off therapy post-minor stroke; off therapy post-major stroke; IC bleed; Post-IC bleed; MI; post-MI; death. Effectiveness: RR of events Source: clinical RCTs and manufacturer's network MA	Mean utilities: EQ-5D; TTO elicitation; Median utilities: SG elicitation- Utilities applied to stable states and stroke related events Source: published literature AE: Marginal decrement from major bleeding to utility (EQ-5D) associated with bleeding events Source: Published literature

STA (TA249): Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation; 2012 (30)	
Manufacturer's Markov model; 4 separate health states: independent disability, moderate disability; dependent; death Key: clinical events: ischemic stroke; intra cranial haemorrhage; haemorrhagic stroke; extra cranial bleeds; systemic embolism; transient ischemic attack; and acute MI. Effectiveness: Baseline death risk (dependent on CHADS2 score), events RR' and treatment effects' RR. All cause mortality estimated from UK life tables adjusted for $CHADS_2$ score Source: clinical RCT, manufacturer's MTC, published literature.	Utility: Mean EQ-5D values; TTO elicitation; assumptions. Applied to separate health states. Source: clinical RCT and published literature from RCT. AE: Marginal decrement from major bleeding to utility (EQ-5D) associated with bleeding events Source: Published literature and assumptions
STA (TA197): Dronedarone for atrial fibrillation and atrial flutter; 2010 (31)	
Manufacturer's DES model; 4 main health states(normal sinus rhythm, permanent AF with uncontrolled symptoms, permanent AF with controlled symptoms and death) and 7 events (AF recurrence, ACS, stroke, CHF, treatment discontinuation for any cause, AF symptoms change for permanent patient and death) Effectiveness: Survival analysis risk equations for clinical events. All cause mortality estimated from UK life tables adjusted for $CHADS_2$ score. Treatment effects applied as ORs. Source: clinical RCT, published literature, manufacturer's MTC	Utility: mean EQ-5D values assigned to health states Source: Observational study AE: utility decrements elicited by TTO in general public Source: AIC study conducted by manufacturer in 127 subjects
MTA (TA120): The effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure; 2007(32)	
TAG de-novo Markov model, with submodels for each device and OPT. 28 separate health states reflecting the occurrence of the key clinical events: routine device replacements, peri-operative complications, infections, device upgrades, left lead dislodgments, hospitalisation due to heart failure, hospitalisation due to arrhythmia, heart transplant, surgical failure and death. Each health state in the model has a corresponding probability tree to model transition probabilities according to clinical events. Effectiveness: Survival curves for cardiovascular mortality (SCD and worsening of HF) by treatment, RR risk for other key clinical events with treatment effects applied as RR reductions. Source: clinical RCTs, published literature, expert opinion, assumptions.	Utility: EQ-5D and TTO (elicited); mean values assigned according to NYHA classes; Utility on hospitalisation due to heart failure: SG (elicited) Source: published literature

MTA (TA88): The effectiveness and cost effectiveness of dual chamber pacemakers compared to single chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation; 2005(33)	
2 TAG Markov models, according to the underlying cause of bradycardia (AVB or SSS); numerous discrete health states that reflect main outcomes following pacemaker insertion, and include: complications of insertion, remaining well with the pacemaker; pacemaker syndrome (mild or severe); upgrade to dual chamber pacemaker; atrial fibrillation; heart failure; stroke; generator expiry or death. Effectiveness: Time-constant cardiovascular mortality rates, Events RR Source: clinical RCTs, MTC, published literature	Utility: Mean utilities elicited through TTO and applied to health states; mean EQ-5D values; clinical expert elicitation. Source: clinical RCT, published literature.

AE: Adverse Events; MTA: Multiple Technology Appraisal; STA: Single Technology Appraisal; MA: Meta-analysis TAG: Technology Appraisal Group; TTO: Time trade-off; SG: Standard Gamble, RCT: randomised controlled trial; CHF: congestive heart failure; MTC: mixed treatment comparison; AIC: Academic in confidence; NVAF: Non-Valvular Atrial Fibrillation; IC: intra-cranial; ONS: Office of national statistics; BP: Blood pressure; LVEF: Left ventricular ejection force; RR: Relative risk; HR: Hazard rate; OR: Odds ratio; SR: Systematic review.

In summary, the following evidence would be required to compare providers or the cost-effectiveness of interventions for cardiac arrhythmia:

- Device interventions (type of device, new or repair/substitution)
- Pharmaceutical interventions (type of intervention, treatment discontinuation, adverse events)
- Clinical variables that characterise disease severity in heart failure patients (NYHA)
- Surgical rates (type of intervention, success rate, peri and post-surgical complications)
- Cerebrovascular, bleeding and thromboembolic events (type of event, rates, disability level following event)
- Hospitalisation (rates, cause, length of stay)
- HRQoL data (prior to surgical procedure and at follow-up)
- Death rates (cardiac and surgical related, all cause)

The majority of this evidence would need to be dated and linked through timings of collection.

4.3.2 Fields collected in National Audit of Cardiac Rhythm Management

The national audit of cardiac rhythm management (NACRM) is composed of two questionnaires for two distinct types of clinical interventions in cardiac arrhythmia: implantation of cardiac devices (collected in the spreadsheet Device-dataset-5502n-14032014); and interventional procedures for management of cardiac rhythm disorders, namely ablation procedures (collected in the spreadsheet eps-dataset-v305-26032014). The ablation dataset also collects PROM data through two questionnaires, namely EQ-5D and the Atrial Fibrillation Effect on Quality Of Life questionnaire (AFTEQ), with both questionnaires being applied prior to the ablation procedure, and at 6 and 12 months of follow-up. There are only three mandatory fields in the devices and ablation datasets (hospital identifier, patient case record number, procedure date). However, there are a minimum number of fields that are part of the cardiac rhythm management (CRM Minimum Data Standard) (on which hospitals are assessed for completeness). The Minimum Data Standard fields, and the remaining fields are provided in the Appendix.

For cardiac devices the data provide information on patient demographics (hospital identifier, patient case record number, NHS number, age, sex, postcode); baseline data (date of first implant, pre-device aetiology, pre-device symptom, Electrocardiogram (ECG) indication for device, functional status (NYHA), left ventricular ejection fraction, ICD Indication, pre-device/Ablation QRS duration);

procedure (Procedure date, first operator (name, General Medical Council (GMC) number), consultant (name, GMC number), intervention category, generator mode (or maximum system capability)); procedure details related to the generator/device (generator mode, generator/device procedure, reason for generator change, generator model, generator serial number); lead extraction (indication for lead extraction); complications (acute complications). For interventional procedures the data provide information on demographics (same as for devices dataset); baseline data (pre procedure aetiology, pre procedure symptom (ablation Indication), other documented arrhythmia, pre procedure arrhythmia); procedure (procedure date, first operator (name, GMC number), consultant (name, GMC number), procedure type, ablation procedure, ablation attempted, success, acute complications); atrial fibrillation ablation details (European Heart Rhythm Association atrial fibrillation classification, NYHA functional status); follow-up for atrial fibrillation ablation (complications (post discharge), frequency of palpitations, duration of palpitations).

4.3.3 Comparing fields in the NACRM with variables used in existing HTAs

The existing models either use survival curves to model mortality, (all cause, cardiovascular and non-cardiovascular) or assume time-constant mortality rates. There is information in the NACRM on clinical interventions (date of procedure/device implantation, generator mode (identifies the type of device), procedure type, ablation success) which would provide some of the information required to compare alternative treatments. The mortality data could be used to model survival, as death related to procedure is collected in the acute and late complications fields. However, this would still be insufficient to distinguish between cardiovascular and non-cardiovascular death, as not all causes of death are collected within the audit. The field late complications captures key clinical events, namely complications (including death) related to either device implantation or ablation procedures occurring within one year of the procedure, but is not included in the minimum data standard of the audit. Furthermore, there are other key clinical events that would not be captured by this audit, such as readmissions to hospital due to clinical deterioration (e.g. hospitalisation due to HF worsening). The NACRM only collects data on antiarrhythmic drugs on patients with AF, with no other medication data being collected in the two datasets of the audit.

Clinical variables such as NHYA functional status (no limitation of physical activity, slight limitation of ordinary physical activity, marked limitation of ordinary physical activity, symptoms at rest or minimal activity), European Heart Rhythm Association AF classification (no symptoms, mild symptoms, severe symptoms, disabling symptoms), and Left ventricular ejection force (LVEF)

(measure of severity of left ventricular disfunction), as well as pre-device aetiology (apparently normal heart, ischaemic heart disease, congenital, cardiac surgery, catheter ablation, percutaneous structural cardiac intervention, cardiomyopathy, endocarditis, myocarditis, valve disease - operated/intervened, cardiac transplant, channelopathy, myotonic dystrophy), and pre-procedure aetiology (apparently normal heart, pre-excitation (delta wave), ischaemic heart disease, valve disease, hypertensive heart disease, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, myocarditis, channelopathy), could be used to case-mix patients when comparing performance or cost-effectiveness of interventions. Pre-device/ pre-procedure aetiology could also be used to inform the clinical pathway(s) relevant to structure the model. Furthermore, the audit collects data on the type of procedures, device implanted (where applicable) and success rates of surgical procedures (implantation or ablation), which would provide information required to compare interventions.

Patient related outcome measures are already collected in the NACRM, the EQ-5D and AFTEQ, although only for patients undergoing ablation procedures. The extension of the collection of PROM data to all patients in the NACRM (preferably the EQ-5D), could improve the ability of the audit to inform cost-effectiveness analysis of interventions. The value of collecting PROM data in cardiac arrhythmias may be greater than in other conditions where it is possible to map clinical variables to a preference-based measure. In this particular case, mapping from clinical variables could be very challenging, given that these variables are usually disease specific and there are several underlying cardiovascular diseases that can be the cause of cardiac arrhythmia.

The mandatory fields in the NACRM are insufficient to inform cost-effectiveness analysis of interventions and policies in cardiac arrhythmia. However, the minimum data standard subdataset has considerably more information that would be useful to model decision problems in this cardiovascular condition. Nevertheless, there are a number of fields that are not included in the minimum data standard, and that would provide valuable information in this context. For example, the PROM data collected in the audit is not currently part of the minimum data standard dataset and is only collected for atrial fibrillation dataset. The late complications fields would also provide important follow-up data, and would be especially relevant to model survival within models, as it reports cardiovascular related causes of death. It is worth noting that the complications that are collected are mostly directly related to the procedure, and do not capture adverse events of medication. As mentioned above, the NACRM collects limited data on medication, with only data related to anti-arrhythmic drugs in patients with AF being collected. Given that these patients may

also be prescribed anticoagulant drugs that can impact on HRQoL through adverse events (e.g. bleeding), and by potentially modifying the rate of thromboembolic events leading to disability, information on AEs would be worth including in the audit fields related to anticoagulant medication. Alternatively, these data could be retrieved by linking the NACRM dataset to other national audit datasets that collect data on related conditions (e.g. the National Heart Failure Audit (NHFA)) which could be done via NHS number. The limitation here would be that not all patients would be registered in both datasets. This would also be the case for clinical events leading to hospital readmission, which are also not collected in the audit.

Depending on the completion rates of non-mandatory fields in the audit, with additional fields added or linkage to other datasets, it is possible that the NACRM could be used to compare the cost-effectiveness of interventions or policies.

4.4 Recommendations for cardiac arrhythmia

In summary, no evidence was identified on the validity and responsiveness of the EQ-5D in cardiac arrhythmia, although the instrument was considered to have good acceptability (Section 4.1). Nevertheless, the validity of EQ-5D has been demonstrated in other related conditions, such as heart failure, as well as more generally in the cardiovascular area. Furthermore, EQ-5D derived utility weights have been widely used in cost-effectiveness studies in cardiac arrhythmia, and NACRM already collects EQ-5D data in patients with atrial fibrillation who undergo atrial ablation procedures. In addition, and although many variables of importance are already collected in the audit, there are concerns about the completion rates of fields not included in the CRM Minimum Data Standard and that not all relevant fields to perform robust economic evaluations are collected in the audit. Potential recommendations (PR) and areas for future research (FR) are discussed below. All suggested future research areas are indicative and would require a discussion and detailed proposal if required.

As the EQ-5D questionnaire is already collected in the NACRM for ablation procedures, it would be of value to extend the collection of the questionnaire to the devices implantation dataset (PR.1). Furthermore, as there is a dearth of evidence on the psychometric properties of EQ-5D, the data collected in the audit could be used to examine these properties, so as to validate the use of EQ-5D in this condition (FR.1). Research on this topic is already being conducted by the National Institute for Cardiovascular Outcomes Research.(17)

There are concerns whether the NACRM collects suffiently detailed information to compare providers or perform economic evaluations. The inclusion of mandatory information on the use of anticoagulant drugs and the occurrence of adverse events associated with these drugs, with special attention to bleeding and cerebrovascular events, would increase the flexibility of the secondary use of the data (PR.2). Depending on the completion rates of the Minimum Data Standard Dataset consideration should be given to making these fields mandatory (PR.3).

Table 5: Recommendations and associated future research for cardiac arrhythmia

PR.1	*Extend EQ-5D-5L collection so that it is conducted for both elements of the NACRM, i.e. the device and the ablation procedures dataset. implantation of cardiac devices (collected in the spreadsheet Device-dataset-5502n-14032014)*
FR.1	*Assess the psychometric properties of the EQ-5D-5L in patients with cardiac arrhythmias using data collected in the audit*
PR.2	*Collect mandatory information on the use of anticoagulant drugs and the occurrence of adverse events associated with these drugs, with special attention to bleeding and cerebrovascular events*
PR.3	*Depending on completion rates of Minimum Data Standard Dataset, consider making these fields mandatory*

5. RESULTS FOR HEART FAILURE

5.1 Evidence of appropriateness of EQ-5D in heart failure (WP1.1)

Six studies included in the updated review in CVD conditions (Section 4.1.4) assessed the psychometric properties of EQ-5D in heart failure, and provided positive evidence of construct (both convergent and known-group) validity, but poor responsiveness. Full details on the assessment of the appropriateness of EQ-5D in heart failure are presented in Section 4.1.5.

5.2 Routinely collected proxy measures in heart failure (WP1.2)

As the EQ-5D was found to be acceptable for CVD conditions, no additional searches for alternative measures were conducted.

5.3 Evidence for economic evaluations in heart failure (WP1.3)

5.3.1 Cost-effectiveness modelling approach used in recent HTAs in heart failure

Three TAs relating to heart failure were identified from the searches, one of these is currently in development with anticipated issue date of June 2014.(27) One of the TAs examined the clinical and cost-effectiveness of CRT in addition to optimal OPT compared to OPT alone for the treatment of people with heart failure (due to LVSD and cardiac dyssynchrony) or people with both an increased risk of SCD as a result of ventricular arrhythmias and heart failure.(27) Another TA examined the clinical and cost-effectiveness of CRT for people with heart failure and evidence of dyssynchrony by comparing CRT-P and CRT-D devices each with OPT, and with each other.(32) The third TA examined the clinical and cost-effectiveness of ivabadrine in addition to standard care compared to standard care alone for the treatment of chronic heart failure.(34)

All TAs used Markov models to examine the cost-effectiveness of the interventions under appraisal. The models comprised of discrete health states and key clinical events which represented the clinical pathway for people with heart failure (or with heart failure and increased risk of SCD) at the point of the intervention. The number of health states varied across models from two to 28 discrete health states, depending on if the occurrence of clinical events was modelled as individual health states or grouped within health states. Cardiovascular mortality (due to worsening of heart failure or SCD) was modelled mostly by using survival data from clinical trials (survival curves and hazard ratios). Other key clinical events encompassed hospitalisations, surgical complications, device related procedures (in TAs on CRT) and heart transplants, and their occurrence was modelled based mostly on trial data (relative risks). When trial data were not used, relative risks were estimated based on individual studies in the published literature or on evidence synthesis of trial estimates conducted

within the TAs. Disease severity in the model was based on the NYHA classification for heart failure severity. In two of the TAs, the distribution of patients by NYHA classes at model entry was derived from trial data, and changes over time were assumed to occur as observed on trial or not to occur at all (if evidence did not suggest disease severity changes post-intervention).(27;32) In another TA, the NYHA distribution was predicted by a regression model that estimated the likelihood of changing NYHA class given treatment and time spent in a particular severity class.(34)

Two of the studies quality adjusted survival by assigning mean utility values to the discrete health states. These utilities were sourced from the published literature, and weighted according to NYHA distribution in the health state.(27;32) One study used a regression model to predict utilities within the alive health state, according to predicted NYHA distribution over time. The regression model also allowed predicting utility decrements from hospitalisations (from heart failure, cardiovascular causes and all causes) and utility benefit from interventions. This regression model relied on patient level data taken from the study used to provide the primary clinical evidence.(34) The majority of utility estimates in the three TAs used EQ-5D data,(27;32) although one TA also used time trade-off and standard gamble elicited utility values from published literature to inform the model.(32)

Table 6: Summary of existing models in heart failure

Model approach	Method used to model utilities
MTA (ID:481): Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure (review of TA95 and TA120); 2014(27)	
TAG de-novo Markov model 4 separate health states: stable, hospitalisation, transplanted and dead. Key clinical events: hospitalisation due to heart failure or arrhythmia, transplant, device failure, death, peri-operative complications of implant procedure, routine device replacements, lead displacement, infections, and device upgrades. Effectiveness: Survival curves for cardiac mortality (SCD and HF) RR risk for other key clinical events, treatment effects applied as RR reductions. Source: clinical RCTs , MA, published literature	Utility: EQ-5D; mean values assigned to health states according to NYHA classes. Source: published literature, observational analysis of RCT data, assumptions
STA (TA267): Ivabradine for the treatment of chronic heart failure; 2012 (34)	
Markov model 2 separate health states: alive, dead. Key clinical events: hospitalisation due to HF, cardiovascular causes and all causes; changes in NYHA class; and death (non-cardiovascular, and cardiovascular HF	Utility: EQ-5D; mean values assigned to NYHA classes at model entry; Utility decrements from hospitalisations (from hearth failure, cardiovascular causes and all causes) and utility benefit from intervention predicted by mixed regression models. Source: sub-study of RCT

related and non HF related). Effectiveness: Regression models applied to estimate events occurrence with the exception of non-cardiovascular mortality, which was estimated from UK life tables. Source: clinical RCT, published literature.	
MTA (TA120): The effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure; 2007(32)	
TAG de-novo Markov model, with submodels for each device and OPT. 28 separate health states reflecting the occurrence of the key clinical events: routine device replacements, peri-operative complications, infections, device upgrades, left lead dislodgments, hospitalisation due to heart failure, hospitalisation due to arrhythmia, heart transplant, surgical failure and death. Each health state in the model has a corresponding probability tree to model transition probabilities according to clinical events. Effectiveness: Survival curves for cardiovascular mortality (SCD and worsening of HF) by treatment, RR risk for other key clinical events with treatment effects applied as RR reductions. Source: clinical RCTs, published literature, expert opinion, assumptions.	Utility: EQ-5D and TTO (elicited); mean values assigned to separate health states according to NYHA classes; Utility on hospitalisation due to heart failure: SG (elicited) Source: published literature

AE: Adverse Events; MTA: Multiple Technology Appraisal; STA: Single Technology Appraisal; MA: Meta-analysis TAG: Technology Appraisal Group; TA: Technology Appraisal; TTO: Time trade-off; SG: Standard Gamble, RCT: randomised controlled trialBP: Blood pressure; LVEF: Left ventricular ejection force; RR: Relative risk; HR: Hazard rate, SR: Systematic review.

