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The appropriateness of intention to treat decisions for invasive therapy in coronary artery disease in The Netherlands

Annejet P Meijler, Henk Rigter, Steven J Bernstein, Jan K Scholma, Joseph McDonnell, Arno Breeman, Jacqueline B Kosecoff, Robert H Brook

Abstract

Objective—To determine the appropriateness of intention to treat decisions concerning coronary artery bypass grafting (CABG) and percutaneous transluminal coronary angioplasty (PTCA) for patients with coronary artery disease in The Netherlands.

Design—Prospective study of intention to treat decisions using a computerised expert system.

Setting—“Presentation” sessions in 10 tertiary referral heart centres in 1992.

Patients—3207 consecutive patients: 1618 CABG and 1589 PTCA candidates.

Main outcome measure—Percentage of invasive treatment decisions rated appropriate, uncertain, or inappropriate by the expert system.

Results—PTCA decisions were common for patients with one-vessel disease and CABG decisions for patients with three-vessel and left main disease. PTCA decisions outnumbered CABG decisions in acute myocardial infarction. Of CABG decisions, 84% were rated appropriate, 12% uncertain, and 4% inappropriate. The proportions for PTCA decisions were 39% appropriate, 31% uncertain, and 29% inappropriate. Type C lesion was the main determinant of inappropriateness of PTCA decisions. If type C lesions were downgraded to type A/B lesions the rate of inappropriate PTCA decisions dropped to 6%.

Conclusions—Clinicians in tertiary referral centres in The Netherlands favoured CABG if vessel disease was extensive or involved the left main artery, and PTCA for patients with less extensive disease and with acute myocardial infarction. Few CABG decisions were inappropriate. The main determinant of inappropriateness of PTCA decisions was its intended use in patients with type C lesions.

Methods

Patients and data collection

When the prospective part of DUCAT began, in 1992, 13 heart centres had the exclusive right to perform CABG and PTCA in The Netherlands. Any cardiologist in The Netherlands who has diagnosed coronary artery disease may present information about the patient to an interventional cardiologist or cardiopulmonary surgeon at one of these centres. The presentation, which can occur in person or by letter, fax message, or telephone, eventually leads to an intention to treat decision in favour of CABG, PTCA, or medical treatment. Ten heart centres, five from university and five from non-university hospitals (see appendix), took part in this study, which was approved centrally by the ethics committee of the University Hospital of Rotterdam. Of the remaining three centres (all from university hospitals) two refused to participate because of objections put forward by one or more of their clinicians, while the third was reassembling its specialists’ staff and therefore could not accept the invitation. Enrolment in the study began, depending on the centre, between February and May 1992, with the goal of recruiting a consecutive sample of patients from each centre. Enrolment in each centre was stopped as soon as one quarter of the expected 1992 case...
load of eligible patients had been included in the study. Patients who had previously had CABG (n = 483) or in whom CABG was to be combined with other surgery were excluded. We enrolled 3980 patients. Of these 3647 (92%) had significant coronary artery disease. Significant coronary artery disease was defined by the DUCAT panel as a minimum of 50% narrowing of the left main artery in left main disease, at least one artery with 70% narrowing and other arteries with 50% narrowing in multivessel disease, and one artery with 70% narrowing in one-vessel disease.5

For 1621 patients at the centres (41%) the decision was to recommend CABG, for 1600 (40%) PTCA (any form), and for 757 medical treatment. Information about the decision was missing for two patients. In this paper we focus on the decisions in favour of invasive treatment (n = 3221). For one PTCA and three CABG candidates we failed to collect all the data necessary to determine the appropriateness of the decision and we deleted the 10 cases of “palliative PTCA” for patients with non-cardiac terminal disease. Thus our results pertain to 3207 consecutive patients, 1618 CABG and 1589 PTCA candidates. In two of the 10 centres 10–20% of the sample were missed due to data collection problems. As this incomplete intake did not affect the outcome of any of the analyses, the data from these two centres were not deleted.

