

# Cost-Effectiveness of Accelerated Perioperative Care and Rehabilitation After Total Hip and Knee Arthroplasty

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**Background:** Accelerated perioperative rehabilitation protocols following total hip and knee arthroplasties are currently being implemented worldwide, but the cost-effectiveness of these protocols from a societal perspective is not known. We compared the cost-effectiveness of an accelerated perioperative care and rehabilitation protocol with that of a more standard protocol for patients treated with total hip and knee arthroplasty.

**Methods:** A cost-effectiveness study was undertaken as a study piggybacked on a randomized clinical trial comparing early outcomes of an accelerated and intensive postoperative rehabilitation regimen with those of a more standard rehabilitation protocol. We assessed eighty-seven patients (forty-two who received the standard protocol and forty-five who received the accelerated protocol) for a total of twelve months. Costs from the time of the patient's visit immediately before the operation to one year postoperatively were calculated with use of activity-based costing analysis. Postoperative quality-adjusted life-years (QALYs) were calculated from validated patient diaries and questionnaires at fifteen time points. The primary objective was to determine whether one intervention was dominant over the other during a twelve-month period or, if neither was dominant, to determine the incremental cost-effectiveness ratio.

**Results:** The result of the randomized clinical trial showed the accelerated intervention to be effective, with a reduction in the length of the hospital stay and a gain in health-related quality of life at the three-month follow-up time point. The cost-effectiveness study showed the accelerated protocol to be significantly less expensive than the standard protocol ( $p = 0.036$ ), with an average reduction in cost of 18,880 Danish kroner (95% confidence interval, 1899 to 38,152) (approximately US \$4000). Patients treated with the accelerated protocol following hip arthroplasty had an additional average gain of 0.08 QALY (95% confidence interval, 0.02 to 0.15) compared with the patients who received the standard protocol ( $p = 0.006$ ); this led to a 98% dominance of the accelerated protocol over the standard protocol. No significant or clinically relevant difference in the numbers of QALYs associated with the two protocols was observed for the patients treated with knee arthroplasty.

**Conclusions:** An accelerated perioperative care and rehabilitation protocol can be both cost-saving and clinically more effective after total hip arthroplasty, whereas it can be cost-saving with no observed significant difference in effect, from a societal perspective, after knee arthroplasty.

**Level of Evidence:** Economic and decision analysis Level I. See Instructions to Authors for a complete description of levels of evidence.

In Denmark, 12,000 total hip and knee arthroplasties are performed each year<sup>1</sup>. The total hospital costs for those procedures were approximately 700 million Danish kroner (DKK) (110 million U.S. dollars) in 2005<sup>2</sup>. New protocols designed to optimize perioperative care and rehabilitation have been given several different names, such as "accelerated in-

**Disclosure:** The authors did not receive any outside funding or grants in support of their research for or preparation of this work. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which the authors, or a member of their immediate families, are affiliated or associated.

tervention” or “clinical pathway.” An accelerated intervention is defined as a multimodal intervention taking place in a multidisciplinary or interdisciplinary organization in order to shorten the time to recovery<sup>3-7</sup>. In contrast, clinical pathways have been implemented in the United States in an effort to reduce the length of the hospital stay and thereby control hospital costs, with less focus placed on consequences for patients and society<sup>8</sup>.

While clinical pathways for hip and knee replacement have been shown to reduce the length of the hospital stay and costs<sup>9</sup>, their major impact is from a hospital perspective. However, to establish the cost-effectiveness of these interventions, they should be assessed from a societal perspective<sup>10</sup>. The efficacy of accelerated perioperative care and interventions has recently been established<sup>11</sup>, but to our knowledge there is no evidence regarding their cost-effectiveness. We therefore investigated, from a societal perspective, the cost-effectiveness of an accelerated perioperative care and rehabilitation intervention, compared with a more standard protocol, following total hip and knee arthroplasty.