In summary, the following evidence would be required to compare providers or the cost-effectiveness of interventions for heart failure:

- Device interventions (type of device, new or repair/substitution)
- Pharmaceutical interventions (type of intervention, treatment discontinuation, adverse events)
- Clinical variables that characterise disease severity in heart failure patients (NYHA)
- Surgical rates (type of intervention, success rate, peri and post-surgical complications)
- Hospitalisation (rates, cause, length of stay)
- HRQoL data (prior to surgical procedure and at follow-up)
- Death rates (cardiac and surgical related, all cause)

The majority of this evidence would need to be dated and linked through timings of collection.

5.3.2 Fields collected in National Heart Failure Audit

The fields in the NHFA are collected through a questionnaire (the spreadsheet Dataset version 4.2.1). Items in the datasets can be labelled core mandatory, core or non-core. The difference between core mandatory and core is that for the former a value must be included in the corresponding field, whereas for core fields, records can be included even without a value (although it is expected that such data is included), and still generate a record. Non-core includes all fields that are not expected to be included (but can be recorded for specific projects). The core mandatory fields, the remaining core and non-core fields are provided in the Appendix. The data provide information on patient registration (hospital identifier, local patient identifier, patient name, age, sex and postcode); admission details (date of admission, main place of care, specialist input, breathlessness, peripheral oedema); medical history (ischaemic heart disease, device therapy, valve disease, hypertension, diabetes, asthma, chronic obstructive pulmonary disease), physical examination (weight, heart rate, systolic blood pressure); investigations on discharge (haemoglobin, urea, creatinine, serum sodium, serum potassium, electrocardiogram, echo); treatment on discharge (angiotensin-converting-enzyme inhibitor, angiotensin receptor blocker, beta blocker, loop diuretic, thiazide or metolazone, mineralocorticoid receptor antagonist, digoxin); discharge and referral (confirmed diagnosis of heart failure, heart failure management plan, stable on oral therapy after discharge planning, review appointment with the heart failure multidisciplinary team, date of review appointment, referral to heart failure nurse follow-up, referral to cardiac rehabilitation, referral to cardiology follow-up, date of discharge, stable on oral therapy after discharge planning, death in hospital).

5.3.3 Comparing fields in the National Heart Failure Audit with variables used in existing HTAs

The existing models use survival curves to model mortality, (all cause, cardiovascular and non-cardiovascular). There is some information in the NHFA on clinical interventions (main place of care, specialist input, device therapy, treatment on discharge) which would provide some of the information required to compare alternative treatments. The mortality data could be used to model overall mortality, but it will not allow distinction between cardiovascular and non-cardiovascular death, as cause of death is not collected within the audit. Furthermore, the NHFA will only provide data on death occurring at the hospital. Relative risks of hospitalisation due to heart failure worsening could potentially be estimated by using readmission data (date and breathlessness). Transitions to stable state could also be modelled based on discharge data (stable on oral therapy after discharge planning).

The NHFA collects referral data (referral to cardiothoracic surgery, referral to transplant) that can be used to inform the occurrence of further clinical events, but these items are not mandatory. Furthermore, the audit does not provide data on surgical complications and device related procedures, which are relevant for those patients requiring CRT or heart transplant.

Breathlessness (no limitation of physical activity, slight limitation of ordinary physical activity, marked limitation of ordinary physical activity, symptoms at rest or minimal activity) and investigations such as electrocardiogram or echocardiogram (allow detecting LVSD and AF) could be used to case-mix patients when comparing performance or cost-effectiveness of interventions.

Patient related outcome measures are not currently collected in the NHFA. The inclusion of a preference-based HRQoL questionnaire (preferably the EQ-5D), could improve the ability of the NHFA to inform cost-effectiveness analysis of interventions. An alternative might be to map from a clinical variable currently collected in the NHFA, breathlessness (corresponding to NYHA classification for severity), to a preference-based measure, which would be compatible with the modelling approaches used in previous TAs. This alternative would have the disadvantage of potentially underestimating the impact of interventions for which effects in HRQoL are not exclusively mediated through improvement in clinical severity defined according to changes in NYHA class. Furthermore, the NYHA is only collected at admission and readmission, and for mapping purposes it would be valuable to collect this measure at discharge too to capture potential benefits of interventions.

Assuming the mandatory fields have relatively high completion rates, with the exception of HRQoL, the information currently collected in the existing NHFA would provide the majority of information required to model the cost-effectiveness of interventions and policies in heart failure. The identified gaps in mortality data could potentially be overcome by using external data (e.g. Office of National Statistics data). Similarly, data on events related to surgical complications and device related procedures could be obtained by linking the NHFA dataset to other national audit datasets, namely the CRM datasets.

As shown in Section 4.1.5 there is positive evidence of the validity of EQ-5D in heart failure, but the evidence base regarding responsiveness could be improved by methodologically sound research in the area. To our best knowledge the collection of PROMs within the NHFA is not currently being considered.

5.4 Recommendations for heart failure

In summary, the EQ-5D appears to be appropriate in patients with HF, and the current heart failure audit collects much of the information required to conduct economic evaluations. Nevertheless, the audit does not collect any HRQoL data, and death rates by cause are not collected. The issues and corresponding PR and areas for FR are discussed below. All suggested FR areas are indicative and would require a discussion and detailed proposal if required.

In section 4.1, it was concluded tha EQ-5D is appropriate to use in cardiovascular conditions, including in heart failure. Considering that the NHFA does not currently collect any preference-based measure that can inform economic evaluation, it is recommended that EQ-5D (EQ-5D-5L) is collected as part of the audit (PR.4). Nevertheless, there was very limited data on the responsiveness to change of EQ-5D across cardiovascular conditions, and existing evidence suggested that this was poor for the particular case of heart failure. As the methods used to assess responsiveness of EQ-5D were not without flaws, future research could aim to examine this property in heart failure patients using the NHFA data (FR.2).

The NHFA already collects a wealth of information on the clinical status of patients admitted to hospital for treatment of their condition, and the associated interventions and care received whilst in hospital and on discharge. However, cause of death is not currently collected. This field would be of importance for longer term extrapolation of survival and should be considered for mandatory collection (PR.5). More detailed research on analyses of fields currently collected in the NHFA is

currently being undertaken under a separate research project within this programme of work (WP3) (FR.3).

Table 7: Recommendations and associated future research for heart failure

PR.4	*Collect the EQ-5D (EQ-5D-5L) in the NCA*
FR.2	*Assess the responsiveness of the EQ-5D-5L to changes in NYHA (already collected in the NCA)using data collected in the audit*
PR.5	*Collect mandatory information on cause of death*
FR.3	*Analyses of fields currently collected in the heart failure NCA is currently being undertaken under a separate research project within this programme of work (WP3)*

6. RESULTS FOR CORONARY ANGIOPLASTY

6.1 Evidence of appropriateness of EQ-5D in coronary angioplasty (WP1.1)

Five studies included in the updated review in CVD conditions (Section 4.1.4) assessed the psychometric properties of EQ-5D in coronary angioplasty, and provided positive evidence of acceptability, and construct (both convergent and known-group) validity, but showed poor reliability. Full details on the assessment of the appropriateness of EQ-5D in coronary angioplasty are presented in Section 4.1.5.

6.2 Routinely collected proxy measures in coronary angioplasty (WP1.2)

As the EQ-5D was found to be acceptable for CVD conditions, no additional searches for alternative measures were conducted.

6.3 Evidence for economic evaluations in coronary angioplasty (WP1.3)

6.3.1 Cost-effectiveness modelling approach used in recent HTAs in coronary angioplasty

Five TAs relating to coronary angioplasty were identified from the searches, one of these is currently in development with an anticipated issue date of July 2014,(35) and corresponds to the review of a previous TA.(36) Three of the TAs examined the clinical and cost-effectiveness of platelet aggregation inhibitors for the treatment of people who have suffered an ACS and are medically managed or underwent revascularisation (namely percutaneous coronary intervention (PCI) and CABG).(35-37) Another TA examined the clinical and cost-effectiveness of a direct thrombin inhibitor, bivalirudin, compared to heparin in addition to glycoproteins inhibitors for patients with ST elevation myocardial infarction (STEMI) intended for PCI.(38) Although these four TAs did not assess coronary angioplasty procedures, they assessed the cost-effectiveness of alternative adjunctive pharmacological interventions in patient populations that included patients intended for or undergoing revascularisation. On TA152, the clinical and cost-effectiveness of drug-eluting stents vs. bare metal stents was compared in patients with coronary heart disease. (39)

All TAs on ACS patient populations used two-part models to examine the cost-effectiveness of the interventions under appraisal. The models comprised a short-term element that included a decision tree to model clinical events following an ACS (between three days to one year after the episode), and a long-term Markov model (15 months to lifetime) that modelled the subsequent clinical pathway and prognosis for those patients that survived within the short-term model.(35-38) The most common reason for employing a two-part model was to separately characterise the impact of treatments over the initial acute period and the post-acute period (or trial follow-up period vs,

longer term). Often an assumption was made that relative effectiveness of particular treatment would be confined to the acute or trial period (e.g. TA182, TA236) but that the longer term consequences associated with particular events incurred during this period would be different. It is worth noting that in other cardiovascular conditions, such as cardiac arrhythmias and heart failure (Sections 4.3 and 5.3), the flexibility provided by the two-part models is not as relevant, given that the longer-term chronic nature of these conditions can be adequately reflected by a single Markov model. In these conditions, while risk of event may vary over time, the concept of the 'acute' and 'post-acute' periods is less applicable, and hence a Markov process is used throughout as opposed to essentially dichotomising the period of risk.

The main clinical events incorporated in the models reflected the occurrence of further ACS (fatal and non-fatal), stroke (fatal, and non-fatal, with different types and subsequent level of disability considered for the latter), revascularisation procedures (PCI and CABG), bleeding and other-cardiovascular and non-cardiovascular mortality. Baseline risks and relative risks of clinical events in the short-term model were modelled based mostly on trial data (survival analysis), while risks and relative risks of clinical events on the longer-term element of the models were sourced from the published literature.(35-38) In one TA, observational data from the Myocardial Ischaemia National Audit Project (MINAP) and General Practitioner Research Database was used to estimate risk of non-fatal events in the long-term Markov model.(37) The only TA that was not specific to an ACS patient population did not provide a detailed description of the model, which hinders the assessment of how effectiveness was modelled. Nevertheless, the authors state that there was no evidence of differences in mortality and myocardial infarction rates between patients in whom bare metal stents were implanted vs. those with drug-eluting stents, and thus effectiveness measures were limited to rates of repeat vascularisation, namely target lesion revascularisation (TLR) and target vessel revascularisation (TVR), and reductions in number of lesions treated for patients who had undergone repeat revascularisations in the 12 months following the index PCI. Rates of TLR and TVR, and number of lesions treated in repeat revascularisations for the different interventions were estimated from meta-analyses of published clinical trials, and adjusted using observational UK data that provided estimates of the proportion of patients likely to benefit from the interventions (i.e. patients for whom revascularisation was performed for at least one lesion that had been previously treated) across risk subgroups. The authors considered this adjustment to be necessary to convert trial efficacy data into estimates that reflected expected effectiveness in UK patients. This model also incorporated estimates of waiting times for different revascularisation procedures (PCI or CABG) to adjust the duration of benefits in the model.(39)

All studies quality adjusted survival by assigning mean utility values to the separate health states. The majority of utilities were derived from mean EQ-5D estimates sourced from external estimates reported in the published literature,(35-38) or from trial and observational UK data.(37;39) In some models, utilities were gender and/or age specific (35;36), and one model weighted utilities according to the level of subsequent disability in the stroke health states (although it was unclear what instrument or assumption was used to classify stroke severity.(35)

Table 8: Summary of existing models in coronary angioplasty

Model approach	Method used to model utilities
MTA (ID:648): Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of TA182); 2013 (35)	
TAG two part model; short term trial-based model plus long-term extrapolation Markov model. Short-term model composed of decision tree for the first three days followed by a Markov model. Clinical events in the model are: primary endpoint events (non-fatal MI, Non-fatal stroke), bleed endpoint event, cardiovascular or bleed death, other death. Long-term de-novo Markov model: Ten initial health states defined by a combination of 1) worst event (none, MI, stroke), 2) Prior events (0, 1, 2, 3+) and 3) Disabled (yes or no). Further health states are defined by the occurrence of clinical events (and dependent on previous health state): Fatal MI, Nonfatal MI, Fatal HS, Nonfatal HS not disabling, Nonfatal HS disabling, Fatal ischaemic stroke/transient ischaemic, Nonfatal ischaemic stroke/transient ischaemic not disabling, Nonfatal ischaemic stroke/transient ischaemic disabling, other vascular death, non-vascular death. Effectiveness: Risk equations for primary endpoints and bleeding events (active treatment period) on short term model; gender specific event incidence risks and event fatality risks (age adjusted) for long-term model; RR of MI, stroke, vascular and non-vascular death for patients with diabetes vs. no diabetes were applied to reflect differences between populations. Source: clinical RCTs, published literature	Utility: mean EQ-5D utility values (gender specific and disability weighted for stroke states) applied to separate health states; disutilities from clinical events applied as decrements for year following event. Source: clinical RCTs, assumptions.
STA (TA236): Ticagrelor for the treatment of acute coronary syndromes; 2011 (37)	
Manufacturer's two-part model: one-year decision tree plus long-term extrapolation Markov model. Decision tree: 4 separate health states (no further event, non-fatal MI, non-fatal stroke and death from any cause). Markov model: 6 separate health states; no further event, non-fatal MI, post MI, non-fatal stroke, post stroke and dead. Non-fatal MI and non-fatal stroke health states are tunnel states that allow for a worse prognosis for patients in the year in which a non-fatal event occurs compared to subsequent years. Effectiveness: Survival analysis to estimate	Utility: mean EQ5D values assigned to each separate health state Source: clinical RCT, assumptions(Published literature utility estimates applied in sensitivity analysis)

	baseline risk and HR of clinical events on short term model. In the long-term model fatal events RRs are applied to mortality estimates from UK life tables, and non-fatal event rates were estimated from an observational database. Sources: clinical RCTs, published literature, manufacturer study based on MINAP and General Practice Research Database.	
STA (TA230): Bivalirudin for the treatment of ST-segment elevation myocardial infarction; 2011 (38)		
	Manufacturer's two-part model: one-year decision tree plus long-term extrapolation Markov model. Decision tree: Initial angiography and reperfusion therapy, after which they can experience 7 possible subsequent events: no relevant complications, minor bleed, major bleed, stroke, repeat MI, repeat revascularisation and death. Markov model: 2 separate health states; alive and dead Effectiveness: RR of clinical events for patients treated with bivalirudin applied to baseline risks on the comparator arm, independent of index treatment (PCI, CABG or conservative treatment) in the short-term model; long term model assumes that life-expectancy for those surviving the initial period was identical for both bivalirudin and heparin with GPI, and based on UK register data. Source: clinical RCT, published literature	Utility: mean EQ5D values from a single observational UK study were assigned to patients in the initial period (0.683) and in the long-term model (0.718), from a cohort study that followed up patients for 1-year after being diagnosed with acute MI. Source: Published literature
STA (TA182): Prasugrel for the treatment of acute coronary artery syndromes with percutaneous coronary intervention; 2009(36)		
	Manufacturer's two-part Markov model: short term trial-based model plus long-term extrapolation Markov model. Short-term model is composed of a decision tree for the first three days followed by a Markov model (15 months). Clinical events in the model are: primary endpoint events (non-fatal MI, non-fatal stroke), bleed endpoint event, cardiovascular or bleed death, other death. Long-term Markov model; same structure as for trial-based Markov model. Effectiveness: Risk equations for primary endpoints and bleeding events (active treatment period) on short term model; mortality RRs in revascularised STEMI and unstable angina/NSTEMI compared to general coronary heart disease population, applied to UK age and gender adjusted life tables for long term model. Source: Clinical RCTs; published literature	Utility: Baseline utility (mean EQ-5D age and sex specific) taken from UK population norms; ongoing utility EQ-5D decrements for ACS and stroke/MI from single study; Major bleeding assumed to impose 25% utility decrement during 14 days. Source: Published literature; assumptions TAG critiqued the use of utility values as they were not directly measured on the population of interest (heart disease). The TAG applied a condition specific long-term utility decrement based on a US survey study. Limitations of this approach were recognised by the TAG.

MTA (TA152): Coronary artery disease - drug-eluting stents (review TA71); 2008 (39)		
	Model is not described within the report, but it is said that the modelling approach is the same as for the previous appraisal (TA71) with minor modifications. Previous TAG projected survival model: Surviving patients can suffer the following events: fatal and non-fatal acute MI, fatal and non-fatal stroke, repeat revascularisations, acute renal failure and severe bleeding.[39] Effectiveness: As model structure is not described, and differences from TA71 are not clear, it is difficult to assess how effectiveness was modelled. Nevertheless, the emphasis was on assessing the reduction in revascularisation rates and number of lesions treated in revascularisation procedures, as no differences in mortality or acute MI incidence were found between interventions. Authors state that they have adjusted trial efficacy data by combining MA estimates with prevalence rates of revascularisation by subgroup (defined according to the presence of risk factors). Risk factors for non-elective patients were previous CABG and small vessels, and for elective patients, calcification, angulation, restenotic lesion, and triple vessel disease. Source: MA of published clinical RCTs, observational data	Utility: The authors used EQ-5D values from a UK survey study for symptomatic angina, after PCI and after CABG health states. For the remaining health states (which were not described) the utility estimates applied were as for TA71, which were mainly sourced from a clinical trial.

HS: health states; AE: Adverse Events; MTA: Multiple Technology Appraisal; GPI: Glycoproteins inhibitors; STA: Single Technology Appraisal; MI: Myocardial Infarction; HS: Haemorrhagic stroke; TAG: Technology Appraisal Group; TIA: Transient ischaemic attack; TA: Technology Appraisal; RCT: randomised controlled trial; RR: Relative risk.