On the basis of the indications and definitions provided by the DUCAT panel,5 we designed and pilot tested in six centres a data collection form to capture the data needed to determine the appropriateness of intention to treat decisions. The form had entries for presenting the following: symptoms and problems; level of angina according to the Canadian Cardiovascular Society classification; use of antianginal medication and contraindications for this treatment; degree, type (A, B, or C),5 and location of luminal narrowing in coronary arteries; outcome of exercise stress tests; estimate of left ventricular function; location, date, and type (Q or non-Q) of myocardial infarction; and perioperative risk factors.5 All variables were defined by the DUCAT panel.5 We also collected data on: patients' age; composition of the team of clinicians who made the intention to treat decision; the way the case was presented; medical history including myocardial infarctions and coronary revascularisations; dyspnoea; coronary artery collaterals; and the clinicians' estimate of how urgent revascularisation was needed. Sources for all this information were the angiogram as read by the clinicians of the heart centre, the discussion at the “presentation” sessions, the abstracted medical record submitted by the referring cardiologist, letters and fax messages, and notes taken by centre clinicians.

The data collectors (n = 18) were affiliated with the heart centres; 11 were junior physicians, five were specialised administrative staff, and two were health services researchers. Data collectors were trained in a one day session.

To test for interobserver agreement we asked the data collectors to abstract independently data from six videotaped “presentation” sessions. From their notes we derived the corresponding appropriateness scores and compared these with the scores considered to be correct by DUCAT research team. Cohen's κ was 0·80. To increase data reliability we collected data for two weeks before beginning enrolment, during which time DUCAT staff and data collectors discussed each case. We maintained throughout the study a call-in line to allow data collectors to forward queries to DUCAT staff. We conducted site visits to several centres each week, held plenary meetings of DUCAT staff and data collectors every four to six weeks, and rapidly checked incoming data forms for inconsistencies.

Clinicians from the DUCAT panel were available to reread angiograms from patients from their own centre in those cases (on average less than 2%) where data collectors failed to extract all of the angiographic information from the data sources. To protect the privacy of the patients, completed forms were coded in the heart centres before being relayed to the DUCAT office. Thus patients' identity was not revealed to the DUCAT research team.

**ANALYSIS**

We have described elsewhere how the DUCAT panel rated indications for coronary revascularisation and assigned appropriateness categories (appropriate, uncertain, inappropriate) to indications.6 In brief, an indication was defined to be appropriate if the expected benefits of performing that procedure exceeded the risks compared with another treatment. The 12 panelists, six interventional cardiologists and six cardiopulmonary surgeons, evaluated three sets of indications, presented as a choice between two treatments, namely: (1) CABG v medical treatment, (2) PTCA v medical treatment, and (3) CABG v PTCA. The panelists were instructed to judge the indications assuming that complete revascularisation was to be the goal. Indications were rated on a 9 point scale with 1 representing an extremely inappropriate indication and 9 an extremely appropriate indication. Indications were considered to be appropriate if the appropriateness score (that is, the panel's median rating) was from 7 to 9, uncertain if the score was from 4 to 6, and inappropriate if the score was from 1 to 3. Indications were also classified as uncertain when panelists' ratings were split, that is, when at least four panelists gave a 1–3 rating and at least four others a 7–9 rating.

The appropriateness scores were programmed into the computerised medical review system (MRS), developed by Value Health Sciences (USA). The data were entered into a relational database. Based on their primary symptom or problem, patients were grouped into six mutually exclusive clinical “chapters”: (1) asymptomatic, (2) chronic stable angina, (3) unstable angina, (4) acute myocardial infarction, (5) recent myocardial infarction, between one and 30 days before the first “presentation” session, and (6) near sud-
den death. We assigned an appropriateness score to each intention to treat decision using the relevant items on the data form. Decisions were classified by the MRS as appropriate, uncertain, or inappropriate if they corresponded to indications scored appropriate, uncertain, or inappropriate by the panel. Results are presented as percentages of group totals, with 95% confidence interval (CI). Percentage intervals were calculated with the normal approximation and truncated at 0 and 100.