### Materials and Methods

A cost-utility study was piggybacked on a randomized clinical trial performed at the Orthopedic Clinic in the Regional Hospital Holstebro, Denmark, from August 2005 to February 2007<sup>11</sup>. The randomized clinical trial was performed to study the effect of accelerated intervention, defined as specialized proactive care and early intensive mobilization and exercise, compared with that of a regimen that was less personalized and less intensive. The randomized clinical trial included eighty-seven patients treated with total hip arthroplasty or with unicompartamental or total knee arthroplasty. The outcome measures of the randomized clinical trial were the length of the stay in the hospital, gain in health-related quality of life from baseline to three months postoperatively, and adverse effects within the first three months postoperatively. The main results of that study were a reduction in the mean length of the hospital stay from eight days (95% confidence interval, 7.1 to 8.4) in the standard-protocol group to five days (95% confidence interval, 4.2 to 5.6) in the accelerated-protocol group ( $p < 0.001$ ). This was accompanied by a larger gain in the health-related quality of life of 0.08 (95% confidence interval, 0.004 to 0.16) in the accelerated-protocol group ( $p = 0.03$ ). No significant or clinically relevant differences in adverse effects were observed.

In the current cost-effectiveness study, we followed all eighty-seven patients for an additional nine months and focused on both costs and cost-effectiveness in the first year postoperatively. The procedures followed in this study were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The study protocol was approved by the Medical Ethics Committee of Ringkøbing and Southern Jutland Counties, and The Danish Data Protection Agency.

### Patients

All patients who were scheduled to undergo elective primary total hip arthroplasty, total knee arthroplasty, or unicompartamental knee arthroplasty at our center were consecutively invited to participate in the study. All patients meeting the inclusion criteria were provided written and oral information about the study at the initial visit, and interested patients gave written consent. The inclusion criteria were a planned elective primary total hip arthroplasty, total knee arthroplasty, or unicompartamental knee arthroplasty. Exclusion criteria were neurological impairment to a degree that the patient could not understand the instructions for participation and a lack of written consent prior to hospitalization.

We determined that a cost saving resulting from a two-day reduction in the length of the hospital stay would be clinically relevant. We performed a power analysis and determined the need for at least forty patients in each group with alpha set at 0.05 and beta set at 0.80. Altogether, 117 patients were eligible for the study (Fig. 1). Twenty-three patients refused to participate, and those twenty-three patients had an average age (and standard deviation) of  $67 \pm 10.4$  years, a female-to-male ratio of 14:9, and a total hip arthroplasty-to-total knee arthroplasty ratio of 10:13. An additional four patients did not meet the inclusion criteria. This left ninety patients for randomization. Forty-five patients were allocated to each group. Three patients in the standard-protocol group (two scheduled to be treated with total hip arthroplasty and one scheduled to be treated with knee arthroplasty) were excluded after randomization. One patient was excluded because the surgery was cancelled as a result of an infection, and two were excluded because they wanted the surgery to be performed outside of the inclusion period. This left eighty-seven patients to receive the allocated intervention. The patients were randomized to either a standard-intervention group or a new accelerated-intervention group by a secretary who was not otherwise involved in the study and who drew an opaque envelope from a box. After randomization, the patients filled in a baseline questionnaire to establish their preoperative health-related quality of life. Other data on patient characteristics were drawn from hospital registers. The patient characteristics of both groups are presented as an electronic appendix.

### Protocol: Both Groups

The patients in both groups were treated with identical surgical and anesthetic procedures according to Danish guidelines, one of which is the use of cemented implants for total hip arthroplasties performed in patients over sixty-five years of age<sup>12,13</sup>. Five experienced surgeons performed all of the operations. Three surgeons performed total hip and total knee arthroplasties at a ratio of 2:1, the fourth surgeon performed only total hip arthroplasties, and the fifth surgeon performed total knee and total hip arthroplasties at a ratio of 9:1. The surgeons were equally represented in both intervention groups. Medications for pain relief were identical in the two groups and consisted of OxyContin or OxyNorm (oxycodone) and paracetamol; Zofran (ondansetron) was used for