In summary, the following evidence would be required to compare providers or the cost-effectiveness of interventions for coronary angioplasty patients:

- Pharmaceutical interventions (type of intervention, treatment discontinuation, adverse events)
- Aetiology requiring angioplasty
- Procedure rates (type of intervention, success rate, peri and post-procedure complications)
- Hospitalisation (rates, cause, length of stay)
- Further cardiovascular events (ACS, revascularisation, stroke)
- HRQoL data (prior to surgical procedure and at follow-up)
- Death rates (cardiac and procedure related, all cause)

6.3.2 Fields collected in National Audit of Percutaneous Coronary Interventional Procedures

The fields in the National Audit of Percutaneous Coronary Interventional Procedures (NAPCI) are collected via a questionnaire (the spreadsheet BCISversion5_6_1). Although there is an expectation that all fields are completed, there are a minimum number of fields that are part of the NAPCI Minimum Data Standard, [personal communication with Tracy Whittaker, National Audit Project Manager for the PCI and Congenital Heart Disease Audits, 5th June 2014] and that are involved with risk stratified outcome assessment.(40) The Minimum Data Standard fields and remaining fields are provided in the Appendix. The data provide information on patient demographics (NHS number, age and gender); pre-procedure details (indication for intervention, procedure urgency, cardiogenic shock, date/time of symptom onset, date/time arrival at first hospital, date/time arrival at PCI hospital); procedure details (vessels attempted, date/time of first balloon inflation, PCI hospital outcome); previous medical history (diabetes, medical history, history of renal disease); and discharge details (status at discharge, discharge date).

6.3.3 Comparing fields in the National Audit of Percutaneous Coronary Interventional Procedures with variables used in existing HTAs

Survival analysis was used in previous TAs to model mortality, and the data collected in the NAPCI audit through the variable 'status at discharge' could be used to model all cause mortality. However, cause of death is not collected within the audit, and therefore it is not possible to distinguish between cardiovascular and non-cardiovascular mortality. Furthermore, the audit only collects data on death occurring at the hospital, which can be a limitation. The NAPCI provides data on clinical

interventions (drug therapy before intervention, glycoproteins used during number of stents, number of drug eluting stents, drug(s) eluted by stents, arterial access (femoral, brachial or radial) which would provide some of the information required to compare alternative treatments, but none of these data are part of the minimum data standard and its completeness may be limited compared to other fields in the audit. The NAPCI collects data on PCI outcomes that include complications (haemorrhagic and embolic cerebrovascular events, transient ischaemic attack/reversible ischemic neurologic deficit, reinfarction), as well as revascularisation procedures (CABG and PCI) following initial PCI that can be used to inform the occurrence of further clinical events occurring within the same hospital episode. There are other fields that also collect data related to complications (procedural complications, arterial complications, bleeding up to discharge), but these are not part of the minimum standard data. Importantly, the audit does not collect data on all types of stroke (thrombotic stroke is not specifically considered on the PCI outcomes field) or data related to severity of disability following cerebrovascular events, which is anticipated to impact on HRQoL, as well as costs.

Previous models have defined patient subgroups or adjusted effectiveness and utility estimates based on sex, age, comorbidities (namely diabetes), underlying disease (ACS, stable angina), type of admission (elective, non-elective). These data are collected in the audit and could be used to case-mix patients when comparing performance or cost-effectiveness of interventions.

The NAPCI does not currently collect patient related outcome measures. The inclusion of a preference-based HRQoL questionnaire (preferably the EQ-5D), could improve the ability of the audit to inform cost-effectiveness analysis of interventions. An alternative would be to apply values from the published literature to clinical events, as has been done in previous models. However, as mentioned before, the audit only collects data on those events that occur during the time spent in hospital following the initial PCI.There is a very important limitation to this approach, as it may fail to capture the impact on HRQoL of the interventions, given that it may not be related to the occurrence of clinical events alone, but also to any beneficial effect on symptoms (e.g. relief of chest pain caused by myocardial ischaemia). It is worth noting that in previous TAs, the focus was not on HRQoL differences driven by improvement in symptoms as they aimed to examine adjunctive therapies or different types of stents, rather than the surgical procedure which was the same for every comparison. Collection of a PROM would have a greater potential value to this particular audit, as it would allow HRQoL considerations to be related to events, but also to symptomatic differences that may be evident and are not fully accounted for by events. As it is, it may be difficult to

demonstrate the full symptomatic benefits of interventions over just the hospitalisation period following coronary angioplasty, and PROMs collection should not be limited to this period. It would be preferable that it was performed as for ablation patients in the NACRM, i.e. prior to the procedure, and at longer follow-up time points (6 and 12 months in this particular case), so as to ensure that any symptomatic impact of treatments that is not limited to the hospitalisation period is captured.

Assuming that the audit fields in general have relatively high completion rates, with the exception of HRQoL, the information currently collected in the existing NAPCI would provide a considerable amount of the information required to model the cost-effectiveness of interventions and policies in coronary angiography. Limitations on the collection of mortality data could be partially overcome by incorporating external data, namely by linkage to mortality registers, or by using estimates from the published literature. Linking the PCI audit to other datasets could not only allow the calculation of longer term mortality rates, but also the distribution of patients between cardiovascular and non-cardiovascular deaths. Even if mortality registers do not allow identifying cause of death, this can be ascertained through linkage to other audits or registers (e.g. Hospital Episode Statistics). For example, if there is a record of a previous coronary heart disease or cerebrovascular disease hospitalisation recorded in the 30-day period which precedes a patient's death, then this might be used to inform cause of death. As illustrated by previous models, cause of death is important for the purposes of extrapolation, since it may not be reasonable to assume that a single mortality function can be applied to both short and longer term parts of the model. A potential alternative approach to overcome gaps in mortality data might be to use external evidence on the expected rate of non-cardiovascular mortality and remove this from the mortality estimates reported in the audit, and then to model non-cardiovascular mortality separately (e.g. using cause-exclusion life table data). Clinical events occurring after hospital discharge or not recorded in the audit (e.g. thrombotic strokes) could also be sourced from the published literature with the exception of further PCI interventions, since patients' NHS number could be used to track readmissions. Similarly, the distribution of patients according to disability severity following cerebrovascular events could also be sourced from the published literature. An alternative to inform the occurrence of clinical events would be to use the NHS number to link the PCI audit to other audits which collect data related to cardiovascular events (e.g. the MINAP for ACS, and the national adult cardiac surgery audit (NACSA) for revascularisations with CABG).

6.4 Recommendations for coronary angioplasty

In summary, the EQ-5D appears to be appropriate in patients undergoing coronary angioplasty, and the current PCI audit collects some of the information required to conduct economic evaluations. Nevertheless, the audit does not collect any HRQoL data, and could be improved by the inclusion of more fields and or making their collection mandatory. The issues and corresponding PR and areas for FR are discussed below. All suggested FR areas are indicative and would require a discussion and detailed proposal if required.

As shown in Section 4.1 there is positive evidence of the validity of EQ-5D in coronary angioplasty, most specifically for known-group and convergent validity, although no evidence was available on reliability and responsiveness. There was also some evidence that EQ-5D exhibits ceiling effects in this condition. Nevertheless, EQ-5D was considered an appropriate measure to estimate HRQoL in coronary angioplasty, and its inclusion in the PCI audit would improve the audit's ability to inform cost-effectiveness analysis in coronary angioplasty especially if its collection also encompasses time points beyond the initial hospitalisation period. To our best knowledge the collection of PROMs within the PCI audit is not currently being considered, so it is recommended that EQ-5D (EQ-5D-5L) is collected within the audit (PR.6). The use of the EQ-5D-5L, could potentially reduce any ceiling effects (86) in patients in less severe stages of cardiovascular disease. As no available evidence was available on reliability and responsiveness of the EQ-5D, future research could aim to examine these properties in coronary angioplasty patients using the NAOCI data (FR.4).

The PCI audit already collects considerable information of relevance for the economic evaluation of interventions in coronary angioplasty (described in Section 6.3.3). However, fields such as cause of death, type of stroke and severity of disability following stroke are not currently collected. The importance of these fields has been highlighted in Section 6.3.3, and should be considered for mandatory collection (PR.7). Furthermore, it is also recommended that fields regarding pharmacological and surgical interventions in coronary angioplasty patients (drug therapy, number and type of stents and type of arterial access), which are already collected in the audit, are considered for mandatory collection or inclusion in the Minimum Data Standard dataset to ensure high completion rates (PR.8).

Table 9: Recommendations and associated future research for coronary angioplasty

PR.6	*Collect the EQ-5D (EQ-5D-5L) in the NCA prior to procedure, after procedure and at least one longer follow-up time point*
FR.4	*Assess the psychometric properties of the EQ-5D-5L using data collected in the audit*
PR.7	*Collect mandatory information on cause of death, type of stroke and severity of disability following stroke*
PR.8	*Make collection of data on drug therapy, number and type of stents and type of arterialaccess mandatory or at least part of the Minimum Data Standard dataset*

7. RESULTS FOR CARDIAC SURGERY

7.1 Evidence of appropriateness of EQ-5D in cardiac surgery (WP1.1)

Four studies included in the updated review in CVD conditions (Section 4.1.4) assessed the psychometric properties of EQ-5D in cardiac surgery, and provided positive evidence of acceptability and construct (both convergent and known-group) validity, but showed poor reliability. Furthermore, there was evidence of potential ceiling effects for the EQ-5D in this condition. Full details on the assessment of the appropriateness of EQ-5D in cardiac surgery are presented in Section 4.1.5.

7.2 Routinely collected proxy measures in Cardiac Surgery (WP1.2)

As the EQ-5D was found to be acceptable for CVD conditions, no additional searches for alternative measures were conducted.

7.3 Evidence for economic evaluations in cardiac surgery (WP1.3)

7.3.1 Cost-effectiveness modelling approach used in recent HTAs in cardiac surgery

The searches identified two TAs relating to cardiac surgery. One of the TAs examined the clinical and cost-effectiveness of ticagrelor compared to clopidogrel for the treatment of ACS in patients managed medically, and those who are managed with PCI or CABG.(37) Another TA examined the clinical and cost-effectiveness of a direct thrombin inhibitor, bivalirudin compared to heparin in addition to glycoproteins inhibitors for patients with STEMI intended for PCI. The modelling approach in this TA assumes that all patients receive an initial angiography for diagnostic purposes, and are then allocated to a primary treatment intervention with the majority of patients undergoing PCI.(38) None of these TAs assessed cardiac surgery procedures; they assessed the cost-effectiveness of alternative adjunctive pharmacological interventions in patient populations that included patients intended for or undergoing revascularisation. Furthermore, they only include one type of procedure collected in the NACSA, namely CABG. Nevertheless, CABG is the most frequent procedure for which data is collected in the NACSA. (41) Other types of surgery included in the audit are heart valve replacement or repair and aortic surgery.

The two TAs used two-part models to examine the cost-effectiveness of the interventions under appraisal. The models comprised a short-term element that included a decision tree to model clinical events within one year following an ACS, and a 39 years long-term Markov model (assumed to be lifetime) that modelled subsequent clinical pathway and prognosis for those patients that survived within the short-term model. The rationale for employing a two-part model has been

described previously in Section 6.3, and mostly this modelling approach allows the impact of treatments over the initial acute period and the post-acute period (or trial follow-up period vs longer term) to be characterised separately. The main clinical events incorporated in the models reflected the occurrence of further ACS (fatal and non-fatal), stroke (fatal, and non-fatal, with different types and subsequent level of disability considered for the latter), revascularisation procedures (PCI and CABG), bleeding and other-cardiovascular and non-cardiovascular mortality. Baseline risks and relative risks of clinical events in the short-term model were modelled based mostly on trial data (survival analysis), while relative risks of clinical events on the longer-term element of the models were sourced from the published literature.(37;38) In one TA, observational data from the MINAP and General Practitioner Research Database was used to estimate risk of non-fatal events in the long-term Markov model.(37)

All studies quality adjusted survival by assigning mean utility values to the discrete health states. These mean utilities were derived from EQ-5D data sourced from external published literature(37;38) and from the clinical trial that also informed the effectiveness estimates in the short-term element of the model.(37) Unlike other models used to examine the cost-effectiveness of pharmacological interventions in patients revascularised with PCI,(35) these models did not explicitly weight utilities according to disability in the stroke health states.

Table 10: Summary of existing models in cardiac surgery

Model approach	Method used to model utilities
STA (TA236): Ticagrelor for the treatment of acute coronary syndromes; 2011 (37)	
Manufacturer's two-part model: one-year decision tree plus long-term extrapolation Markov model. Decision tree: 4 discrete health states (no further event, non-fatal MI, non-fatal stroke and death from any cause). Markov model: 6 separate health states; no further event, non-fatal MI, post MI, non-fatal stroke, post stroke and dead. Non-fatal MI and non-fatal stroke health states are tunnel states that allow for a worse prognosis for patients in the year in which a non-fatal event occurs compared to subsequent years. Effectiveness: Survival analysis to estimate baseline risk and HR of clinical events on short term model. In the long-term model fatal events RRs are applied to UK life tables mortality estimates, and non-fatal event rates were estimated from an observational database. Sources: clinical RCTs, published literature, manufacturer study based on MINAP and General Practice Research Database.	Utility: mean EQ-5D values assigned to each separate health state Source: clinical RCT, assumptions(Published literature utility estimates applied in sensitivity analysis)
STA (TA230): Bivalirudin for the treatment of ST-segment elevation myocardial infarction; 2011(38)	
Manufacturer's two-part model: one-year decision tree plus long-term extrapolation Markov model. Decision tree: Initial angiography and reperfusion therapy, after which they can experience 7 possible subsequent events: no relevant complications, minor bleed, major bleed, stroke, repeat MI, repeat revascularisation and death. Markov model: 2 discrete health states; alive and dead Effectiveness: RR of clinical events for patients treated with bivalirudin applied to baseline risks on the comparator arm, independent of index treatment (PCI, CABG or conservative treatment) in the short-term model; long term model assumes that life-expectancy for those surviving the initial period was identical for both bivalirudin and heparin with GPI, and based on UK register data. Source: clinical RCT, published literature	Utility: mean EQ-5D values from a single observational UK study were assigned to patients in the initial period (0.683) and in the long-term model (0.718), from a cohort study that followed up patients for 1-year after being diagnosed with acute MI. Source: Published literature

AE: Adverse Events; MTA: Multiple Technology Appraisal; STA: Single Technology Appraisal; MI: Myocardial Infarction; GPI: Glycoproteins inhibitors; TAG: Technology Appraisal Group; TIA: Transient ischaemic attack; TA: Technology Appraisal; RCT: randomised controlled trial; RR: Relative risk.

In summary, the following evidence would be required to compare providers or the cost-effectiveness of interventions for cardiac surgery patients:

- Pharmaceutical interventions (type of intervention, treatment discontinuation, adverse events)
- Aetiology requiring cardiac surgery
- Procedure rates (type of intervention, success rate, peri and post-procedure complications)
- Hospitalisation (rates, cause, length of stay)
- Further cardiovascular events (ACS, revascularisation, stroke, level of disability following stroke)
- HRQoL data (prior to surgical procedure and at follow-up)
- Death rates (cardiac and procedure related, all cause)

The majority of this evidence would need to be dated and linked through timings of collection.

7.3.2 Fields collected in National Adult Cardiac Surgery Audit

The fields in the NACSA are collected via a questionnaire (the spreadsheet NACSAdatasetV4.1). Similarly to the PCI audit, there is an expectation that all fields are completed, but a Minimum Data Standard is still in development. Nevertheless, a record cannot be submitted to the audit without the completion of the fields: date of birth, procedure type, procedure date, height and weight. Mandatory fields and fields on which hospitals are assessed for completeness and the remaining fields are provided in the Appendix. The data provide information on: patient demographics (age and gender); cardiac history (recent MI); previous interventions (previous cardiac surgery, date of last cardiac operation); additional medical history and risk factors (creatinine at time of surgery, renal function/dialysis, history of pulmonary disease, history of neurological dysfunction, extracardiac arteriopathy, pre-operative heart rhythm); cardiac investigations (left ventricular function ejection fraction category, pulmonary artery systolic pressure); pre-operative status and support (intravenous nitrates or any heparin, intravenous inotropes prior to anaesthesia, ventilated (pre-operation), cardiogenic shock, date and time of operation, operative urgency, number of previous heart operations, responsible consultant surgeon, responsible consultant anaesthetist); procedures classified by group (CABG, valve, major aortic, other cardiac procedures); other cardiac procedures; valve surgery (reason for repeat aortic valve operation, native mitral valve pathology, reason for repeat mitral valve operation, native tricuspid valve pathology, reason for repeat tricuspid valve operation, native pulmonary valve pathology, reason for repeat pulmonary valve operation); pre-operative, intra-operative and post-operative cardiac support devices (reason for repeat aortic

valve operation, native mitral valve pathology, reason for repeat mitral valve operation, native tricuspid valve pathology, reason for repeat tricuspid valve operation, native pulmonary valve pathology, reason for repeat pulmonary valve operation); cardiopulmonary bypass data (height and weight); and post-operative course (patient status at discharge, date of discharge/ date of death in hospital). Although the patient NHS number is not mandatory, whenever this field is not completed the Central Cardiac Audit Database (CCAD) will attempt to obtain it from the National Strategic Tracing Service using the patient's name, date of birth and postcode.

7.3.3 Comparing fields in the National Cardiac Surgery Audit with variables used in existing HTAs

Survival analysis was used in previous TAs to model mortality, and therefore the data collected in NACSA audit through the variables 'status at discharge' and date of discharge/ date of death in hospital could be used to model all cause mortality. However, cause of death is not collected within the audit, and therefore it is not possible to distinguish between cardiovascular and non-cardiovascular mortality. The collection of in-hospital death alone can limit the use of the audit to inform cost-effectiveness analysis. Nevertheless, it may be reasonable to assume that in-hospital death is procedure-related, especially if it occurs within a short period after the operation. The collection of data related to the occurrence of clinical events after index surgery in the NACSA includes complications requiring return to surgical theatre ('Return to Theatre'; Appendix) and cerebrovascular accidents ('New post-operative neurological dysfunction'; Appendix). The 'Return to Theatre' field captures re-operation due to bleeding or tamponed, valvular problems, graft problems, other cardiac problems, sternum re-suturing and surgery for deep sternal wound infection. The collection of further events is limited to the period of hospitalisation following the initial surgery.

The NACSA audit provides data on the type of surgical procedures (CABG, valve, major aortic, other cardiac procedures) and cardiac support devices used (intra-aortic balloon pump, impeller device use, ventricular assist device use, other support device), which would provide some of the information required to compare alternative treatments.

Clinical events such as MI will not be captured by the variable 'Return to Theatre' as there is no specific entry for this type of cardiac problem and, furthermore, they may occur without requiring a return to the theatre. The 'New post-operative neurological dysfunction' field records the occurrence of stroke-related events, as well as lower extremities paraplegia and paraparesis. However, it does not identify the type of stroke (other than distinguishing between transient and

permanent) and the level of disability following the cerebrovascular event (unless it causes paralysis or weakness of the legs). Furthermore, these two fields are not part of the completeness assessment dataset, which may negatively impact on their rate of completion compared to other fields.

The NACSA collects a number of patient risk factors (identified in Table A15, Appendix) that allow the estimation of the EuroSCORE,(42) a risk stratification system to predict early mortality in cardiac surgical patients. This score can also be used to adjust mortality estimates based on patient characteristics to allow comparison of interventions across different patient case-mix. Furthermore, clinical measures collected for stable patients, such as the NYHA and CCSC scores ('Angina status pre-surgery' and 'Dyspnoea status pre-surgery' respectively), number of previous MIs, and diabetes management, could also be used to case-mix patients when comparing performance or cost-effectiveness of interventions. It is worth noting that these fields may be affected by issues regarding their rate of completion, as they are not part of the completeness assessment dataset (unlike the EuroSCORE fields).