### Results

#### GENERAL AND CLINICAL CHARACTERISTICS

The median age of the patients selected for invasive treatment was 62 years, and 7% were aged 75 years and older. Seventy four per cent were men. Thirty eight per cent had a history of an old myocardial infarction (> 1 month ago) and 11% had had prior PTCA treatment. Left main vessel disease was present in 9%, three-vessel disease in 33%, two-vessel disease in 28%, one-vessel disease in 29%, and non-significant disease in 2% of the patients. Most patients had chronic stable angina (61%), while unstable angina (19%) and recent myocardial infarction (15%) were also frequently seen. The remainder of the patients were asymptomatic (2%) or presented with acute myocardial infarction (2%) or near sudden death (0-4%). As severity of anatomical disease increased, CAGB decisions became more common than PTCA decisions, which dominated in one-vessel disease (table 1). In most clinical chapters the frequency of CAGB and PTCA decisions was roughly the same. An exception was acute myocardial infarction, where 86% of the decisions were in favour of PTCA (table 2).

### Table 1

**Intention to treat decisions for patients referred for coronary revascularisation in The Netherlands by level of anatomic disease**

<table>
<thead>
<tr>
<th>Anatomical disease</th>
<th>Number of decisions (%)</th>
<th>CAGB</th>
<th>PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-significant coronary artery disease</td>
<td>50</td>
<td>11(22-0)</td>
<td>39(78-0)</td>
</tr>
<tr>
<td>One-vessel, – PLAD</td>
<td>620</td>
<td>21 (3-4)</td>
<td>599 (96-6)</td>
</tr>
<tr>
<td>One-vessel, – PLAD</td>
<td>309</td>
<td>36 (11-7)</td>
<td>273 (88-3)</td>
</tr>
<tr>
<td>Two-vessel, – PLAD</td>
<td>489</td>
<td>142 (29-0)</td>
<td>347 (71-0)</td>
</tr>
<tr>
<td>Two-vessel, + PLAD</td>
<td>404</td>
<td>219 (54-0)</td>
<td>186 (46-0)</td>
</tr>
<tr>
<td>Three-vessel</td>
<td>1046</td>
<td>908 (86-8)</td>
<td>138 (13-2)</td>
</tr>
<tr>
<td>Left main</td>
<td>289</td>
<td>282 (97-6)</td>
<td>7 (2-4)</td>
</tr>
<tr>
<td>Total</td>
<td>3207</td>
<td>1618 (50-5)</td>
<td>1589 (49-5)</td>
</tr>
</tbody>
</table>

Numbers, with row percentages in parentheses. CAGB, coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty; PLAD, posterior left anterior descending artery.

### Table 2

**Intention to treat decisions for patients with coronary artery disease in The Netherlands by clinical chapter**

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Number of decisions (%)</th>
<th>CAGB</th>
<th>PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>68</td>
<td>40 (58-8)</td>
<td>28 (41-2)</td>
</tr>
<tr>
<td>Chronic stable angina</td>
<td>508</td>
<td>1054 (52-4)</td>
<td>891 (45-8)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>608</td>
<td>282 (46-4)</td>
<td>326 (53-6)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>51</td>
<td>7 (13-7)</td>
<td>44 (86-5)</td>
</tr>
<tr>
<td>Recent myocardial infarction</td>
<td>472</td>
<td>214 (49-3)</td>
<td>258 (54-7)</td>
</tr>
<tr>
<td>Near sudden death</td>
<td>13</td>
<td>10 (76-9)</td>
<td>3 (23-1)</td>
</tr>
</tbody>
</table>

Numbers, with row percentages in parentheses. Restricted to decisions for patients with significant coronary artery disease.

### Appropriateness of Decisions

Of the CAGB decisions, 84% were judged appropriate, 12% uncertain, and 4% inappropriate. Inappropriateness was more common for PTCA decisions, of which 39% were classified as appropriate, 31% as uncertain, and 29% as inappropriate. That an intention to treat decision is appropriate does not necessarily mean that the treatment chosen is the best. Panel scores indicated that PTCA was to be preferred in 3% of the appropriate CAGB decisions, but if CAGB and PTCA decisions were both rated appropriate the panel never preferred surgery to angioplasty.

All CAGB decisions for patients with left main disease were classified as appropriate, as were 95% of those for patients with three-vessel disease. In contrast, only one of 21 CAGB decisions for patients with one-vessel disease not including the proximal left anterior descending artery (PLAD) was considered to be appropriate, while 12 of these CAGB decisions were inappropriate. Panel scores indicated that PTCA was judged appropriate for 49% of the patients with one-vessel disease and 33% of the patients with two-vessel disease. PTCA was considered to be inappropriate for 67% of the patients with three-vessel disease and for five out of seven patients with left main disease. Inappropriateness was not only associated with intention to treat, but also with intention not to treat. For instance, of the seven patients with left main disease referred for PTCA, three actually had angioplasty of the left main coronary artery, two (with 50–69% stenosis) of the left main coronary artery underwent PTCA of the PLAD, and in two another type of single vessel PTCA was performed, leaving a 70–99% stenosis of the left main coronary artery untouched.