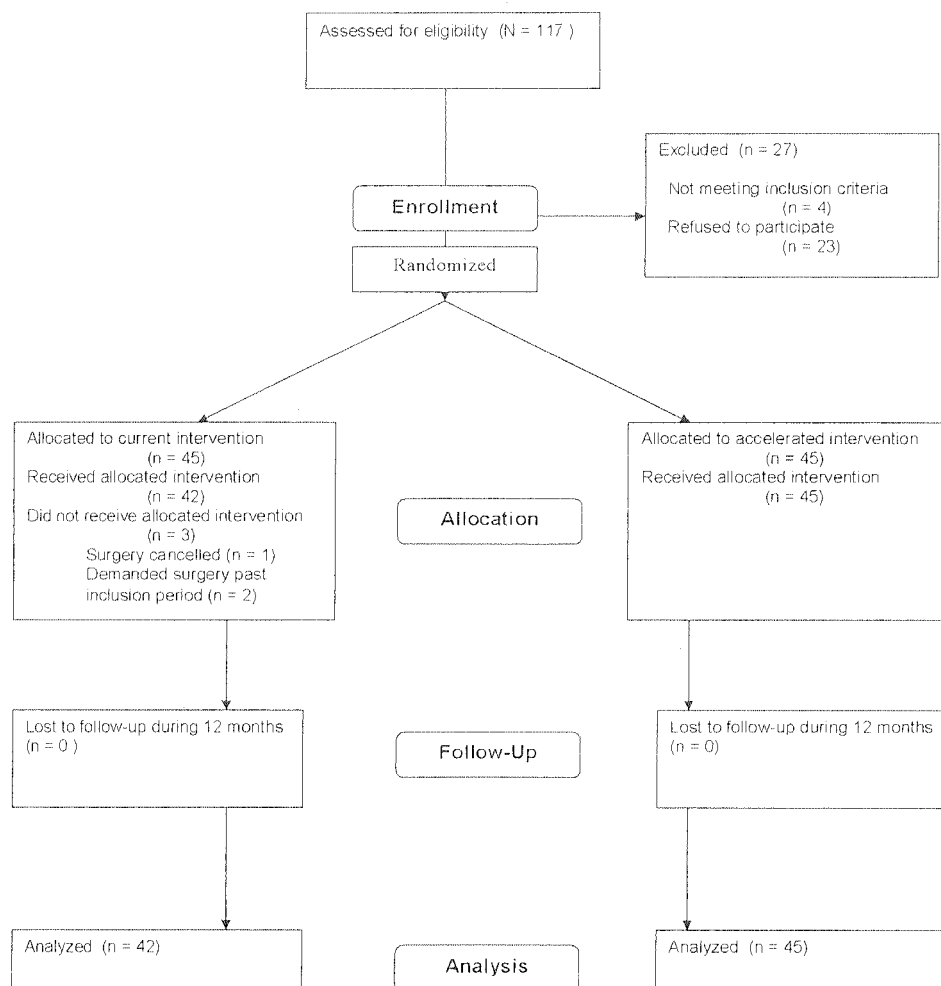


Fig. 1

Flow chart of patients in the two intervention arms.

nausea reduction, and magnesium tablets were given for bowel regulation.

The standard and accelerated protocols are summarized in Table I. A detailed description of the accelerated protocol has been published previously<sup>14</sup>.

### Discharge

All patients were discharged to home. The discharge criteria were the same for both groups: absence of any signs of wound problems; the patient's willingness to be discharged; satisfactory pain control; awareness of procedures for safely discontinuing the use of medication; knowledge of restrictions; the ability to walk safely with or without walking aids, to walk up and down stairs, and to perform home exercises; knowing how to increase home exercises; the ability to perform personal care; and, in the group treated with knee arthroplasty, achievement of at least 90° of knee flexion. Surgeons who were not otherwise involved in the study determined, in agreement with the patients, when the discharge criteria were fulfilled; no patient asked to postpone discharge after having fulfilled the other discharge criteria.