The NACSA audit does not currently collect patient related outcome measures. The inclusion of a preference-based HRQoL questionnaire (preferably the EQ-5D), could improve the ability of the audit to inform cost-effectiveness analysis of interventions. Similarly to coronary angioplasty case, an alternative would be to apply values from the published literature to clinical events, as has been done in previous models. However, the audit does not collect all relevant clinical events, such as further ACS, and only collects data on those events that occur during the time spent in hospital following the initial PCI. As for coronary angioplasty, this approach may fail to capture the full impact on HRQoL by the interventions, as HRQoL may not be related to the occurrence of clinical events alone, or to any beneficial effect on symptoms. It is worth noting that in previous TAs, the focus was not on HRQoL differences driven by improvement in symptoms as they aimed to examine adjunctive therapies, rather than the surgical procedure. Furthermore, both TAs include CABG only, while the audit encompasses all major cardiac surgery procedures. Therefore, there may be other clinical events that were not identified as relevant to the assessment of interventions in cardiac surgery and would need to be collected in the audit too. The issues regarding the need to account for potential symptomatic differences between interventions that may be evident and are not fully accounted for by events would also apply in the case of cardiac surgery. Although NYHA and CCSC scores are collected in the NACSA, which capture some of the symptomatic dimensions and can potentially be mapped onto HRQoL measures, the collection is limited to stable patients in the pre-operative stage, and therefore not very useful in this context. The collection of a PROM would allow HRQoL

considerations to be related to events, but also to symptomatic differences. As it is it may be difficult to demonstrate the full symptomatic benefits of an intervention over just the hospitalisation period following cardiac surgery, PROM collection should not be limited to this period. It would be preferable if HRQoL data was collected as for ablation patients in the NACRM, i.e. prior to the procedure, and at longer follow-up time points (6 and 12 months in this particular case), so as to ensure that any symptomatic impact of treatments that is not limited to the hospitalisation period is captured.

Assuming that the audit fields in general have relatively high completion rates, with the exception of HRQoL, the information currently collected in the existing NACSA would provide a considerable amount of the information required to model the cost-effectiveness of interventions and policies in coronary angiography. Limitations on the collection of mortality data could be partially overcome by incorporating external data, namely by linkage to mortality registers, or by using estimates from the published literature. Linking the NACSA to other datasets could not only allow the determination of longer term mortality rates, but also the distribution of patients between cardiovascular and non-cardiovascular. Even if mortality registers do not allow the identification of the cause of death, this can be ascertained through linkage to other audits or registers (e.g. Hospital Episode Statistics), as described for coronary angioplasty in Section 6.3. A potential alternative approach to overcome gaps in mortality data might be to use external evidence on the expected rate of non-cardiovascular mortality and remove this from the mortality estimates reported in the audit, and then to model non-cardiovascular mortality separately (e.g. using cause-exclusion life table data). Clinical events occurring after hospital discharge or not recorded in the audit (e.g. ACS, PCI, bleeding complications not resulting in cardiac surgical interventions) could also be sourced from the published literature. The occurrence of further cardiac surgery procedures could also be tracked via patients' NHS number to check for further admissions. Similarly, the distribution of patients according to disability severity following cerebrovascular events could also be sourced from the published literature. An alternative to inform the occurrence of clinical events would be to use the NHS number to link the NACSA audit to other audits which collect data related to cardiovascular events (e.g. the MINAP for ACS, and the PCI audit for coronary angioplasty procedures). These considerations apply mostly to the most frequent cardiac surgery procedure in the audit, i.e. CABG. Linkages to other audits and registers may be of relevance for less frequent cardiac surgery procedures, namely valve repair/replacement, aortic procedures and heart transplant, but identifying them would require further exploration of the clinical pathways following these procedures.

7.4 Recommendations for cardiac surgery

In summary, the EQ-5D appears to be appropriate in patients undergoing cardiac surgery, and the current NACSA collects some of the information required to conduct economic evaluations. Nevertheless, the audit does not collect any HRQoL data, and could be improved by including more fields and/or making some existing fields collection mandatory. The issues and corresponding PR and areas for FR are discussed below. All suggested FR areas are indicative and would require a discussion and detailed proposal if required.

As shown in Section 4.1.5 there is positive evidence of the validity of EQ-5D in cardiac surgery, most specifically for known-group and convergent validity, although no evidence was available on reliability and responsiveness. There was also some evidence that EQ-5D exhibits ceiling effects in this condition. Nevertheless, EQ-5D was considered an appropriate measure to estimate HRQoL in cardiac surgery, and its inclusion in the NACSA would improve the audit's ability to inform cost-effectiveness analysis in cardiac surgery, especially if its collection also encompasses time points beyond the initial hospitalisation period. To our best knowledge the collection of PROMs within the NACSA is not currently being considered, so it is recommended that EQ-5D (EQ-5D-5L) is collected within the audit. (PR.9) Furthermore, the use of the EQ-5D-5L, could potentially reduce any ceiling effect (86) in patients in less severe stages of cardiovascular disease. As no available evidence available on reliability and responsiveness of the EQ-5D, future research could aim to examine these properties in cardiac surgery patients using the NAPCI data (FR.5).

The NACSA audit already collects considerable information of relevance for the economic evaluation of interventions in cardiac surgery (described in Section 7.3.3). However, fields such as cause of death, type of stroke, severity of disability following stroke, and ACS and PCI on follow-up, are not currently collected. These fields' importance has been highlighted in Section 7.3.3, and should be considered for mandatory collection (PR.10). Furthermore, it is also recommended that fields regarding pharmacological and surgical interventions in cardiac surgery patients (drug therapy, number and type of stents and type of arterial access), which are already collected in the audit, are considered for mandatory collection or inclusion in a Minimum Data Standard dataset to ensure high completion rates (PR.11).

Table 11: Recommendations and associated future research for cardiac surgery

PR.9	*Collect the EQ-5D (EQ-5D-5L) in the NCA prior to procedure, after procedure and at least at one longer follow-up time point.*
FR.5	*Assess the psychometric properties of the EQ-5D-5L using data collected in the audit*
PR.10	*Collect mandatory information on cause of death, type of stroke, severity of disability following stroke, and ACS and PCI on follow-up.*
PR.11	*Depending on completion rates of completeness assessment dataset, consider making these fields mandatory*

8. RESULTS FOR ACUTE CORONARY SYNDROME

8.1 Evidence of appropriateness of EQ-5D in acute coronary syndrome (WP1.1)

Five studies included in the updated review in CVD conditions (Section 4.14) assessed the psychometric properties of EQ-5D in ACS, and provided positive evidence of acceptability and construct (both convergent and known-group) validity, but showed poor reliability. Full details on the assessment of the appropriateness of EQ-5D in ACS are presented in Section 4.1.5.

8.2 Routinely collected proxy measures in acute coronary syndrome (WP1.2)

As the EQ-5D was found to be acceptable for CVD conditions, no additional searches for alternative measures were conducted.

8.3 Evidence for economic evaluations in acute coronary syndrome (WP1.3)

8.3.1 Cost-effectiveness modelling approach used in recent HTAs in acute coronary syndrome

Five TAs relating to ACS were identified from the searches, one of these is currently in development with an anticipated issue date of July 2014, (35) and corresponds to the review of a previous TA.(36) Three of the TAs examined the clinical and cost-effectiveness of platelet aggregation inhibitors for the treatment of people who have suffered an ACS and are medically managed or underwent revascularisation procedures (PCI or CABG).(35-37) Another TA examined the clinical and cost-effectiveness of a direct thrombin inhibitor, bivalirudin, compared to heparin in addition to glycoprotein inhibitors for patients with STEMI intended for PCI.(38) Another TA examined the clinical and cost-effectiveness of statins for the prevention of coronary heart disease (including ACS).(43)

All TAs except one used two-part models to examine the cost-effectiveness of the interventions under appraisal. The models comprised a short-term element that included a decision tree to model clinical events following an ACS (between three days to one year after the episode), and a long-term Markov model (15 months to lifetime) that modelled the subsequent clinical pathway and prognosis for those patients that survived within the short-term model.(35;37) As mentioned in Section 14.3, the two-part model aimed to separately characterise the impact of treatments over the initial acute period and the post-acute period (or trial follow-up period vs. longer term). Often an assumption was made that the relative effectiveness of a particular treatment would be confined to the acute or trial period (e.g. TA182, TA236) (36;38) but that the longer term consequences associated with particular events experienced during this period would be different. The main clinical events incorporated in the models reflected the occurrence of further ACS (fatal and non-fatal), stroke

(fatal, and non-fatal, with different types and subsequent level of disability considered for the latter), revascularisation procedures (PCI and CABG), bleeding and other-cardiovascular and non-cardiovascular mortality. Baseline risks and relative risks of clinical events in the short-term model were modelled based mostly on trial data (survival analysis), while risks and relative risls of clinical events on the longer-term element of the models were sourced from the published literature (35-38) or from trial data.(37) In one TA, observational data from the MINAP and General Practitioner Research Database was used to estimate risk of non-fatal events in the long-term Markov model. (37) Another TA applied a Markov model to examine the cost-effectiveness of statins in the primary and secondary prevention coronary heart disease (including ACS).(43) In this model, the risk of events was sourced by UK observational studies and treatment effect of statins was applied as a relative risk reduction from a meta-analysis. The transition probabilities for secondary events (i.e. following one other cardiovascular event) could be different (depending on the type of event) for the first year, but remained constant in subsequent years. Other cause mortality risk estimated from national statistics for the overall population.(43)

All studies quality adjusted survival by assigning mean utility values to the separate health states. The majority of utilities were derived from mean EQ-5D estimates sourced from external estimates reported in the published literature.(35-38;43) One study used time trade-off elicited utility values to inform stable angina health states. (43) In some models, utilities were gender and/or age specific,(35;36) and one model weighted utilities according to levels of disability in the stroke health states (although it was unclear what instrument or assumption was used to classify stroke severity).(35)

Table 12: Summary of existing models in acute coronary syndromes

Model approach	Method used to model utilities
MTA (ID:648): Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of TA182); 2013 (35)	
TAG two part model; short term trial-based model plus long-term extrapolation Markov model. Short-term model composed of decision tree for the first three days followed by a Markov model. Clinical events in the model are: primary endpoint events (non-fatal MI, non-fatal stroke), bleed endpoint event, cardiovascular or bleed death, other death. Long-term de-novo Markov model: Ten initial health states defined by a combination of 1) worst event (none, MI, stroke), 2) Prior events (0, 1, 2, 3+) and 3) Disabled (yes or no). Further health states are defined by the occurrence of clinical events (and dependent on previous health state): Fatal MI, Nonfatal MI, Fatal HS, Nonfatal HS not disabling, Nonfatal HS disabling, Fatal ischaemic stroke/transient ischaemic, Nonfatal ischaemic stroke/transient ischaemic not disabling, Nonfatal ischaemic stroke/transient ischaemic disabling, other vascular death, non-vascular death. Effectiveness: Risk equations for primary endpoints and bleeding events (active treatment period) on short term model; gender specific event incidence risks and event fatality risks (age adjusted) for long-term model; RR of MI, stroke, vascular and non-vascular death for patients with diabetes and vs. no diabetes were applied to reflect differences between populations. Source: clinical RCTs; published literature	Utility: mean EQ-5D utility values (gender specific and disability weighted for stroke states) applied to separate health states; disutilities from clinical events applied as decrements for year following event. Source: clinical RCTs, assumptions.
STA (TA236): Ticagrelor for the treatment of acute coronary syndromes; 2011 (37)	
Manufacturer's two-part model: one-year decision tree plus long-term extrapolation Markov model. Decision tree: 4 separate health states (no further event, non-fatal MI, non-fatal stroke and death from any cause). Markov model: 6 separate health states; no further event, non-fatal MI, post MI, non-fatal stroke, post stroke and dead. Non-fatal MI and non-fatal stroke health states are tunnel states that allow for a worse prognosis for patients in the year in which a non-fatal event occurs compared to subsequent years.	Utility: mean EQ5D values assigned to each separate health state Source: clinical RCT, assumptions(Published literature utility estimates applied in sensitivity analysis)

Effectiveness: Survival analysis to estimate baseline risk and HR of clinical events on short term model. In the long-term model fatal events RRs are applied to UK life tables mortality estimates, and non-fatal event rates were estimated from an observational database. Sources: clinical RCTs, published literature, manufacturer study based on MINAP and General Practice Research Database.	

STA (TA230): Bivalirudin for the treatment of ST-segment elevation myocardial infarction; 2011 (38)	
Manufacturer's two-part model: one-year decision tree plus long-term extrapolation Markov model. Decision tree: Initial angiography and reperfusion therapy, after which they can experience 7 possible subsequent events: no relevant complications, minor bleed, major bleed, stroke, repeat MI, repeat revascularisation and death. Markov model: 2 separate health states; alive and dead Effectiveness: RR of clinical events for patients treated with bivalirudin applied to baseline risks on the comparator arm, independent of index treatment (PCI, CABG or conservative treatment) in the short-term model; long term model assumes that life-expectancy for those surviving the initial period was identical for both bivalirudin and heparin with GPI, and based on UK register data. Source: clinical RCT, published literature	Utility: mean EQ-5D values from a single observational UK study were assigned to patients in the initial period (0.683) and in the long-term model (0.718), from a cohort study that followed up patients for 1-year after being diagnosed with acute MI. Source: Published literature

STA (TA182): Prasugrel for the treatment of acute coronary artery syndromes with percutaneous coronary intervention; 2009(36)	
Manufacturer's two-part Markov model: short term trial-based model plus long-term extrapolation Markov model. Short-term model is composed of a decision tree for the first three days followed by a Markov model (15 months). Clinical events in the model are: primary endpoint events (non-fatal MI, non-fatal stroke), bleed endpoint event, cardiovascular or bleed death, other death. Long-term Markov model; same structure as for trial-based Markov model. Effectiveness: Risk equations for primary endpoints and bleeding events (active treatment period) on short term model; mortality RRs in revascularised STEMI and unstable angina/NSTEMI compared to general	Utility: Baseline utility (mean EQ-5D age and sex specific) taken from UK population norm; ongoing utility EQ-5D decrements for ACS and stroke/MI from single study; Major bleeding assumed to impose 25% utility decrement during 14 days. Source: Published literature; assumptions TAG critiqued the use of utility values as they were not directly measured on the population of interest (heart disease). The TAG applied a condition specific long-term utility decrement based on a US survey study. Limitations of this approach were recognised by the TAG.

	coronary heart disease population, applied to UK age and gender adjusted life tables for long term model. Source: Clinical RCTs; published literature	
MTA (TA94): Statins for the Prevention of Coronary Events; 2006 (43)		
	TAG's Markov model: 24 separate health states;: event free, MI, stable angina, unstable angina, CHD death, TIA, stroke, cerebrovascular death, death other causes, post MI, MI given CVD history, MI given CHD history, post stable angina, post unstable angina, post TIA, post stroke, post stroke given cerebrovascular disease history, post stroke given CHD history, fatal CHD event given CHD history, fatal CHD event given cerebrovascular disease history, fatal cerebrovascular event given CHD history, fatal cerebrovascular event given cerebrovascular disease history, death other causes following a first event. Effectiveness: CHD and cerebrovascular disease baseline risk of events modelled by age and gender from UK observational studies and treatment effect from statins applied as a relative risk reduction. Model allowed for differences in first year transition probabilities for secondary events, with these probabilities being constant in subsequent years. Other cause mortality risk estimated from national statistics for the overall population. Source: Observational studies, MA, published literature	Utility: Mean EQ-5D utilities for baseline utility and most clinical events, although TTO-elicited utilities were applied to stable angina. It was assumed that there was no disutility due to the use of statins. Source: Reanalysis of UK population norm utilities; Published literature

AE: Adverse Events; MTA: Multiple Technology Appraisal; CHD: Coronary heart disease; STA: Single Technology Appraisal; MI: Myocardial Infarction; HS: Haemorrhagic stroke; TAG: Technology Appraisal Group; TIA: Transient ischaemic attack; TA: Technology Appraisal; RCT: randomised controlled trial; RR: Relative risk.

In summary, the following evidence would be required to compare providers or the cost-effectiveness of interventions for ACS:

- Pharmaceutical interventions (type of intervention, treatment discontinuation, adverse events)
- Underlying conditions and type of ACS
- Procedure rates (type of intervention, success rate, peri and post-procedure complications)
- Hospitalisation (rates, cause, length of stay)
- Further cardiovascular events (ACS, revascularisation, stroke, level of disability following stroke)
- HRQoL data (at occurrence of index ACS and at follow-up)
- Death rates (cardiac and procedure related, all cause)

The majority of this evidence would need to be dated and linked through timings of collection.

8.3.2 Fields collected in Myocardial Ischaemia National Audit

The MINAP collects clinical data about patients that can present with either of the two types of MI – STEMI and non-ST elevation MI (NSTEMI) – for which management of the condition differs. As treatment of MI will also depend on the type of hospital in which the patient receives treatment, MINAP distinguishes between two types: interventional (providing emergency or primary PCI) and non-interventional hospital (does not have a facility to perform primary PCI). Therefore, the data collection form has been divided depending on the type of heart attack and the type of hospital.

The fields in the MINAP are collected via a questionnaire, which includes four forms: main generic, reperfusion, interventional audit and Takotsubo cardiomyopathy form. The questionnaire data are collected on an Excel spreadsheet (minap-dataset-v10.3.2). The Takotsubo cardiomyopathy is not formally part of MINAP dataset, and it is only completed if the discharge diagnosis is Takotsubo cardiomyopathy. For this reason, only items collected on the three remaining datasets were examined. Fields in the datasets have been classified as mandatory, expected to be completed for a useful overview of care, or for local use, with the classification varying depending on whether the patient suffered a STEMI or a NSTEMI. The mandatory and non mandatory fields are listed in the Appendix for STEMI and NSTEMI respectively. For STEMI patients the data provide information on demographics (hospital identifier, NHS number, patient name (surname and forename), age, sex, postcode, General practitioner (GP) /Primary care trust (PCT) code); admission details (initial

diagnosis, procedure performed at the interventional hospital, date/time of symptom onset, date/time of call for help, ambulance job number, date/time arrival at hospital, admission method, referring hospital code); reperfusion (initial reperfusion treatment, electrocardiogram determining treatment location of initial reperfusion treatment, date/time of reperfusion treatment, delay before treatment, reason reperfusion treatment not given, additional reperfusion treatment , patient location at time of STEMI); examinations (systolic blood pressure, heart rate, Killip class); tests (serum glucose, creatinine, raised cardiac markers, peak troponin); drug therapy at discharge (beta blocker, angiotensin converting enzyme inhibitor or angiotensin receptor blocker, statin, aspirin, thienopyridine inhibitor, aldosterone antagonist, Ticagrelor); diabetes or hyperglycaemia management (as an inpatient); complications (death in hospital); cardiac arrest (location), investigations and interventions (daycase transfer date, interventional centre code); discharge details (date, diagnosis, destination); and interventional audit data in the case of interventional hospitals (date/time of arrival at non interventional hospital, assessment at non interventional hospital, assessment at interventional centre, intended reperfusion procedure, procedure performed, reason for no angiogram performed, reason for no intervention performed). Data mandatorily collected for NSTEMI patients is generally the same, with a few exceptions regarding which items are collected in admission details, reperfusion, previous medical history, drug therapy, complications, investigations and interventions, and discharge details. Interventional audit data is not collected for NSTEMI patients, and it is not applicable.