Appropriateness also varied with clinical chapter (table 3). CAGB decisions were always appropriate for patients with near sudden death, almost always for patients with unstable angina, and less often for asymptomatic patients. The same trend applied to PTCA decisions, although the proportion of appropriate PTCA decisions was smaller than that for CAGB. The proportion of inappropriate PTCA decisions was large for relatively non-acute conditions such as asymptomatic status and chronic stable angina.

### Sensitivity Analysis

The DUCAT panel raised various issues. First, although the use of PTCA was generally judged to be inappropriate by the panel if a type C, rather than a type A or B, lesion was present, some panelists believed that coronary angioplasty might be justified in cases with as yet poorly defined subsets of type C lesions. A second issue discussed by the panel was complete versus incomplete revascularisation. When rating the indications the panel acknowledged that the general goal of PTCA is complete revascularisation, but it also stated that incomplete revascularisation may sometimes be acceptable, for instance when a stenosis has lost its importance because the formation of collaterals has restored the blood flow.
supply or when the myocardial area served by the stenosed vessel is not viable anymore. Finally, during the panel meeting a few panelists were concerned about the definition of two of the variables underlying the indications, that is, “adequate medical therapy” and “significant coronary artery disease”. For all these reasons we performed sensitivity analyses of inappropriate PTCA decisions by assessing the impact of changing assumptions and definitions of clinical variables thought to be important by the DUCAT panel for choosing between treatments for patients with coronary artery disease (table 4).

We began by examining the impact of type C lesions on the rate of inappropriate treatment decisions. Some type C lesions may have a better prognosis than other type C lesions. As our data did not allow a distinction to be made in subsets of type C lesions, we analysed the effect of considering all type C lesions as if they were type A or B. We found that the rate of inappropriate PTCA decisions dropped from 29% to 6%. Distinguishing between type C and type A or B lesions did not affect the rate of inappropriate CABG decisions.

Next, we determined the appropriateness of decisions in relation to the extent of revascularisation the clinicians at the heart centres planned to achieve. We considered two approaches to this issue. The first was to downgrade the number of diseased vessels, for example from three to two if the clinicians elected to treat only two vessels in a patient with three-vessel disease. The panel rejected this analysis plan because the data on benefits and risks are based on total extent of anatomical disease. The second approach, which we followed, was to change lesion type, knowing that the presence of a type C lesion was a major determinant of inappropriateness of PTCA decisions. Clinicians at the heart centres selected incomplete revascularisation for 79% of the patients with multivessel disease. In 7% of these cases the patient had one or more type C lesions that were not considered for coronary angioplasty but still contributed to the outcome “inappropriate” if complete revascularisation was taken to be the goal. We downgraded type C lesions to type A or B lesions solely for the stenoses the clinicians decided to leave untouched. The rate of inappropriate PTCA decisions decreased from 29% to 19%, whereas the rate of inappropriate CABG decisions remained unchanged.

Other changes in assumptions and definitions had less effect on the rate of inappropriate PTCA decisions. We give two examples. One of the variables selected by the DUCAT panel was the extent of medication the patient was receiving at the time of the decision. For patients with chronic stable angina, adequate medical treatment was defined as the use of triple medication (a β blocker, calcium channel blocker, and a nitrate), unless contraindications existed for the administration of medication. However, some believe that treatment with drugs from two out of the three classes may also constitute adequate medical treatment.89 Only 32% of patients with chronic stable angina in our study received triple antianginal medication; another 43% received dual medication. We examined the effect of changing the definition of adequate medical treatment to dual rather than triple medication. The rate of inappropriate PTCA decisions fell from 29% to 25%.