### Attempts to Reduce Bias in the Study

The standard-protocol patient group and health-care staff were separated from the accelerated-protocol patient group and health-care staff during the study period, and the health-care staffs were not allowed to discuss the interventions with each other. Two newly employed therapists, a physiotherapist and an occupational therapist, blinded to the standard protocol were mainly responsible for the rehabilitation in the accelerated-protocol group. Health-care personnel carrying out the standard protocol were not aware of the procedures in the accelerated-protocol group. Because the length of the hospital stay was related to both the intervention and the outcome, surgeons who were not otherwise involved in the study decided when the discharge criteria were fulfilled. We used validated questionnaires<sup>15</sup>, diaries<sup>16</sup>, and registers<sup>17</sup> for all data collection.

### Economic Evaluation

The analysis was based on a societal perspective, and the time frame was fixed to one year per patient. The analysis was a marginal analysis (investigating only areas that were different). The cost-effectiveness of the accelerated intervention was esti-

**TABLE I Protocols for Standard and Accelerated Interventions for Eighty-seven Patients Treated with Total Hip or Knee Arthroplasty in Denmark from 2005 to 2006**

Standard-Protocol Group	Accelerated-Protocol Group
Information given separately to each individual patient on the day of admission	Patients receive information in groups at an outpatient clinic visit prior to hospitalization
Hospitalization on the day before surgery	Hospitalization on the day of surgery
Patients treated with arthroplasty placed randomly among other patients	All patients treated with arthroplasty placed together in one separate part of the ward
Various nurses in charge of care, and various occupational therapists and physiotherapists responsible for mobilization	One nurse in charge of a multidisciplinary team of nurses, occupational therapists, and physiotherapists
Nutrition screening	Nutrition screening and special focus on daily consumption of 1.5 L of fluid, including two protein beverages
Mobilization and exercise started on the first postoperative day	Mobilization and exercise started on the day of surgery
Individual and gradual mobilization according to the patient's tolerance	Intensive mobilization of patients in teams after preset daily goals
Four hours of mobilization daily	Eight hours of mobilization daily
No difference in operating theater	
No difference in pain relief, nausea control, or bowel regulation	

mated by relating the incremental cost of the two interventions to the incremental effect, in quality-adjusted life-years (QALYs), of the two interventions. The resulting incremental cost-effectiveness ratio represents the cost per QALY gained in a cost-utility analysis<sup>10</sup>. In cases where the new intervention was both less costly and more effective, an estimate of the percent dominance was obtained from a bootstrap simulation. The uncertainty of the incremental cost-effectiveness ratio was also estimated by using bootstrap simulation. A bootstrap simulation is a non-parametric method in which a random sample of the same size as the original sample is drawn several times with replacement from the original data. The results of the bootstrap sampling are

presented in a cost-effectiveness plane. The cost-effectiveness plane is constructed from the crossing of the x axis and the y axis. Incremental effect is plotted on the x axis and incremental cost, on the y axis. The four resulting quadrants represent the potential outcomes in terms of cost and effect. In the upper right quadrant, the new intervention is more effective but also more costly than the comparator; in the lower right quadrant, it is more effective and less costly; in the lower left quadrant, it is less effective and less costly; and in the upper left quadrant, it is less effective and more costly<sup>10</sup>. A cost of DKK 160,000 per QALY gained<sup>18</sup>, a cost saving of at least DKK 1000 with no significant or clinically relevant difference in health-related quality of life, or a

**TABLE II Incremental Costs\*, Derived with Univariate and Multivariate Analyses, Between Standard and Accelerated-Intervention Groups Treated with Total Hip Arthroplasty or with Total or Unicompartamental Knee Arthroplasty**

Analysis	Stratified Analysis					
	Crude Analysis (All Patients; N = 87)		Total Hip Arthroplasty (N = 56)		Total or Unicompartamental Knee Arthroplasty (N = 31)	
	Incremental Cost (95% Confidence Interval†) (DKK‡)	P Value§	Incremental Cost (95% Confidence Interval†) (DKK‡)	P Value§	Incremental Cost (95% Confidence Interval†) (DKK‡)	P Value§
Univariate	-18,880 (-1899 to -38,152)	0.036				
Multivariate#	-18,086 (-7002 to -34,834)	0.004	-14,925 (-669 to -28,576)	0.029	-27,258 (-650 to -78,739)	0.083