8.3.3 Comparing fields in the Myocardial Ischaemia National Audit with variables used in existing HTAs

The existing models used survival analysis to model mortality, and therefore the data collected in MINAP through the variable 'death in hospital' could be used to model the different types of mortality (all cause, cardiovascular, and non-cardiovascular). However, the MINAP will only provide data on death occurring at the hospital, which can be a limitation. There is some information in the MINAP on clinical interventions and type of care (procedure performed at the interventional hospital, admission method, and admission ward, drug therapy on discharge, coronary intervention) which would provide some of the information required to compare alternative treatments. The MINAP collects data on complications following ACS (bleeding, reinfarction), as well as reperfusion procedures (for STEMI patients) that can be used to inform the occurrence of further clinical events within the same hospital episode, but these items are not mandatory for all ACS classifications (STEMI and NSTEMI). Moreover, the audit does not provide data on the occurrence of stroke related

events, such as ischaemic and haemorrhagic stroke, and on disability resulting from these events which may have a non-negligible impact on HRQoL and costs.

Previous models have defined patient subgroups or adjusted effectiveness and utility estimates based on sex, age, comorbidities (namely diabetes) and type of ACS (STEMI, NSTEMI, unstable angina). These data are collected in the audit and could be used to case-mix patients when comparing performance or cost-effectiveness of interventions. There is also a non-mandatory field in MINAP for previous clinical history that could be of interest in this context, as previous models have explicitly incorporated clinical history in their model structure.(43)

MINAP does not currently collect patient-reported outcome measures. The inclusion of a preference-based HRQoL questionnaire (preferably the EQ-5D-5L), could improve the ability of the audit to inform cost-effectiveness analysis of interventions. An alternative would be to apply values from the published literature to clinical events, as has been done in previous models. However, as it has been highlighted before, the MINAP does not collect all relevant data regarding clinical events, namely the occurrence of ischaemic and haemorrhagic strokes and level of disability following stroke. Even if the audit collected all relevant clinical events, applying utility weights to the clinical events alone may fail to capture the impact on HRQoL of the interventions if this extends beyond changing the frequency of the events and has an effect on symptoms too. Similarly to the PCI audit, collection of a PROM would allow HRQoL considerations to be related to events, but also to symptomatic differences that may be evident and are not fully accounted for by events. The issue regarding duration of follow-up period for the collection of PROMs in the PCI audit also applies here, as it may be difficult to demonstrate the full symptomatic benefits of interventions over just the hospitalisation period following ACS. Therefore, the collection of PROMs beyond the initial hospitalisation episode would be useful to ensure that any longer term symptomatic impact of treatments is captured.

Assuming the mandatory fields have relatively high completion rates, with the exception of HRQoL, the information currently collected in the existing MINAP would provide a considerable amount of information required to model the cost-effectiveness of interventions and policies in ACS. Although mortality data is only collected for the period until discharge, external published data, linkage to other datasets (mortality registers, Hospital Episode Statistics, other audits) or longitudinal linkage across multiple MINAP entries (for patients that suffer further hospitalisations due to ACS) could be incorporated to overcome this limitation. Another alternative is to use risk scores, such as the Global

Registry of Acute Cardiac Events (GRACE), to estimate cardiovascular mortality, as well as the risk of future MI events, in hospital and at 6 months.(44) All the variables required to estimate GRACE are already collected within the audit (age, Killip class, pulse rate, systolic blood pressure, serum creatinine, ST-segment deviation, cardiac arrest at admission, elevated cardiomarkers). Another risk score that can be used to predict all cause mortality, myocardial infarction, or urgent revascularisation is the Thrombolysis in Myocardial Infarction (TIMI).(45) However, not all variables required to estimate this score are mandatory variables in MINAP, namely the place where aspirin was administered (allows assessment of whether it was administered within 7 days of the initial event), and TIMI only predicts short-term outcomes (at 14 days after index event). Another limitation of the MINAP to inform cost-effectiveness studies is that it provides incomplete coverage of other relevant clinical events that may occur during the initial episode. This limitation could potentially be addressed by linking data to other audits, such as the PCI audit for those patients undergoing coronary angioplasty (or coronary angiography, as this audit covers both procedures) to determine procedure related complications (e.g. cerebral, haemorrhagic stroke). However, the linkage to the NAPCI would in itself be affected by the same issues that were identified in that audit (Section 14.3), i.e. not all types of stroke are recorded, and level of disability following stroke is also not collected. Follow-up data which is limited to some complications (bleeding, reinfarction) and repeated revascularisation (reperfusion) occurring within the same hospital episode could be supplemented by risk estimates taken from the published literature. Clinical events occurring after the hospital episode for which the patient was initially admitted would also have to be sourced from the published literature with the exception of further ACS events, as patients' NHS number could be used to track readmissions. It is worth noting that it is unclear in the audit whether further events within the same hospital episode, such as reinfarction would generate a new entry on MINAP, or just be collected on the field 'reinfarction', which is not part of the minimum data standard. Furthermore, even by linking a patient longitudinally across multiple MINAP entries and to other relevant datasets, issues would remain regarding events that are not captured within the MINAP or NAPCI registries (e.g death outside hospitalisation, ischaemic stroke, non-ischaemic stroke unrelated to procedure, stroke disability and issues about symptoms more generally).

8.4 Recommendations for acute coronary syndrome

In summary, the EQ-5D appears to be appropriate in ACS patients, and the current MINAP collects some of the information required to conduct economic evaluations. Nevertheless, the audit does not collect any HRQoL data, and could be improved by including more fields and/or making their

collection mandatory. The issues and corresponding PR and areas for FR are discussed below. All suggested FR areas are indicative and would require a discussion and detailed proposal if required.

As shown in Section 4.1, the validity of EQ-5D in ACS was demonstrated across all examined psychometric properties. There was no evidence regarding the responsiveness of this measure, and reliability examined at health dimension level was found to be poor in one study included in the review. There were also issues regarding the existence of potential ceiling effects in this condition. Nevertheless, the overall evidence was positive and EQ-5D is considered an appropriate measure to estimate HRQoL in ACS. The inclusion of this measure would improve the audit's ability to inform cost-effectiveness analysis in this condition, especially if its collection also encompasses time points beyond the initial hospitalisation period. To our best knowledge the collection of PROMs within the NACSA is not currently being considered, so it is recommended that EQ-5D (EQ-5D-5L) is collected within the audit.(PR.12, FR.5) As mentioned in previous sections, the use of the EQ-5D-5L could potentially reduce any ceiling effect(86) in patients in less severe stages of cardiovascular disease. Alternatively and provided that all relevant clinical events could be collected or sourced from external sources, utility weights from the published literaturature could be applied to clinical events to generate quality adjusted life years (QALYs).

The MINAP already collects the majority of relevant information for the economic evaluation of interventions in ACS (described in Section 8.3.3). However, fields such as occurrence and type of stroke, severity of disability following stroke are not currently collected. These fields importance has been highlighted in Section 8.3.3, and should be considered for mandatory collection (PR.13).

Table 13: Recommendations and associated future research for acute coronary syndrome

PR.12	*Collect the EQ-5D (EQ-5D-5L) in the NCA at admission and at least one longer-term follow-up time point.*
FR.6	*Assess the psychometric properties of the EQ-5D-5L using data collected in the audit*
PR.13	*Collect mandatory information on occurrence and type of stroke, severity of disability following stroke.*

9. SUMMARY

9.1 Summary of evidence used to inform the conclusions for WP1.1

Cardiovascular conditions: An existing review (3) was updated and a total of 12 primary studies were included in the update. As there was substantial overlap between the study populations, and a very limited amount of evidence for some of the individual CVD conditions the evidence is summarised collectively. Overal, the review provides evidence that the EQ-5D is adequate in CVD, being acceptable in the majority of studies and having good construct validity (known group and convergent). There was some evidence of ceiling effects (although this is unlikely to be observed in the hospitalised patients within the CVD audits), and there was very little evidence on its reliability. Additional evidence was required on its sensitivity to detecting small changes in HRQoL over time.

Table 14: Summary of evidence on EQ-5D for CVD conditions

Measure (N)	Acceptability	Reliability	Construct (KGV; Convergent)	Responsiveness (Change over time; Ceiling effects)	
EQ-5D (12)	Fair to good	Poor (little evidence)	Good	Poor (mostly uncertain)	Evidence of ceiling effects (more pronounced at health dimension level)
Adequate, with some uncertainty surrounding responsiveness.					

9.2 Summary of evidence required for use in economic evaluations (WP1.3)

Cardiac arrhythmia: The NACRM currently collects the EQ-5D and the condition-specific AFTEQ in a patient questionnaire administered pre and post (6 month and 12 month) the ablation procedure. However, only patients undergoing ablation procedures complete the questionnaire and if this could be extended to all patients within the audit, this would increase the scope of the audit data in relation to performing economic evaluations and comparing providers. Although there is currently insufficient information in the mandatory fields to conduct formal economic evaluations, the data standard subset has additional information that could be used, subject to completion levels. In particular, the following information would ideally be required for informing economic models: normal sinus rhythm, permanent AF with uncontrolled symptoms, permanent AF with controlled symptoms, and death rates, type of intervention (CRT-P, CRT-D, dual-chamber or single chamber pace-makers, implantable cardioverter defibrillators) and associated success/complication rates,

cardiac resynchronisation therapy, anti-coagulant drugs and thromboembolic, ischaemic and bleeding events.

Heart Failure: Although no PROMs are currently collected in the NHFA, it may be possible to utilise the NYHA breathless severity data to obtain proxy preference-based utility scores to generate QALYs in economic evaluations. However, the NHFA data are only collected on admission and re-admission. To inform the benefits of interventions, they would also need to be collected post intervention and on discharge from hospital. In addition, the collection of EQ-5D-5L directly within the audit would capture the benefits of interventions and procedures directly thus reduce the uncertainty inherent within mapping functions. Excluding HRQoL information, the current NHFA collects much of the information required to conduct formal economic evaluations and to compare providers, and it is possible that the gaps identified (mortality and surgical complications) may be available in external datasets if these could be linked in some way.

Coronary angioplasty: Although the PCI audit does not collect PROMs, due to the discrete nature of the health states in the typical clinical pathway, it would be possible to utilise evidence in the literature to populate HRQoL values in economic evaluations. However, the inclusion of a PROM (preferably the EQ-5D-5L) within the audit would enable direct comparison of providers and interventions using the audit data. In addition, depending on the timing of collection, EQ-5D-5L collected via the audit, could provide useful information on the longer-term effects (for example 6 month and 12 month post discharge) on HRQoL associated with reductions in symptoms, rather than the immediate direct effect of specific interventions and procedures (i.e. during hospitalisation). Excluding HRQoL information, the NAPCI does collect much of the information required to conduct formal economic evaluations and to compare providers. Again it may be possible to use external datasets to subsidise gaps in the evidence collected (e.g. mortality and surgical complication rates) for economic evaluations, but this would not be particularly informative when comparing providers.

Cardiac surgery: The NACSA audit does not collect PROMs, and as discussed for the PCI audit, while it may be possible to utilise evidence from the literature when conducting economic evaluations of interventions, this form of information is not particularly informative when comparing providers and it is recommended that the EQ-5D-5L is collected within the audit with follow-up data to capture the longer-term HRQoL benefits of interventions. Excluding the HRQoL information, the information collected within the audit would suffice to compare providers and would provide a substantial amount of the evidence required to conduct formal economic evaluations of interventions

(assuming a relatively high completion rate for all fields). The exceptions are again the mortality information, surgical complications and longer term information on subsequent events. The latter may be available from external datasets if these could be linked in some way.

Acute coronary syndrome: The MINAP does not collect PROMs and as discussed for the PCI audit, while it may be possible to utilise evidence from the literature when conducting economic evaluations of interventions, this form of information is not particularly informative when comparing providers and it is recommended that the EQ-5D-5L is collected within the audit with follow-up data to capture the longer-term HRQoL benefits of interventions. Excluding the HRQoL information, the information collected within the audit would provide a considerable amount of the information required to model the cost-effectiveness of interventions and policies in ACS assuming relatively high completion levels.

In summary, while the evidence collected in the individual audits will allow comparison of providers in many cases, it is clear that the mandatory fields in most of the audits will not provide sufficient detailed information to perform formal economic evaluations. The main omission is the lack of PROMs which limits the flexibility of the data in terms of comparing either providers or interventions used in routine clinical practice. However, many of the audits contain optional fields which would be useful for economic evaluations and enforcing the collection of key variables is recommended in many of the audits. A recurrent issue relates to the level of detail and the timing of the variables collected. To be useful for economic evaluations, many of the variables used have to be synchronised in terms of timing of collection, and many need to be collected over periods of time to assess progression or relapse etc.

Finally, subject to synchronising the fields collected, linking the CVD audits could produce a synergistic effect in terms of the evidence required to inform parameters within formal economic evaluations or to compare providers. However, exploring this possibility is outside the scope and time restrictions of the current project.

APPENDIX: CARDIOVASCULAR CONDITIONS

The tables in this Appendix provide additional information for the reviews (WP1.1, 1.2 and 1.3) conducted for CVD conditions.

Table A1: Characteristics of included studies included in the systematic review for cardiovascular conditions (WP 1.1)

Study ref Author, Year	Country	Disease/treatment stage	Treatment (if any)	Study type (e.g. cross sectional, RCT, cohort)	Study objective
Schweikert, 2006[a](5)	Germany	Patients with acute coronary syndromes ACS (MI , coronary artery bypass, angina)	No treatment, single cohort Questionnaires given at admission, at discharge and three months after discharge	Consecutive patients attending inpatient cardiac rehabilitation following ACS	To analyse the acceptance and feasibility, discriminative ability construct validity, criterion validity, reliability and responsiveness of the EQ-5D
van Stel, 2006[a](23)	The Netherlands	Patients with symptomatic coronary stenosis	OctoPump standard on-pump CABG vs off-pump CABG OctoStent Off-pump CABG vs PTCA Questionnaires given prior to intervention, at 1, 3, 6 and 12 months after the intervention.	Two RCTs: OctoPump OctoStent	To assess the equivalency of SF-6D and EQ-5D cross-sectionally, in domain content, in scoring distribution, and in the amount of change measured after intervention
Nowels, 2005(25)	United States	Patients who suffered a MI (2 to 25 months prior to study)	No treatment, single cohort Questionnaires given before appointment.	Cross-sectional study set at multi-site cardiology group practice	To assess cross-sectional validity of EQ-5D after MI.
Eurich, 2006[a](46)	United States and Canada	Patients with heart failure older than 30 years old and LVSD	No treatment, single cohort Questionnaires given at baseline	Cohort study Patients attending outpatient services	Evaluate the relative responsiveness of selected disease-specific and generic HRQoL measures.

			and at 6 weeks.		
Spertus, 2005[a](47)	North America	Patients with heart failure older than 30 years old and LVSD	No treatment, single cohort Questionnaires applied at baseline and at 6.7± 2.6 weeks.	Cohort study Patients attending outpatient services	Compare the ability of selected disease-specific and generic HRQoL measures to reflect short-term changes in the clinical status of outpatients with heart failure.
De Smedt, 2013[b](12)	Europe (22 countries)	Patients hospitalised for CABG, PCI, acute MI or myocardial ischemia	No treatment, single cohort Patients interviewed 6 months to 3 years after index hospital admission	Cross-sectional survey study	To investigate the validity and reliability of the EQ-5D, SF-12 and HADS
Sut, 2011[b(]13)	Turkey	Patients with ACS (MI and unstable angina pectoris)	No treatment, single cohort Patients interviewed at hospital	Cross-sectional study	To evaluate the construct validity of the Turkish version of the EQ-5D in patients with ACS
Garster, 2009[b](14)	United States	Population-based sample that included individuals without CHD, and with CHD of varying severity. Patients with heart failure older than 35 years old and LVSD	No treatment. Patients interviewed over phone in first study (NHMS), and at the heart failure clinic on the parallel study (COMHS)	Cross-sectional studies NHMS COMHS	To compare HRQoL differences with CHD in generic indexes and a proxy specific score in a nationally representative sample of US adults
Kontodimopoulos, 2011[b(]15)	Greece	Patients with chronic heart failure admitted for elective cardiac surgery	No treatment, single cohort. Patients interviewed at hospital	Cross-sectional survey study Consecutive patients admitted for elective cardiac surgery	To compare EQ-5D and SF-6D utilities across groups of chronic heart failure with varying disease severity
Feeny, 2012[b](16)	United States	Patients with congestive heart failure, older than 35 years old and LVSD (and patients undergoing	No treatment. Questionnaires given at baseline and at 6 months	Prospective cohort study	To examine agreement in classifying patients as better, stable or worse.

		cataract extraction surgery)	follow-up		
De Smedt, 2014[b](19)	Europe (20 countries)	Patients hospitalised for CABG, PCI, acute MI or myocardial ischemia	No treatment, single cohort Patients interviewed 6 months to 3 years after index hospital admission	Cross-sectional survey study	To compare EQ5D and SF-6D utility scores in a large European sample of patients with stable CHD
Withers, 2014[b](17)	UK	Cardiac arrhythmia patients treated with catheter ablation	No treatment, single cohort Pre and post-procedure questionnaires sent to patients at the same time. Reminders were sent to non-responders within 16-29 days of first contact.	Retrospective audit data Consecutive patients treated with catheter ablation	To assess the feasibility of administering PROMs in patients treated with ablation for cardiac arrhythmias, and to conduct the first stage of development and testing of a new PROM tool.