Furthermore, we addressed the issue of non-significant coronary artery disease. We classified invasive treatment decisions for patients with non-significant coronary artery disease as inappropriate. Two DUCAT panelists felt that subliminal lesions (between 50% and 70% narrowing in cases where none of the stenoses produced a narrowing of 70% or more) may occasionally warrant invasive intervention. Because we had recorded any lesion of 50% or more, we could trace subliminal lesions of 50–69% in patients with non-significant coronary artery disease. Thirty five of the 39 PTCA candidates with non-significant coronary artery disease had at least one vessel with such a subliminal lesion. If these cases were considered to have significant disease and then rerated for appropriateness, the rate of inappropriate PTCA decisions was 27.5% rather than 29%.

We then studied what happened to the rate of inappropriate PTCA decisions if we combined the downgrading of all type C lesions to type A or B lesions, the change in definition of adequate medical treatment to dual rather than triple medication and the reclassification of cases with subliminal lesions to significant.

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Table 3  Appropriateness of invasive treatment decisions by clinical chapter

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Appropriate</th>
<th>Inappropriate</th>
<th>Appropriate</th>
<th>Inappropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>70.0 (55.8 to 84.2)</td>
<td>12.5 (2.3 to 22.7)</td>
<td>17.5 (3.7 to 32.1)</td>
<td>57.1 (38.8 to 75.4)</td>
</tr>
<tr>
<td>Chronic stable angina</td>
<td>82.1 (9.8 to 84.4)</td>
<td>4.5 (3.2 to 5.8)</td>
<td>30.2 (27.2 to 33.2)</td>
<td>33.4 (30.3 to 36.5)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>94.3 (91.6 to 97.0)</td>
<td>0.0</td>
<td>75.5 (70.8 to 80.2)</td>
<td>9.8 (6.6 to 13.0)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>85.7 (59.8 to 100.0)</td>
<td>14.3 (0.0 to 40.2)</td>
<td>32.9 (27.2 to 36.0)</td>
<td>18.2 (6.8 to 29.0)</td>
</tr>
<tr>
<td>Recent myocardial infarction</td>
<td>82.2 (77.1 to 87.3)</td>
<td>3.7 (1.2 to 6.2)</td>
<td>39.1 (33.1 to 45.1)</td>
<td>27.9 (22.4 to 33.4)</td>
</tr>
<tr>
<td>Near sudden death</td>
<td>100.0</td>
<td>0.0</td>
<td>66.7 (13.4 to 100.0)</td>
<td>33.3 (0.0 to 86.6)</td>
</tr>
</tbody>
</table>

Table 4  Sensitivity analyses of inappropriate PTCA decisions

<table>
<thead>
<tr>
<th>Change</th>
<th>Fall in rate of inappropriate PTCA decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Type C lesions to type A or B</td>
<td>29.3% to 6.4%</td>
</tr>
<tr>
<td>2 Triple medication to dual medication</td>
<td>29.3% to 25.0%</td>
</tr>
<tr>
<td>3 Cases with non-significant coronary artery disease omitted</td>
<td>29.3% to 27.5%</td>
</tr>
<tr>
<td>All changes combined, in the order indicated</td>
<td>29.3% to 4.0%</td>
</tr>
</tbody>
</table>

PTCA, percutaneous transluminal coronary angioplasty.
The appropriateness of intention to treat decisions for invasive therapy in coronary artery disease in The Netherlands

The rate of inappropriate decisions became 4% (table 4).

Discussion

We prospectively evaluated the appropriateness of intention to treat decisions for invasive treatment of patients with coronary artery disease made in tertiary referral centres in The Netherlands. Of the CABG decisions, 4% were inappropriate, compared with 29% of the PTCA decisions if complete revascularisation was taken to be the goal. PTCA was more often chosen than CABG in cases of one- and two-vessel disease not involving the PLAD. The patient’s primary symptom did not clearly influence which invasive treatment was selected, except for acute myocardial infarction, where PTCA was preferred to CABG.

The rate of inappropriate CABG decisions was low. This is in line with the outcomes of recent retrospective studies in the state of New York and two Canadian provinces, which reported rates of 2–5%.10 11 The appropriateness studies done so far jointly point to a worldwide decrease in the rate of inappropriate use of CABG in the past 10 years.12–15 One reason may be that CABG is mainly used at present in patients with severe coronary artery disease, where CABG has been shown to improve survival. PTCA has replaced CABG for minor coronary artery disease.