\*Ordinary least square regression. Cost estimate A (total average costs) was used in the analyses. †The 95% confidence interval was derived from a bootstrap of 2000 replicates. ‡Five Danish kroner (DKK) approximately correspond to one U.S. dollar. §Tested with the nonparametric percentile method. #In the multivariate analysis, incremental cost was adjusted for any preoperative primary-care cost, health-related quality of life at baseline, sex, age, a diagnosis of osteoarthritis or not, a cemented implant or not, whether the patient was employed or not, and whether a hip or knee arthroplasty was performed.

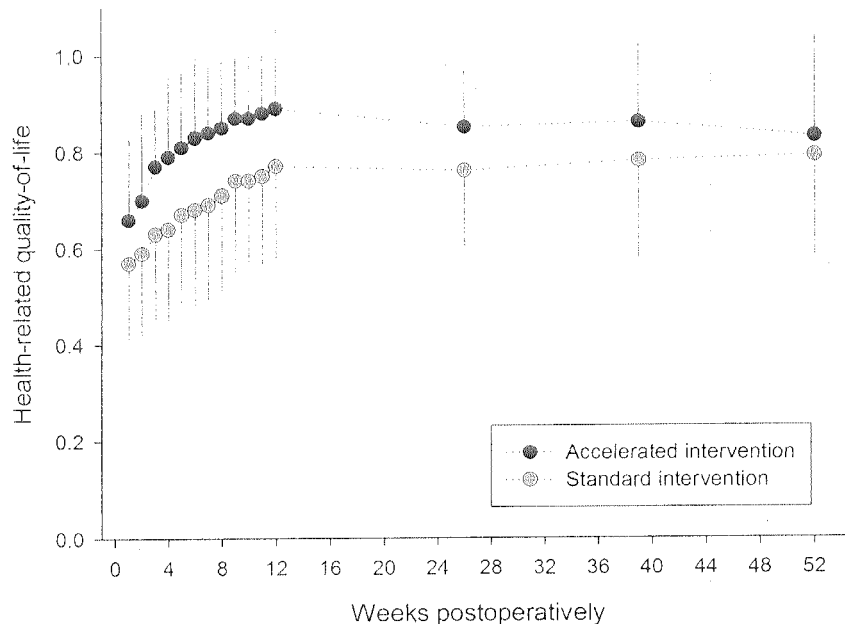


Fig. 2  
Mean health-related quality-of-life scores, with standard deviations, measured at fifteen postoperative time points, for fifty-six patients treated with primary total hip arthroplasty followed by either the accelerated or the standard intervention.

gain in health-related quality of life of at least 0.05 with no significant or clinically relevant difference in cost was considered sufficient for a decision of implementation.

#### Costs

The primary cost estimate was the average total cost (cost estimate A). Postoperative productivity loss was calculated with a maximum of three months of absence from paid work (friction cost method)<sup>19</sup>. We obtained all costs for medical care, medication, and physiotherapy during the twelve weeks prior to hospitalization from a regional register<sup>17</sup> in order to adjust the postoperative costs for preoperative costs. We started estimation of costs on the information day (the day of the patient's visit to receive information about the protocol and for consultation with the surgeon, anesthetist, and nurse), four days before the surgery, for the accelerated-intervention group and on the day of admission, which was the day before the surgery, for the standard-intervention group. Time ended at the one-year follow-up visit, at which a questionnaire was used. We estimated the total costs at the patient level using a mix of activity-based costing analysis (time studies) and the step-down method of allocation of overhead costs to all departments involved in the patient's care up to the final department (the orthopaedic ward). To cover the perioperative and postoperative patient path, we defined seven cost activity centers: (1) information day, (2) boarding of the patient at the hospital, (3) care in the hospital, (4) rehabilitation in the hospital, (5) patient needs (e.g., nonprescription medication, home changes, and transportation) in the follow-up period, (6) primary care in the follow-up period, and (7) hospital