Table A2: Participant characteristics studies included in the systematic review for cardiovascular conditions (WP 1.1)

Ref Man ID	Study ref Author, Year	Number of participants recruited	Age in years mean (sd); range	male %	Ethnicity (%)	Other characteristics (%)	Missing data (patients completing study) include reasons for non-completion if given
	Schweikert, 2006 (24)	114	55(7.6); 30-65	85	NR	MI: 51 Coronary artery bypass: 42 Angina: 7 NYHA class I: 83 NYHA class II: 9 NYHA class III: 3 NYHA class IV: 0	106 patients included in analysis 8 patients excluded from analysis: 5 withdrew and 3 had incomplete documentation for administrative reasons. Missing and invalid responses in the EQ-5D self-classifier ranged from 0.6% (admission) to 2.9% (discharge).
	van Stel, 2006(23)	560(281+280)	60.2 (9.3)	70.4	NR	-	% of missing data (BL and post-intervention respectively): EQ-5D: 9.1%; 15.9% 5.9% (33) patients lost to follow-up 4.6% (BL) and 4.1% (post-intervention) patients did not fill in the questionnaires
	Nowels, 2005(25)	123	64 (NR)	69	NR	One previous MI: 80 Two previous MI: 17 Three previous MI: 3 Median time since last MI: 176.5days (range 25-872 days) CCSC I: 74 CCSC II: 19 CCSC III: 6 CCSC IV: 1	111 patients appeared for appointment 20 patients of scheduled patients refused consent 99 patients completed study
	Eurich, 2006(46)	476	60(13)	75	Caucasian: 73 African-American: 23 Other: 4	NYHA class I: 11 NYHA class II: 43 NYHA class III: 41 NYHA class IV: 5	Only 298 who had complete data were included in the study. No other reason provided.
	Spertus, 2005(47)	547	61(13)	75	White: 70	NYHA class I: 11NYHA class II: 41 NYHA class III: 44 NYHA class IV: 6	Only 476 who had complete data were included in the study. No other reason provided.

						5 patients died during the study
	De Smedt, 2013(18)	8,966	63.2 (9.5)	74.6	NR	Primary education: 25.3 Secondary education 56.7 Higher education: 18.0	8,745 were included in the analysis
	Kahyaoglu, 2011(48)	138	63.9 (9.3)	72.1	NR	MI : 45.1 unstable angina pectoris: 54.9	16 patients did not agree to respond to the scales 122 patients were included in the analysis
	Garster, 2009(14)	NHMS: 3,844 COMHS: 154	No CHD: 58.9 (14.0) CHD only: 69.9 (10.2) CHD + medication: 68.9 (10.7)	No CHD: 41.2 CHD only: 57.0 CHD + medication: 49.1	No CHD: 66.2 (White); 28.8 (Black) CHD only: 75.9(White); 20.4 CHD + medication: 62.4 (White); 30.7 (Black)	No CHD: 3,350 patients CHD only: 265 patients CHD + medication: 218 patients CHD only: 28.3 (CABG), 37.0 (coronary angiography) CHD + medication: 33.0 (CABG), 52.3 (coronary angiography)	NHMS: 3,844 patients completed the study (46.% response rate) COMHS: 154 patients completed the study, no other information reported
	Kontodimopoulos, 2011(15)	256	65.80 (71.7)	71.7	NR	Self-assessed severity: Very severe: 17.1 Severe: 35.9 Medium: 21.5 Mild: 15.5 Very mild:10.0 Comorbid conditions: Unstable angina: 23.5 Diabetes: 21.9 Hypertension: 61.8 Acute MI: 32.	251 patients included (98% response rate)
	Kaplan, 2011(49)	Heart failure cohort: 160	NR Age reported by categories, rather than	77	White: 79 Black: 12 Asian: 3 Other: 1		Patients completing EQ-5D at baseline, 1 month and 6 months follow-up: 155; 136; 110.

		mean value.		Missing: 5		
Feeny, 2012(16)	Heart failure cohort: 160	NR Age reported by categories, rather than mean value.	77	White: 79 Black: 12 Asian: 3 Other: 1 Missing:5		Data available at baseline and 6 months follow-up for 110 patients Complete data for both time points for 86 patients. Patients with missing data were older than those without (statistically significant difference) No other information reported
De Smedt, 2013(18)	8,966	63.1 (9.2)	75	NR	Cardiac revascularisation as recruiting diagnosis: 60 Reporting diabetes: 23.2 History of stroke: 4.5 Reported at least one recurrent coronary event since recruiting diagnosis: 13.3	7,472 were included in the analysis (those that had complete data for both EQ-5D and SF-6D)
Withers, 2014(17)	800	57.8 (Range: 17-88))	55	NR	Atrial fibrillation:23.0	791 were included in the analysis (patients were removed from the study as they were identified as duplicates (had moved houses or been retreated) or deceased

SD, standard deviation; yr, year; NR, not reported; MI, Myocardial infarction; CHD, coronary heart disease; CABG, coronary artery bypass grafting; NYHA, New York Heart Association; BL, baseline; CCSC, Canadian Cardiovascular Society Class; NHMS, National health measurement study; COMHS, Clinical outcomes and measurement of health study

Table A3: Valuation and descriptive methods used in studies included in the systematic review for cardiovascular conditions (WP 1.1)

	GENERIC MEASURES			OTHER MEASURES USED			
Study ref Author, Year	**Descriptive system**	**Tariff used**	**Mean (SD); 95% CI**	**Condition-specific HRQL measures**	**Clinical measures**	**Qualitative questions**	**Missing data; completion rates of measures; etc.**
Schweikert, 2006(24)	EQ-5D SF-36	European (0-100)[Greiner, 2003]		MacNew	None	None	Acceptance of EQ-5D assessed by proportion of missing responses on EQ-5D
van Stel, 2006(23)	EQ-5D SF-6D	UK [Dolan, 1996]	EQ-5D at baseline 0.64 (SD NR; median 0.69) SF-6D at baseline 0.62 (SD NR; median 0.60)	None	None	None	% of missing data (BL and post-intervention respectively): EQ-5D: 9.1%, 15.9%; SF-6D:16.9%, 22.6%; SF-6D:16.9%, 22.6%; SF-6D after imputation of SF-36 missing items:10.9%, 16.8%;
Nowels, 2005(25)	EQ-5D SF-36	UK [Dolan, 1996]	0.73(SD NR)	QLMI	CCSC	None	Only 99 patients completed the study
Eurich, 2006(46)	EQ-5D RAND12	UK [Dolan, 1996] US [Shaw et al, 2005]	EQ-5D at baseline, UK tariff: 0.66 (SD 0.26) RAND12 at baseline: **PCS:** 35.0 (SD 10.7) **MCS:** 48.4 (SD 11.4)	KCCQ	None	None	Only 298 patients with complete data included in the study
Spertus, 2005(47)	EQ-5D	UK [Dolan, 1996]	EQ-5D at baseline:	KCCQ	NYHA 6-MW	None	Only 476 patients with complete data included in the study

	SF-12		0.67 (SD 0.26) SF-12 at baseline: **PCS:** 35 (SD 11) **MCS:** 49 (SD 12)		Physician global rate of change B-type natriuretic peptide		
De Smedt, 2013(18)	EQ-5D SF-12	UK [Dolan, 1996]	Means are reported by country and range between: EQ-5D: 0.76 (SD NR) SF-12: **PCS:** 42.14 (SD NR) **MCS:** 49.15 (SD NR)	None	HADS	None	Only 8475 patients were included in the analysis
Sut, 2011(13)	EQ-5D Turkish version	NR	0.79 (0.32)	MacNew	None	None	122 patients answered the questionnaires
Garster, 2009(14)	EQ-5D SF-6D SF-36 HUI2 HUI3 QWB-SA	NR	EQ-5D; No CHD: 0.88 (SD 0.15) CHD only: 0.82 (SD 0.15) CHD + medication: 0.74 (SD 0.21)	CVD-specific proxy score	None	None	NHMS: 3,844 patients completed the study (46% response rate) COMHS: 154 patients completed the study, no other information reported

	HALex						
Kontodimopoulos, 2011(15)	EQ-5D SF-6D	UK [Dolan, 1996] SF-6D	EQ-5D: 0.73(SD 0.303; median 0.796); 0.665 – 0.741 SF-6D: 0.710(SD 0.136; median 0.687); 0.693 – 0.727		DASI	None	251 patients included (98% response rate)
Feeny, 2012(16)	EQ-5D SF-6D HUI2 HUI3 QWB-SA SRH	US [Shaw et al, 2005]	NR	MHLF	None	None	Data available at baseline and 6 months follow-up for 110 patients Complete data for both time points for 86 patients.
De Smedt, 2014(19)	EQ-5D	UK [Dolan, 1996]	Median EQ-5D : 0.80 (IQR:0.69-1.00) Median SF-6D: 0.70 (IQR: 0.62-0.82)	None	None	None	Only 7,472 patients were included in the analysis (complete data for both EQ-5D and SF-6D)
Withers, 2014(17)	EQ-5D-5L	Country not reported, refers to the EuroQoL crosswalk[EuroQoL group, 2013]	NR	Modified PPAQ Newly developed arrhythmia specific	None	None	791 patients were included in the analysis

		questionnaire developed

Table A4: Acceptability, reliability and validity assessment in studies used studies included in the systematic review for cardiovascular conditions (WP 1.1)

Author, Year	Method of measuring validity Type of validity, how (e.g. known group/convergent)?	Validity results Group A(n) vs. Group B(n)[ϕ] Mean EQ-5D; mean difference in EQ-5D	Authors' conclusions/notes
Schweikert, 2006(24)	Acceptance and feasibility of EQ-5D assessed by proportion of missing and invalid responses	EQ-5D questionnaire missing range: 0.6 to 2.9% SF-36 missing range: 1.5 to 6.5% MacNew invalid answers range: 1.5 to 2.3% to 4.8%	Instrument well understood and accepted by patients with ACS
	Construct validity, comparing subgroups: MI vs CABG patients: i. % of patients citing no problems in each EQ-5D health dimensions at admission	**MI** (% no; moderate; extreme problems) **Mobility:** 81.5; 18.5; 0 **Self-care:** 100; 0; 0 **Usual activities:** 55.8; 36.5;7.7 **Pain:** 51.9; 48.1; 0 **Anxiety/depression:** 50.0; 46.3.0; 3.7 **CABG** (% no; moderate; extreme problems) **Mobility:** 61.4; 38.6; 0; p=0.03[a] **Self-care:** 77.3; 22.7; 0; p <0.001[b] **Usual activities:** 25.6; 51.2; 0; p=0.006[c] **Pain:** 15.9; 79.5; 4.6; p=0.002[a] **Anxiety/depression:** 52.3; 45.5; 2.3; p=0.822[a]	% of patients citing no problems significantly higher among patients with MI than for patients after CABG, for all health dimensions except anxiety/depression.
	Criterion validity: Association between EQ-5D self-classifier response level and median SF-36 subscale and McNew scores at admission.	For all EQ-5D health dimensions , the median of the SF-36 and McNew subscales were ranked as expected and significantly different between groups (p<0.001)	Reasonable criterion validity. EQ-5D correlates well with most subscales of SF-36, and MacNew questionnaire. EQ-5D has good test-retest validity, but may be due to ceiling effects.
	Reliability: Proportion of agreement between consecutive measures of EQ-5D self-classifier for patients indicating unchanged HRQoL between time periods.	**Period 1: Health dimension (n): agreement (%), Kappa statistic** **Mobility (n=11):** 73%; k=0.24 **Self-care (n=11):** 100%; k=1 **Usual activities (n=11):** 55%; k=0.17 **Pain (n=11):** 82%; k=0.62 **Anxiety/depression (n=11)::** 65%; k=1 **Period 2 Health dimension (n): agreement**	

		(%), Kappa statistic **Mobility (n=33):** 88%; k=0.53 **Self-care (n=34):** 70%; k=NA[e] **Usual activities (n=33):** 69%; k=0.43 **Pain (n=32):** 82%; k=0.62 **Anxiety/depression (n=34):** 65%; k=0.24	
van Stel, 2006(23)	Acceptability: Not formally assessed, but the percentage of missing data by measure and time point was reported.	% of missing data (BL and post-intervention respectively): EQ-5D: 9.1%, 15.9%; SF-6D:16.9%, 22.6%;	Higher percentage of missing data for SF-6D on both periods
	Discriminative validity: Tendency towards a single level response	% patients reporting no problems at baseline for EQ-5D health dimensions: Mobility: 31.8% Self-care: 93.1% Usual activities: 30.5% Pain: 31.8% Anxiety/depression: 60% % reporting full-health at baseline for EQ-5D index: 13.5% % patients reporting no problems at baseline for SF-6D health dimensions: Pain: 13.0% Mental health: 8.9% Physical functioning: 2.3% Social functioning: 20.1% Role limitations: 14.1% Vitality: 2.7% % patients reporting full-health at baseline for SF-6D score: 0.4%	Evidence of ceiling effect for EQ-5D.

	Convergent validity: Spearman rank correlations between domains of SF-6D and EQ-5D ICC between utility scores of EQ-5D and SF-6D	Spearman correlations between like health dimensions of SF-6D and EQ-5D : Physical functioning and Mobility: 0.31* Physical functioning and Usual Activities: 0.42* Role limitation and Usual Activities: 0.35* Social Functioning and Usual Activities: 0.41* Pain and Pain/Discomfort:0.43* Mental Health and Anxiety/Depression: 0.47* Spearman correlations between remaining health dimensions of SF-6D and EQ-5D : Physical functioning and Self-care: 0.34* Physical functioning and Pain/Discomfort: 0.24* Physical functioning and Anxiety/Depression: 0.11** Role limitation and Mobility: 0.19** Role limitation and Self-care: 0.09 Role limitation and Pain/Discomfort: 0.30* Role limitation and Anxiety/Depression: 0.21* Social Functioning and Mobility: 0.26* Social Functioning and Self-care: 0.20** Social Functioning and Pain/Discomfort: 0.36* Social Functioning and Anxiety/Depression: 0.34* Pain and Mobility: 0.32** Pain and Self-care: 0.23** Pain and Usual Activities: 0.48* Pain and Anxiety/Depression: 0.19** Mental Health and Mobility: 0.04 Mental Health and Self-care: 0.09 Mental Health and Usual Activities: 0.09 Mental Health and Pain: 0.17** Vitality and Mobility: 0.20* Vitality and Self-care: 0.15** Vitality and Usual Activities: 0.27*	Correlation structure was rather diffuse with only moderate correlations, which does not support construct validity. Only mood/mental health exhibited strong correlation with each other, and lower correlations with other health dimensions. Low ICC suggests lack of agreement.

		Vitality and Pain/Discomfort: 0.26* Vitality and Anxiety/Depression: 0.27* ICC between EQ-5D and SF-6D scores:0.45	
Nowels, 2005(25)	Convergent validity: Spearman rank correlations of EQ-5D domains with SF-36 and with QLMI.	Spearman correlations between like domains of SF-36 and EQ-5D: Physical functioning and Mobility: 0.63 Physical functioning and Usual Activities: 0.59 Role limitation (physical) and Usual Activities: 0.62 Social Functioning and Usual Activities:0.50 Pain and Pain/Discomfort: 0.68 Mental Health and Anxiety/Depression: 0.75 Spearman correlations between domains of QLMI and EQ-5D: Symptoms and Mobility: 0.47 Symptoms and Self-care: 0.17 Symptoms and Usual activities: 0.49 Symptoms and Pain and Discomfort: 0.45 Symptoms and Anxiety/Depression: 0.59 Restriction and Mobility: 0.31 Restriction and Self-care: 0.07 Restriction and Usual activities: 0.45 Restriction and Pain and Discomfort: 0.30 Restriction and Anxiety/Depression: 0.53 Confidence and Mobility: 0.34 Confidence and Self-care: 0.07 Confidence and Usual activities: 0.01 Confidence and Pain and Discomfort: 0.38 Confidence and Anxiety/Depression: 0.31 Self-esteem and Mobility: 0.46 Self-esteem and Self-care: 0.17 Self-esteem and Usual activities: 0.56 Self-esteem and Pain and Discomfort: 0.40 Self-esteem and Anxiety/Depression: 0.48	Authors state that convergent validity was demonstrated for the EQ-5D through moderate to high correlations with disease specific and general HRQoL instrument.

		Emotion and Mobility: 0.41 Emotion and Self-care: 0.31 Emotion and Usual activities: 0.43 Emotion and Pain and Discomfort: 0.31 Emotion and Anxiety/Depression: 0.64 Spearman correlations between EQ-5D index and QLMI total score: 0.57	
	Discriminative validity: Comparison of differences in EQ-5D index score between two groups based on their CCSC scores (I vs. II, III, or IV), using Mann-Whitney rank-sum testing. Compared the means of EQ-5D index score between the CCSC class I and CCSC class II with a t-test and the respondents with Mann-Whitney rank-sum testing.	EQ-5D index scores showed excellent discrimination ($p<0.001$) between patients with CCSC I compared to patients with either CCSC II, III or IV collectively. Spearman's correlation coefficient between EQ-5D score and CCSC class grouping was 0.36. Mean EQ-5D (SD) by CCSC: I: 0.78 (0.2) II: 0.72 (0.12) II, III, or III: 0.62 (NR) Non-parametric analysis showed significant differences in mean EQ-5D index scores ($p<0.05$, but t-test did not ($p=0.1$)	Demonstrates that EQ-5D has discriminative validity.

De Smedt, 2013(18)	Known-group validity: Assessment of the relationship of constructs with age, gender and education, using Kruskall-Wallis to test the hypothesis that quality of life would decrease with age, and lower education, and would be lower for females.	EQ-5D mean by groups (Kruskall–Wallis p value<0.001 for all groups): Gender: Male: 0.78 Female:0.69 Age: < 50 years: 0.81 50-59 years: 0.77 60-69 years: 0.76 > 70 years: 0.72 Education level: Primary education: 0.72 Secondary education: 0.76 High education: 0.80	Discriminative validity was confirmed for all HRQoL measures including EQ-5D.
	Convergent validity: Spearman's correlation for theoretically related constructs.	Spearman correlations (CI 95%): EQ-5D index and HADS-A: -0.51 (-0.31;-0.61) EQ-5D index and HADS-D: -0.51 (-0.22;-0.63) EQ-5D index and SF-12 PCS: 0.64 (0.48;0.72) EQ-5D index and SF-12 MCS: 0.47 (0.20;0.61) EQ-5D index and SF-12 Q1: -0.51 (-0.33;-0.63) EQ-5D anx/dep and SF-12 Q6: -0.55(-0.47;-0.66)	Convergent validity was supported by the estimated correlations for all HRQoL measures including EQ-5D. Strong correlation between EQ-5D index and SF-12 Q1 confirmed good criterion validity.
Sut, 2011(13)	Construct validity: Defined as extent to which it correlates with criteria from an established measure, such as valid disease-specific instruments Spearman rank correlations between EQ-5D index and the macNew subscales and global scores	Spearman rank correlations of EQ-5D index and: MacNew emotional subscale: 0.644** MacNew physical subscale: 0.721** MacNew social subscale: 0.557** MacNew global score: 0.688**	Significant Spearman correlations between EQ-5D index scores and MacNew subscales shows the validity of the Turkish version of the EQ-5D (p<0.001).
Garster, 2009(14)	Discriminative validity: Comparison of adjusted and unadjusted	Mean EQ-5D (SE) differences between: No CHD – CHD only: -0.055(0.013); -	Little differences between generic indexes in their sensitivity to coronary heart disease

	mean score differences scores between CHD group ES estimated between severity group	0.047(0.013)[f]; -0.038(0.013)[g] (p<0.001) No CHD – CHD with medication: -0.14(0.022); -0.12(0.023)[f]; -0.084(0.020)[g] (p<0.001) P value by F-test across groups ES for proxy CVD score and EQ-5D, respectively: CHD only vs no CHD: 0.51; 0.32 CHD with medication vs CHD only: 0.62; 0.52 CHD with medication – no CHD: 1.13; 0.84	related HRQoL. Effect sizes were in general of the same magnitude as for the CVD proxy score. Generic indexes can capture differences in HRQoL between populations with and without coronary heart disease.
	Convergent validity: Correlations between proxy CVD scores and generic indexes, partial on age, sex, and race.	Partial correlations between CVD proxy score and EQ-5D index: All NHMS sample: -0.63 NHMS all CHD sample: -0.65	Partial correlations demonstrated that all of the generic indexes correlated highly with the CVD proxy score, in both the NHMS sample as a whole and in a subgroup of only those with CHD.
Kontodimopoulos, 2011(15)	Convergent validity: Correlation and ICC between mean EQ-5D and SF-6D scores	Pearson correlation: 0.647[**] ICC: 0.484, p<0.001	Strong correlation between EQ-5D and SF-6D, despite level of agreement not being high.
De Smedt, 2014(19)	Convergent validity: Spearman rank correlations between utility scores of SF-6D and EQ-5D Spearman rank correlations between health dimensions of SF-6D and EQ-5D ICC between utility scores of SF-6D and EQ-5D	Spearman correlations between like SF-6D and EQ-5D utility scores: r=0.695[***] Spearman correlations between like health dimensions of SF-6D and EQ-5D[*]: Physical functioning and Mobility: 0.446 Physical functioning and Usual Activities:0.504 Role limitation and Usual Activities: 0.390 Social Functioning and Usual Activities: 0.403 Pain and Pain/Discomfort: 0.630 Mental Health and Anxiety/Depression: 0.551 Spearman correlations between remaining health dimensions of SF-6D and EQ-5D[***]: Physical functioning and Self-care: 0.318 Physical functioning and Pain/Discomfort: 0.415 Physical functioning and Anxiety/Depression:	EQ-5D outcomes are significantly correlated with SF-6D values, with ICC indicating moderate agreement between instruments. Moderate correlations found between related health dimensions of the two instruments.