For PTCA we found that 29% of the decisions were judged inappropriate, compared with a 4% rate of inappropriate PTCA procedures in the New York State study.16 When comparing appropriateness rates across panels and across countries, one must acknowledge differences in the way the panels were conducted and indications structured. For example, in New York State the expert panel modified their PTCA ratings if they judged CABG more appropriate than PTCA. A PTCA case that was rated uncertain would be downrated to inappropriate if CABG was preferred, thus increasing the rate of inappropriate PTCA indications. This did not occur in The Netherlands. Conversely, the Dutch panel added one more level of clinical detail to those defined in the New York State study, that is, vessel morphology. In general, the DUCAT panel considered type C lesion to be a contraindication for PTCA; the presence of such a lesion was the main determinant of inappropriateness of PTCA decisions. Assuming in the sensitivity analysis that model cases with a type C lesion were identical to cases with type A or B lesions caused the rate of inappropriate PTCA decisions in our study to fall to 6%, only slightly above the rate in New York State. The New York State panel decided not to consider vessel morphology in their ratings of the appropriateness of PTCA. Ultimately, to determine if there is a difference in the appropriateness of use of medical procedures between the United States and The Netherlands will require the application of US panel scores to Dutch cases and Dutch scores to cases from the United States.

Within one year of the meeting of the DUCAT panel, when data collection for our study started, PTCA was regularly tried as treatment for type C lesions in all heart centres in The Netherlands, accounting for the high rate of inappropriate PTCA decisions. This change in treatment policy in The Netherlands reflects a trend in clinical practice that was seen throughout the world.17–20 However, it remains to be seen if attempts to open type C lesions with coronary angioplasty are justified. For instance, the success rate for angioplasty in chronic total occlusions—one subset of type C lesions—is not impressive so far.17–20 The follow up data on the patients enrolled in the DUCAT study may shed light on this issue.

The importance of lesion type illustrates a more general phenomenon, the imperative of anatomy. Intervventional cardiologists seeing a lesion tend to take invasive action. To some extent anatomical disease has replaced functional disease as the guiding principle for revascularisation, at least in the heart centres in The Netherlands.21 One explanation is that tertiary referral centres function as last resort. Clinicians at these centres may assume that non-invasive treatment options have been exhausted for patients referred to their centre. However, at least some of our findings indicate this assumption to be wrong (for example, see the underuse of medication).

Type C lesion was also a factor in decisions about whether or not revascularisation by PTCA was to be complete. Multivariate regression analysis of PTCA decisions pointed to type C lesion as the least important determinant of choosing for incomplete revascularisation.21 After the DUCAT panel was conducted, data were published indicating that complete revascularisation by PTCA is associated with better long term outcomes. However, there are circumstances when incomplete revascularisation is as effective as complete revascularisation. In patients with mild stenoses (that is, between 50% and 59% luminal narrowing) in vessels at least 1·5 mm in diameter that supply under 10% of the myocardium, there is no evidence of a survival benefit with complete compared with incomplete revascularisation.22 DUCAT is the first study to examine which vessels interventional cardiologists felt were important to treat. Follow up of the patients in DUCAT may help to confirm these clinicians’ intuitive sense or to identify lesions that should have been treated.

Finally, how should appropriateness scores be applied? An American practice of using such scores as part of utilisation review before performing the procedure is not advocated in The Netherlands.23 A better application is to use appropriateness scores for the development of clinical practice guidelines to assist clinicians and patients with difficult decisions. The Netherlands Society of Cardiology is using the DUCAT panel to update the appropriateness scores, as a starting point for developing national guidelines, an option supported by the government of The Netherlands.24 Furthermore the DUCAT...
This work was part of the DUCAT study, funded by the National Health Insurance Board (Ziekenfondsenraad) in The Netherlands. The study design was approved by the medical ethics committee of the University Hospital Dijkzigt in Rotterdam. Participating centres were the heart centres of the University hospitals of Amsterdam, Free University, Groningen, Maastricht, and Utrecht, and all five non-university heart centres in The Netherlands: Onze Lieve Vrouwe Gasthuis, Amsterdam; de Klokkeberg, Breda; St. Catharina, Eindhoven; St Antonius, Nieuwegein; and de Weezenlanden, Zwolle.