readmission in the follow-up period. The total average costs in the seven activity centers were calculated by multiplying the observed volumes of health care by the unit prices. Information-day activities were identified by means of observation and time registration and were validated by health-care staff. The costs of boarding the patient at the hospital were calculated on the basis of data from the hospital central accounting system with use of a step-down allocation of overhead costs to all departments involved in the patient's care up to the final department and by finally estimating a daily hospital-board cost. Care and rehabilitation activities in the hospital were identified by means of observation and time registration and were validated by health-care staff. Patient needs and primary care in the follow-up period were identified from standardized and validated patient diaries<sup>16</sup> and questionnaires<sup>15</sup> and were validated against the hospital patient administrative system and from a register of primary care data in a closed database on the Internet<sup>17</sup>. The register of primary care data holds data on all medical care consultations, prescribed medication, and physiotherapy consultations<sup>18</sup>. The patient diary was handed out on the day of discharge and consisted of a cost questionnaire, to be filled in weekly, regarding all relevant post-hospitalization costs over twelve weeks. The patients brought the diary to the three-month inpatient visit. If they failed to bring the diary or it was incomplete, the patients filled in a retrospective questionnaire or data were obtained by use of the register of primary care data<sup>17</sup>. Cost questionnaires were sent to the patients on the twenty-sixth, thirty-ninth, and fifty-second weeks. If there was a delay in the return of a questionnaire, a new questionnaire was sent, and if that questionnaire was not returned, data were

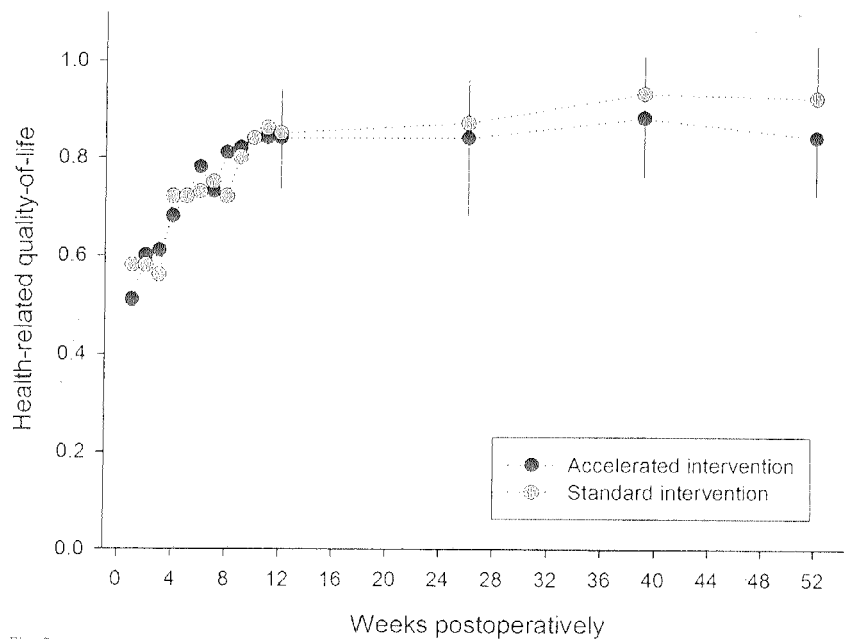


Fig. 3  
Mean health-related quality-of-life scores, with standard deviations, measured at fifteen postoperative time points, for thirty-one patients treated with primary total knee arthroplasty or unicompartmental knee arthroplasty followed by either the accelerated or the standard intervention.

obtained from the register of primary care data<sup>17</sup>. All postoperative patient and primary-care costs were therefore collected for a total of twelve months. Finally, hospital readmissions in the period from discharge to three months after discharge were identified on the basis of data from the hospital patient administrative system.

Preoperative and perioperative cost data were available for all patients. Eight patients (three treated with total hip arthroplasty and two treated with total knee arthroplasty followed by the standard intervention, and two treated with total hip arthroplasty and one treated with total knee arthroplasty followed by the accelerated intervention) did not submit a postoperative diary, and three patients (two treated with total hip arthroplasty followed by the standard intervention and one treated with total hip arthroplasty followed by the accelerated intervention) did not complete any of the postoperative questionnaires. However, data for these patients were obtained with retrospective questionnaires and from the register of primary care data<sup>17</sup>.