		0.281 Role limitation and Mobility: 0.338 Role limitation and Self-care: 0.223 Role limitation and Pain/Discomfort: 0.395 Role limitation and Anxiety/Depression: 0.405 Social Functioning and Mobility: 0.346 Social Functioning and Self-care: 0.313 Social Functioning and Pain/Discomfort: 0.390 Social Functioning and Anxiety/Depression: 0.410 Pain and Mobility: 0.459 Pain and Self-care: 0.321 Pain and Usual Activities: 0.474 Pain and Anxiety/Depression: 0.338 Mental Health and Mobility: 0.268 Mental Health and Self-care: 0.230 Mental Health and Usual Activities: 0.321 Mental Health and Pain: 0.354 Vitality and Mobility: 0.325 Vitality and Self-care: 0.247 Vitality and Usual Activities: 0.371 Vitality and Pain/Discomfort: 0.343 Vitality and Anxiety/Depression: 0.324 ICC between utility scores of SF-6D and EQ-5D: 0.536, $p<0.01$	
	Discriminative validity: Tendency towards a single level response	Patients reporting full health: EQ-5D: 28.8% SF-6D: 4.2%	Ceiling effect observed for EQ-5D instrument.
Withers, 2014(17)	Acceptability of EQ-5D assessed by proportion of complete responses for the overall PROM tool (3 instruments, for pre and post procedure)	Response rate for following initial mailing 45-50%, across centres Overall response rate for following reminders for non-responders: Across centres: 70-75% For all sample: 71.2%	High response rates suggest that the PROM tool is acceptable.

Table A5: Responsiveness assessment studies included in the systematic review for cardiovascular conditions (WP 1.1)

Author, Year	Method of measuring responsiveness (e.g. effect sizes, statistical significance)	Responsiveness results	Authors' conclusions/notes
Spertus, 2005(47)	Degree of clinical change assessed according validated rating of change assessment by cardiologist (7 categories: large (n=5), moderate (n=13), or small deterioration (n=35); no change (n=320); small (n=65), moderate (n=34), or large improvement(n=4)). t-tests to compare differences in mean change scores by change category for patients whose condition had changed as compared to stable patients c-statistics to compare responsiveness of EQ-5D with KCCQ, SF-12, and NYHA by clinical change degree c-statistics represent % of the time that the measure correctly identified patients with clinical change for all possible	EQ-5D (Index and VAS) and SF-12D did not show great sensitivity to changes in clinical condition, as measured by mean change scores. Differences were small and the majority was not statistically significant. Results were presented graphically. The EQ-5D Index c statistics ranged from approximately 0.56 (for small clinical improvements) to approximately 0.69 (for moderate to large clinical deterioration), performing worse than than the KCCQ and NYHA but similarly discriminative abilities to SF-12 PCS and MCS. Results are presented graphically.	KCCQ and NHYA classification had a pattern consistent with the magnitude and direction of change. KCCQ was the most sensitive to clinical changes for groups of patients and for individual patients.

	pairs of patients, one experiencing clinical change and one not.		
Eurich, 2006(46)	Estimated mean changes in score and indices for all measures according to degree of change: ES[a] SRM[b] Clinical change defined according to three criteria: Change in NYHA: improving two NYHA classes, improving one NYHA class, no change in NYHA class, and deteriorating one NYHA class. Change global rating of change assessment (15 points scale): substantially improved (+7, +6, +5), moderately improved (+4,+3,+2), no change (+1, 0, -1), moderately deteriorated (-2, -3, -4), and substantially deteriorated (-5, -6, -7). Difference from baseline to 6-weeks in distanced travelled in the 6 MW test: Substantially improved (≥ +100 meters); moderately improved (+50 to +99	Mean change in EQ-5D index (SD): NYHA change criteria: Improved +2 NYHA Classes (n=2): 0.04 (0.05) Improved +1 NYHA Classes (n=50): 0.02 (0.19) No Change in NHYA Class (n=206): 0.02 (0.20) Deteriorated -1 NYHA Classes (n=40): 0.00 (0.19) Deteriorated -2 NYHA Classes (n=0): - Change global rating of change assessment criteria: Substantially improved (n=7): 0.21 (0.26) Moderately improved (n=53): 0.03 (0.20) No change (n=206): 0.04 (0.19) Moderately deteriorated (n=30): -0.01 (0.19) Substantially deteriorated (n=2): -0.05 (0.07) Change in distance travelled in the 6-MW criteria: Substantially improved (n=28): 0.05 (0.16) Moderately improved (n=40): 0.08 (0.23) Small improvement (n=33): 0.05 (0.17) No change (n=114): 0.01 (0.17) Small deterioration (n=60): 0.06 (0.23) Moderately deteriorated (n=16): 0.03 (0.20) Substantially deteriorated (n=7): 0.00 (0.12) ES and SRM for EQ-5D index, respectively: NYHA change criteria: Improved +2 NYHA Classes (n=2): 0.20; 0.80 Improved +1 NYHA Classes (n=50): 0.08; 0.11 No Change in NHYA Class (n=206): 0.19; 0.25 Deteriorated -1 NYHA Classes (n=40): 0.00; 0.00	HRQoL measures more responsive to improvement than to deterioration in clinical status. Responsiveness will vary for the same generic HRQoL depending on responsiveness indices and external criterion used to identify clinical change.

	meters), small improvement (+25 to +49 meters), no change (+24 to -24 meters), small deterioration (-25 to -99 meters), moderately deteriorated (- 100 to -199 meters), and substantial deterioration (≤ -200 meters). Substantially improved (≥ +100 meters); moderately improved (+50 to +99 meters), small improvement (+25 to +49 meters), no change (+24 to -24 meters), small deterioration (-25 to -99 meters), moderately deteriorated (- 100 to -199 meters), and substantial deterioration (≤ -200 meters).	Deteriorated -2 NYHA Classes (n=0): - Change global rating of change assessment criteria: Substantially improved (n=7): 0.75;0.81 Moderately improved (n=53): 0.13; 0.15 No change (n=206): 0.15; 0.21 Moderately deteriorated (n=30): -0.05; -0.05 Substantially deteriorated (n=2): -0.15; -0.71 Change in distance travelled in the 6-MW criteria: Substantially improved (n=28): 0.21; 0.31 Moderately improved (n=40): 0.29; 0.35 Small improvement (n=33): 0.22; 0.29 No change (n=114): 0.04; 0.06 Small deterioration (n=60): 0.23; 0.26 Moderately deteriorated (n=16): 0.09; 0.15 Substantially deteriorated (n=7): 0.00; 0.00 KCCQ more responsive to clinical change than EQ-5D and RAND 12, across all responsiveness indices and criteria for change. EQ-5D appears to be more responsive for higher degrees of clinical improvement, than for smaller clinical changes, according to both NYHA and global rating of change. This is less evident for the 6 MW. . EQ-5D is slightly less responsive than RAND 12 (the difference is greater when compared to the mental component of RAND-12)	
Feeny, 2012(16)	Agreement between the disease-targeted measure (MLHF) and each of the (EQ-5D, HUI2, HUI3, QWB-SA, and SF-6D) preference-based measures and SRH as to whether patients had improved, were stable, or got worse was assessed	MLHF and EQ-5D (n=86): % agreement: 19% k-statistic: -0.25 (CI 95%: -0.37 to -0.13) Weighted k statistic: -0.30 (CI 95%: -0.45 to -0.15) Delta statistics not reported for individual measures but stated to range between -0.33 (QWB-SA) to 0.26 (self-reported health).	Negligible agreement among measures on classification of patients as worse, stable or improved

	using the of percentage agreement, k (unweighted and weighted), and delta statistic.		
	Comparisons of number of patients experiencing change of HRQoL from baseline to 6 months according to MLHF and according to EQ-5D	Patients who got worse according to MLHF (n=46): Got worse according to EQ-5D:11 Stayed the same according to EQ-5D:16 Showed improvement according to EQ-5D:19 Patients who stayed the same according to MLHF (n=13): Got worse according to EQ-5D:6 Stayed the same according to EQ-5D:2 Showed improvement according to EQ-5D:5 Patients who showed improvement according to MLHF (n=27): Got worse according to EQ-5D:16 Stayed the same according to EQ-5D:8 Showed improvement according to EQ-5D:3	-

Table A6: Minimum Data Standard fields collected in the NACRM device dataset

DEMOGRAPHICS
Hospital identifier, Patient case record number, NHS Number, Date Of birth, Sex, Postcode
BASELINE DATA
Date of first implant, Pre-device Aetiology, Pre-device Symptom, Electrocardiogram Indication for Device, Functional status (NYHA), LVEF , ICD Indication, PreDevice/Ablation QRS duration
PROCEDURE
Procedure Date, First operator (scrubbed) name, First operator (scrubbed) GMC number, Consultant Name, Consultant GMC number, Intervention category, Generator mode (Maximum system capability)
PROCEDURE DETAILS - GENERATOR/DEVICE
Generator/Device Procedure, Reason for generator change, Generator model, Generator serial number
LEAD EXTRACTION
Indication for Lead Extraction
COMPLICATIONS
Acute complications

Table A7: Non-Minimum Data Standard fields collected in the CRM device dataset

DEMOGRAPHICS
Patient name (surname), Patient name (forename), Patient status
BASELINE DATA
Atrial rhythm at time of implant, Functional status (NYHA), QRS morphology (if greater than 120ms)
PROCEDURE
Second operator (scrubbed) name, Second operator (scrubbed) GMC number, Second operator grade, Consultant grade, Fluoroscopy time, Dose area product, Operation report/comment
PROCEDURE DETAILS - GENERATOR/DEVICE
Generator/Device implant site, Generator/Device manufacturer
PROCEDURE DETAILS - LEAD[a]
Lead intervention, Access, Pacing site, Indication for lead revision/change/removal, Lead manufacturer, Lead model, Lead serial number, Lead/Connector type
LEAD EXTRACTION
Methods used, Number of pacing leads removed completely, Number of pacing leads removed partially, Number of coronary sinus leads removed completely, Number of coronary sinus leads removed partially, Number of defibrillation (DF) leads removed completely, Number of DF leads removed partially
COMPLICATIONS
Late complications
FILE CLOSURE
Date of file closure, Device File Closure (reason)

[a] Same set of fields for each type of lead: left ventricular lead (1,2); right ventricular lead (1,2); atrial lead (1,2); nonpacing defibrillation lead (1,2).

Table A8: Minimum Data Standard fields collected in the NACRM interventional procedures dataset

DEMOGRAPHICS
Hospital identifier, Patient case record number, NHS Number, Date Of birth, Sex, Postcode
BASELINE DATA
Pre-procedure Aetiology (Underlying Heart Disease), Pre-procedure Symptom (Ablation Indication), Other Documented Arrhythmia, Pre-procedure Arrhythmia
PROCEDURE
Procedure date, First operator name, First operator GMC number, Consultant name, Consultant GMC number, Procedure type, Ablation procedure, Ablation attempted, Success, Acute complications
ATRIAL FIBRILLATION ABLATION DETAILS
Early Recurrence (within 24hrs)[a], European Heart Rhythm Association atrial fibrillation classification, NYHA functional status
OUTCOME IN HOSPITAL
No fields in the Minimum Data Standard
FOLLOW-UP [b]
Complications (post discharge), Outcomes: frequency of palpitations, Outcomes: duration of palpitations
FOLLOW-UP QoL/PROMs
No fields in the Minimum Data Standard

[a] This field has been deleted in the latest version of the dataset (version 3.05)
[b] Only to be completed if the procedure was atrial fibrillation ablation
Underlined fields are mandatory

Table A10: Core mandatory fields collected in the National Heart Failure Audit

PATIENT REGISTRATION
Hospital identifier Local patient identifier, Patient surname, Patient forename, Date Of birth, Sex, Postcode (of usual address)
ADMISSION/READMISSION DETAILS
Date of admission, Main place of care, Specialist input, Breathlessness[a] (on admission), Peripheral oedema (on admission)
MEDICAL HISTORY
Ischaemic heart disease, Device therapy (prior to or during this admission), Valve disease, Hypertension, Diabetes, Asthma, Chronic obstructive pulmonary disease
TREATMENT ON ADMISSION
No mandatory fields
PHYSICAL EXAMINATION
Weight (on admission/first recorded), Weight (on discharge /last recorded), Heart rate (on admission/first recorded), Heart rate (on discharge /last recorded), Systolic blood pressure (on admission/first recorded), Systolic blood pressure (on discharge /last recorded)
INVESTIGATIONS (all on discharge/last recorded)
Haemoglobin, Urea , Creatinine, Serum Sodium, Serum Potassium, Electrocardiogram, Echo (or other gold standard test e.g. MRI, nuclear scan or angiogram, recorded within 12 months of admission)
TREATMENT ON DISCHARGE[b]
Angiotensin-converting-enzyme inhibitor, Angiotensin receptor blocker, Beta blocker, Loop diuretic, Thiazide or metolazone, Mineralocorticoid receptor antagonist, Digoxin
DISCHARGE AND REFERRAL[b]
Confirmed diagnosis of heart failure , Heart failure management plan, Stable on oral therapy after discharge planning, Review appointment with the heart failure multidisciplinary team, Date of review appointment, Referral to heart failure nurse follow-up, Referral to cardiac rehabilitation, Referral to cardiology follow-up, Date of discharge, , Death in hospital

[a] corresponds to NYHA classification for heart failure severity
[b] if patient survived to discharge

Table A11: Non-mandatory (core and non-core) fields collected in National Heart Failure Audit

PATIENT REGISTRATION
NHS number, Ethnic category, GP name
ADMISSION/READMISSION DETAILS
All fields are mandatory
MEDICAL HISTORY
Device mode (prior to or during this admission), Congenital heart disease, Cerebral vascular accident , Alcohol (units/week), Smoking history
TREATMENT ON ADMISSION
Angiotensin-converting-enzyme(ACE) inhibitor, ACE inhibitor dose, ACE inhibitor contraindication, Angiotensin receptor blocker (ARB), ARB dose, Beta blocker, Beta blocker dose, Beta blocker contraindication, Loop diuretic, Loop diuretic dose, Thiazide or Metolazone, Thiazide dose, Mineralocorticoid receptor antagonist (MRA), MRA contraindication, MRA dose, Aspirin, Aspirin dose, Other oral anti-platelet, Digoxin, Digoxin dose, Calcium channel blocker (CCB), CCB dose, Statin, Statin dose, Warfarin, International normalized ratio (INR), Warfarin dose, Other oral anticoagulant, Other oral anticoagulant dose, Amiodarone, Amiodarone dose, Allopurinol, Allopurinol dose, Nonsteroidal anti-inflammatory drug, Oral nitrates , Nitrate dose, Bronchodilators, Diabetes therapy, Ivabradine, Ivabradine dose, Hydralazine, Hydralazine dose
PHYSICAL EXAMINATION
All fields are mandatory
INVESTIGATIONS (all on discharge/last recorded)
B-type Natriuretic Peptide (BNP), N-terminal prohormone of BNP, QRS duration, MRI systolic dysfunction Chest x-ray cardiothoracic ratio, Chest x-ray pulmonary oedema
TREATMENT ON DISCHARGE[a]
ACE inhibitor dose, ACE inhibitor contraindication, ARB dose, Beta blocker dose, Beta blocker contraindication, Loop diuretic dose, Thiazide dose, MRA contraindication, MRA dose, Aspirin, Aspirin dose, Other oral anti-platelet, Digoxin dose, CCB, CCB dose, Statin, Statin dose, Warfarin, INR, Warfarin dose, Other oral anticoagulant, Other oral anticoagulant dose, Amiodarone, Amiodarone dose, Allopurinol, Allopurinol dose, NSAID, Oral nitrates, Nitrate dose, Bronchodilators, Diabetes therapy, Ivabradine, Ivabradine dose, Hydralazine, Hydralazine dose,
DISCHARGE AND REFERRAL[a]
Referral for cardiothoracic surgery, Referral for transplant, Referral to palliative care services

[a] if patient survived to discharge
Core fields are underlined

Table A12: Minimum Data Standard fields collected in the PCI audit

PATIENT DEMOGRAPHICS
NHS number, Birth date, Sex
PRE-PROCEDURE DETAILS
Indication for Intervention, Procedure Urgency, Cardiogenic shock (Pre-procedure), Date/time of symptom onset[a], Date/Time arrival at First hospital[a] , Date/Time arrival at PCI hospital[a]
PROCEDURE DETAILS
Vessels attempted, Date/Time of first balloon inflation[a], PCI Hospital Outcome
PREVIOUS MEDICAL HISTORY
Diabetes, Medical history, History of renal disease
DISCHARGE DETAILS
Status at discharge, Discharge Date

[a] For primary PCI with symptom onset in community only

Table A13: Non Minimum Data Standard fields collected in the PCI audit

PATIENT DEMOGRAPHICS
Patient Ethnic Group, Administrative category, Postcode of usual address
PRE-PROCEDURE DETAILS
Clinical Syndrome (requiring PCI), Indication for intervention, Canadian Cardiovascular Society angina status (Pre-procedure; Stable only), NYHA Dyspnoea Status (Pre-procedure; Stable only), Admission route (ACS only), Presenting ECG (ACS only), Recent Lysis (ACS only), Cardiac Enzymes/Markers Raised, LVEF Category, LVEF, Number grafts present (Pre-operation), Number grafts patent (Pre-operation), Left main stem stenosis (Pre-PCI), Left anterior descending arteries (LAD) proximal stenosis (Pre-PCI), LAD other stenosis (Pre-PCI), Right coronary arteries (RCA) stenosis (Pre-PCI), Circumflex coronary artery (Cx) stenosis (Pre-PCI), Flow in IRA PreOp (ACS only), Ventilated PreOp, Drug therapy PreOp, Date/time of call for help (STEMI only), Referring Hospital, Date/time of ECG triggering primary PCI pathway (only for those developing STEMI while in hospital), Patient location at time of STEMI onset (for patients treated for acute STEMI only), PCI for stent thrombosis
PROCEDURE DETAILS
Date and time of operation, Consultant Responsible for Procedure, Primary Operator, Primary Operator status, Second Operator, Second Operator status, Third Operator, Third Operator status, Number of vessels attempted (not epicardial territories), Number of lesions attempted, Number of Chronic Occlusions attempted, Number Restenoses attempted, Number Instent stenoses attempted, Number Stents used, Number Drug-eluting stents used, Drug(s) eluted by stent(s) (drug based stents), Glycoproteins IIb/IIIa drug(s) used during procedure, Diagnostic device(s) used during procedure, Procedural device(s) used, Athero-thrombus removal device(s) used, Brachytherapy device(s) used, Emboli protection device(s) used, Circulatory support, Arterial management, Local Procedure Identifier, Follow on (Adhoc) procedure, Training procedure, Research procedure, Research title, Arterial access, Largest balloon/stent used, Longest stented / treated segment, Procedural Complication Arterial Complications, Time to bypass, Patient status during transfer to theatre Why no glycoproteins IIb/IIIA during procedure, Indication for stent, Surgical cover, Left Main Stem Protected, Consultant responsible for procedure GMC Number, Primary Operator GMC number Second Operator GMC number, Third Operator GMC number, PCI for stent thrombosis
POST-PROCEDURE DETAILS
Left Main Stem Stenosis (Post PCI), LAD Proximal Stenosis (Post PCI), LAD Other Stenosis (Post PCI), RCA Stenosis (PCI), Cx Stenosis (PCI), Number Lesions Successful, Number coronary grafts patent PostOp, Flow in infarct related artery PostOp (ACS), Operation report/comment, Device failure, Enzymes PostOp, Bleeding up to discharge
PREVIOUS MEDICAL HISTORY
Previous MI, Previous CABG, Previous PCI, Family history of coronary artery disease, Smoking status
INVESTIGATIONS AND INTERVENTIONS
Height, Weight, Cholesterol, Creatinine, Q Wave on ECG, ECG ischaemia
CARDIAC ARREST AND CARDIOGENIC SHOCK
Out Of Hospital Cardiac Arrest, Presumed date / time of arrest, Ventilation, Arterial blood gas on arrival in cath lab: pH, Arterial blood gas on arrival in cath lab: Lactate, Arterial blood gas on arrival in cath lab: Base excess Glasgow Coma Scale on arrival in cath lab, Therapeutic Hypothermia, Other therapeutic hypothermia

Table A14: Mandatory and completeness assessment fields, collected in the NACSA

PATIENT IDENTIFICATION AND DEMOGRAPHICS
Birth Date[a], Sex[a]
CARDIAC HISTORY
Interval between surgery and last MI[a]
PREVIOUS INTERVENTIONS
Previous cardiac surgery[a] , Date of last cardiac operation
ADDITIONAL MEDICAL HISTORY AND RISK FACTORS
Actual creatinine at time of Surgery[a], Renal function/Dialysis[a], History of pulmonary disease[a], History of neurological dysfunction[a], Extracardiac arteriopathy[a], Pre-operative heart rhythm[a]
CARDIAC INVESTIGATIONS
Left ventricular function, Ejection fraction category[a], Pulmonary artery systolic pressure[a]
PRE-OPERATIVE STATUS AND SUPPORT
Intravenous nitrates or any heparin[a], Intravenous inotropes prior to anaesthesia[a], Ventilated (Pre-Operation)[a], Cardiogenic shock (Pre-Operation)[a], Date and time of operation, Operative urgency[a], Number of previous heart operations[a], Responsible consultant surgeon, Responsible consultant Anaesthetist
PROCEDURES CLASSIFIED BY GROUP
CABG[a], Valve[a], Major Aortic[a], Other Cardiac Procedures[a]
OTHER CARDIAC PROCEDURES
Other Actual Cardiac Procedures[a]
VALVE SURGERY
Reason for repeat aortic valve operation[a], Native mitral valve pathology[a], Reason for repeat mitral valve operation[a], Native tricuspid valve pathology[a], Reason for repeat tricuspid valve operation[a], Native pulmonary valve pathology[a], Reason for repeat pulmonary valve operation[a],
CARDIAC SUPPORT DEVICES - PRE-OPERATIVE
Intra-aortic balloon pump used[a], Impeller device used[a], Ventricular assist device used[a], Other support device used[a]
CARDIAC SUPPORT DEVICES - INTRA-OPERATIVE
Intra-aortic balloon pump used[a], Impeller device used[a], Ventricular assist device used[a], Other support device used[a]
CARDIAC SUPPORT DEVICES - POST-OPERATIVE
Intra-aortic balloon pump used[a], Impeller device used[a], Ventricular assist device used[a], Other support device used[a]
CARDIOPULMONARY BYPASS DATA
Height, Weight
POST-OPERATIVE COURSE
Patient Status at discharge, Date of discharge / Date of death in hospital

[a] Fields required for EuroSCORE risk adjustment of mortality estimates

Underlined fields are mandatory

Table A15: Other fields collected in the NACSA

PATIENT IDENTIFICATION AND DEMOGRAPHICS
Hospital Identifier, NHS Number, Local Patient Identifier, Patient Name (Surname), Patient Name (Forename),Postcode Of Usual Address
ADMISSION DETAILS
Admission Date, Administrative Category
CARDIAC HISTORY
Angina status pre-surgery, Dyspnoea status pre-surgery, Number of Previous MIs,
PREVIOUS INTERVENTIONS
Previous PCI , Date of last cardiac operation
RISK FACTORS FOR ACQUISITION OF CORONARY DISEASE
Diabetes management, Cigarette smoking history, History of hypertension

ADDITIONAL MEDICAL HISTORY AND RISK FACTORS

History of neurological disease

CARDIAC INVESTIGATIONS

Left heart catheterisation, Date of last catheterisation, Extent of coronary vessel disease, Left main stem disease, Severity of Aortic Valve Stenosis (EOA in cm^2), Severity of Aortic Valve Stenosis (Gradient mmHg), Category of aortic valve stenosis

PRE-OPERATIVE STATUS AND SUPPORT

First Operator, First operator grade, First operator - Calman year of trainee, First assistant, First assistant grade, First assistant - Calman year of trainee

CORONARY ARTERY SURGERY

Total number of distal coronary anastomoses, Graft Site, Graft Conduit, Graft Anastomosis

VALVE SURGERY

Number of valves replaced/repaired, Aortic valve haemodynamic pathology, Aortic valve type, Native aortic valve pathology, Native aortic valve other pathology, Other reason for repeat aortic valve replacement, Aortic valve procedure, Aortic valve implant type, Aortic implant prosthesis name, Aortic implant prosthesis model, Aortic valve or ring serial number, Aortic valve or ring size (mm), Mitral valve haemodynamic pathology, Mitral valve type, Native mitral valve other pathology, Other reason for repeat mitral valve replacement, Mitral valve procedure, Mitral valve implant type, Mitral implant prosthesis name, Mitral implant prosthesis model, Mitral valve serial number, Mitral valve size, Tricuspid valve haemodynamic pathology, Tricuspid valve type, Native Tricuspid valve other pathology, Other reason for repeat tricuspid valve replacement, Tricuspid valve procedure, Tricuspid valve implant type, Tricuspid implant prosthesis name, Tricuspid implant prosthesis model, Tricuspid valve serial number, Tricuspid valve size, Pulmonary valve haemodynamic pathology, Pulmonary valve type, , Native pulmonary valve other pathology, Other reason for repeat pulmonary valve replacement, Pulmonary valve procedure, Pulmonary valve implant type, Pulmonary implant prosthesis name, Pulmonary implant prosthesis model, Pulmonary valve serial number, Pulmonary valve size

Aorta procedure

Number of aorta segments operated on, Presentation, Aetiology, Aortic pathology - Root Segment Code 1, Aortic pathology - Ascending Segment Code 2, Aortic procedure – Ascending Segment Code 2, Aortic pathology - Arch Segment Code 3, Aortic procedure – Arch, Segment Code 3, Aortic pathology - Descending Aorta Segment Code 4, "Aortic procedure - Descending Aorta, Segment Code 4", Aortic pathology - Abdomninal Segment Code 5, Aortic procedure - Abdominal Segment Code 5, Neuroprotection

CARDIOPULMONARY BYPASS DATA

Cardiopulmonary bypass, Predominant method of myocardial protection, Cardioplegia – Solution, Cardioplegia – Temperature, Cardioplegia - Infusion mode, Cardioplegia – Timing, Non-cardioplegic myocardial protection

CARDIAC SUPPORT DEVICES - PRE-OPERATIVE

Reason for Intra-aortic balloon pump use, Reason for impeller device use, Reason for Ventricular assist device use, Reason for use of Other Support device

CARDIAC SUPPORT DEVICES - INTRA-OPERATIVE

Reason for Intra-aortic balloon pump use, Reason for impeller device use, Reason for Ventricular assist device use, Reason for use of Other Support device

CARDIAC SUPPORT DEVICES - POST-OPERATIVE

Reason for Intra-aortic balloon pump use, Reason for impeller device use, Reason for Ventricular assist device use, Reason for use of Other Support device

CPB DATA

Height, Weight, Cumulative bypass time, Cumulative cross clamp time, Total circulatory arrest time

POST-OPERATIVE COURSE

Return to Theatre, Deep Sternal wound infection, Deep Sternal wound infection treatment, New post-operative neurological dysfunction, New haemofiltration or dialysis post-operatively, Discharge destination from cardiothoracic ward

GRAFT DATA[a]

Anastamosis contructed by (distal and proximal)

AORTIC VALVE PROCEDURE DATA[a]

Aortotomy, Excision of valve, Decalcification of annulus, Implantation of valve, Closure of aortotomy, De-

airing of heart
MITRAL VALVE PROCEDURE DATA[a]
Bi-caval cannulation, Access to mitral valve, Assessment and repair, Excision of valve and annular debridement, Repair of valve, Ring, Implantation of valve, Atrial closure, De-airing of heart
PREPARATION FOR BYPASS[a]
Sterntomy, Thoracotomy, Cannulation, Weaning, Sternal closure, Thoracotomy closure
RISK SCORING[a]
Additive Euroscore, Logistic Euroscore
CONDUIT HARVEST[a]
Left internal mammary artery, Right internal mammary artery, Lesser saphenous vein, Shorter saphenous vein, Radial, Other vein, Other artery, Sub-procedure

[a] Fields that only are required for the trainee dataset, and that are filled in by the trainees.

Table A16: Mandatory fields collected in the MINAP for STEMI

DEMOGRAPHICS
Hospital identifier, NHS number, Patient surname, Patient forename, Date of birth, Sex, Postcode, GP/ PCT code
ADMISSION DETAILS
Initial diagnosis, Procedure performed at the interventional hospital, Date/time of symptom onset, Date/time of call for help, Ambulance Job Number, Date/time arrival at hospital, Admission method, Referring hospital code
REPERFUSION
Initial reperfusion treatment, Electrocardiogram determining treatment, Location of initial reperfusion treatment, Date/time of reperfusion treatment, Delay before treatment, Reason reperfusion treatment not given, Additional reperfusion treatment , Patient location at time of STEMI
EXAMINATIONS
Systolic blood pressure, Heart rate, Killip class
TESTS
Serum glucose, Creatinine, Raised cardiac markers, Peak troponin
PREVIOUS MEDICAL HISTORY
No mandatory fields
DRUG THERAPY
No mandatory fields
DRUG THERAPY AT DISCHARGE
Beta blocker, Angiotensin converting enzyme inhibitor or angiotensin receptor blocker, Statin, Aspirin, Thienopyridine inhibitor, Aldosterone antagonist, Ticagrelor
DIABETES/HYPERGLYCAEMIA MANAGEMENT
In patient management of hyperglycaemia/diabetes
COMPLICATIONS
Death in hospital
CARDIAC ARREST
Cardiac arrest location
INVESTIGATIONS AND INTERVENTIONS
Daycase transfer date, Interventional centre code
DISCHARGE DETAILS
Date of discharge, Discharge diagnosis, Discharge destination
National Institute for Health and Care Excellence (NI) MI CRITERIA
No mandatory fields
INTERVENTIONAL AUDIT[a]
Date/time of arrival at non interventional hospital, Assessment at non interventional hospital, Assessment at interventional centre, Intended reperfusion procedure, Procedure performed, Reason for no angiogram performed, Reason for no intervention performed

[a] only for interventional hospitals

Table A17: Mandatory fields collected in the MINAP for NSTEMI

DEMOGRAPHICS
Hospital identifier, NHS number, Patient surname, Patient forename, Date of birth, Sex, Postcode, GP/ PCT code
ADMISSION DETAILS
Initial diagnosis, Ambulance Job Number, Date/time arrival at hospital, Admission method, Admission ward, Referring hospital code
REPERFUSION
Electrocardiogram determining treatment
EXAMINATIONS
Systolic blood pressure, Heart rate, Killip class
TESTS
Serum glucose, Creatinine raised cardiac markers , Peak troponin
PREVIOUS MEDICAL HISTORY
Smoking status, Diabetes
DRUG THERAPY
Previous statin use, Thienopyridine platelet inhibitor
DRUG THERAPY AT DISCHARGE
Beta blocker, Angiotensin converting enzyme inhibitor or angiotensin receptor blocker, Statin, Aspirin, Thienopyridine inhibitor, Aldosterone antagonist, Ticagrelor
DIABETES/HYPERGLYCAEMIA MANAGEMENT
In patient management of hyperglycaemia/diabetes
COMPLICATIONS
Bleeding complications, Death in hospital
CARDIAC ARREST
Cardiac arrest location
INVESTIGATIONS AND INTERVENTIONS
Coronary angiography, Coronary intervention, Date/time of referral for investigation/intervention, Delay to performance of angiogram, Angio date/time, Local intervention date, Interventional centre code
DISCHARGE DETAILS
Date of discharge, Discharge diagnosis, Cardiological care during admission
NICE MI CRITERIA
No mandatory fields
INTERVENTIONAL AUDIT[a]
Not applicable

[a] only for interventional hospitals

Table A18: Non-mandatory fields collected in the MINAP for STEMI

DEMOGRAPHICS
Patient ethnicity
ADMISSION DETAILS
Date/time of arrival of first responder, Date/time of arrival of ambulance, Admission ward, Admitting consultant, Where was aspirin/other antiplatelet given?, Place first 12 lead electrocardiogram performed
REPERFUSION
Electrocardiogram QRS complex duration, Site of infarction
EXAMINATIONS
Weight, Height
TESTS
Serum cholesterol, Haemoglobin, Troponin assay, Exercise test, Echocardiography, Radionuclide study, Stress echo, Left ventricular ejection fraction
PREVIOUS MEDICAL HISTORY
Previous MI, Previous angina, Hypertension, Hypercholesterolaemia, Peripheral vascular disease, Cerebrovascular disease, Asthma or COPD, Heart failure, Smoking status, Diabetes, Previous PCI, Previous CABG, Family history of CHD
DRUG THERAPY
Previous beta blocker use, Previous angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB),Previous statin use, Previous thienopyridine inhibitor use, Unfractionated heparin, Low molecular weight heparin, Thienopyridine platelet inhibitor, IV 2b/3a agent, IV beta blocker, Oral beta blocker, Calcium channel blocker, IV nitrate, Oral nitrate, Potassium channel modulator, Warfarin, ACEI or ARB, Thiazide diuretic, Loop diuretic, Thrombolytic drug, Aldosterone antagonist, Fondaparinux, Bivalirudin
DRUG THERAPY AT DISCHARGE
All fields mandatory
DIABETES/HYPERGLYCAEMIA MANAGEMENT
Diabetic therapy at discharge, Date/time of start of insulin infusion
COMPLICATIONS
Bleeding complications, Reinfarction
CARDIAC ARREST
Cardiac arrest date/time (first arrest only), Arrest presenting rhythm, Outcome of arrest
INVESTIGATIONS AND INTERVENTIONS
Date of return to referring hospital
DISCHARGE DETAILS
Followed up by, Cardiological care during admission, Cardiac rehabilitation
NICE MI CRITERIA
Smoking cessation advice given, Dietary advice given during this admission
INTERVENTIONAL AUDIT[a]
All fields mandatory

[a] only for interventional hospitals

Table A19: Non-mandatory fields collected in the MINAP for NSTEMI

DEMOGRAPHICS
Patient ethnicity
ADMISSION DETAILS
Date/time of symptom onset, Date/time of call for help, Date/time of arrival of first responder, Date/time of arrival of ambulance, Admitting consultant, Where was aspirin/other antiplatelet given?, Place first 12 lead electrocardiogram performed
REPERFUSION
Electrocardiogram QRS complex duration
EXAMINATIONS
Weight, Height

TESTS
Serum cholesterol, Haemoglobin, Troponin assay, Exercise test, Echocardiography, Radionuclide study, Stress echo, Left ventricular ejection fraction
PREVIOUS MEDICAL HISTORY
Previous MI, Previous angina, Hypertension, Hypercholesterolaemia, Peripheral vascular disease, Cerebrovascular disease, Asthma or COPD, Heart failure, Previous PCI, Previous CABG, Family history of CHD
DRUG THERAPY
Previous beta blocker use, Previous ACEI or ARB, Previous thienopyridine inhibitor use, Unfractionated heparin, Low molecular weight heparin, IV 2b/3a agent, IV beta blocker, Oral beta blocker, Calcium channel blocker, IV nitrate, Oral nitrate, Potassium channel modulator, Warfarin, ACEI or ARB, Thiazide diuretic, Loop diuretic, Aldosterone antagonist, Fondaparinux, Bivalirudin
DRUG THERAPY AT DISCHARGE
All fields mandatory
DIABETES/HYPERGLYCAEMIA MANAGEMENT
Diabetic therapy at discharge, Date/time of start of insulin infusion
COMPLICATIONS
Reinfarction
CARDIAC ARREST
Cardiac arrest date/time (first arrest only), Arrest presenting rhythm, Outcome of arrest
INVESTIGATIONS AND INTERVENTIONS
Daycase transfer date, Date of return to referring hospital
DISCHARGE DETAILS
Discharge destination, Followed up by, Cardiac rehabilitation
NICE MI CRITERIA
Smoking cessation advice given, Dietary advice given during this admission
INTERVENTIONAL AUDIT[a]
Not applicable

[a] only for interventional hospitals

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