#### Unit Costs

Unit costs were obtained from the central Danish hospital employee register<sup>20</sup>, the register of primary care data<sup>17</sup>, Stat-Bank Denmark<sup>21</sup>, the Dutch Manual for Costing in Economic Evaluations 2002<sup>22</sup>, and patient reporting. The average number of effective working hours was calculated to be 1516 hours by using actual hospital wage and employee data. Costs in activity centers 1 through 4 were calculated in 2005 prices and transformed to 2006 prices after adjusting for inflation. Costs in activity centers 5, 6, and 7 were calculated with use of 2006

prices. Productivity loss for patients engaged in active employment was calculated by using an average wage rate for the age-specific group, while productivity loss for patients not engaged in active employment was calculated with use of the proposed tariff in the Dutch Manual for Costing in Economic Evaluations<sup>22</sup>, after adjusting for inflation.

#### Effects

The effect of the accelerated intervention was determined by using a standardized questionnaire for the measurement of health outcome, the EuroQOL-5D (EQ-5D)<sup>15</sup>. The EQ-5D measures health-related quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression)<sup>15</sup>. The EQ-5D questionnaire was included in the patient diary and was filled in at baseline and then weekly from the first to twelfth week postoperatively. It was also completed at twenty-six, thirty-nine, and fifty-two weeks postoperatively. If return of a questionnaire was delayed, a new questionnaire was sent, and if that questionnaire was not returned, we contacted the patients by telephone at fifty-two weeks. Health-related quality-of-life scores were calculated with use of the "Official Danish Time Trade-Off Scores."<sup>23</sup> The effect in terms of QALYs was calculated by using the fifteen measurement points postoperatively and employing the area-under-the-curve method with the trapezoid rule<sup>24</sup>. These effect data were available for all patients at baseline and at three and twelve months postoperatively, with the exception of the twelve-month follow-up data for one patient, who could not be reached by mail or telephone.

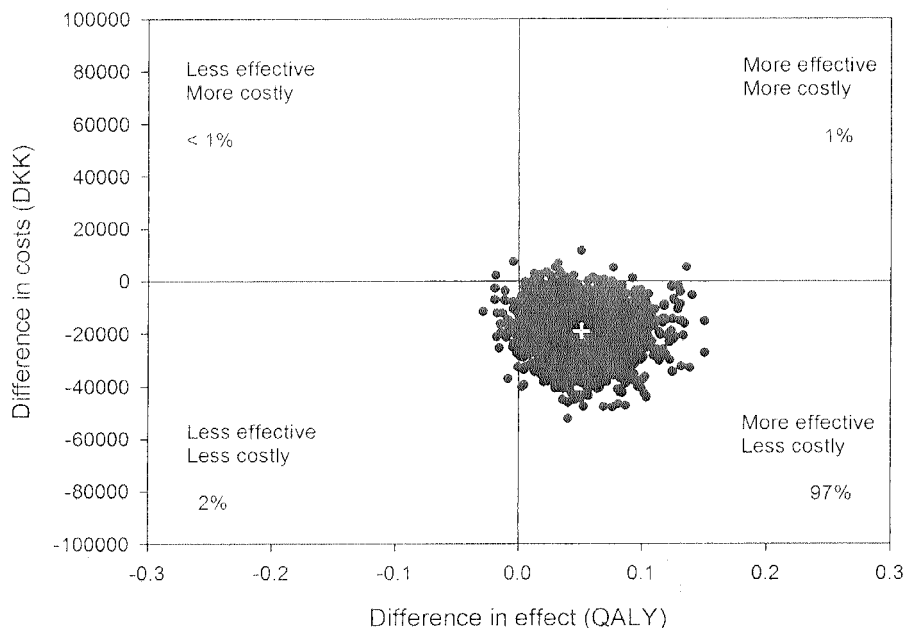


Fig. 4  
Cost-effectiveness plane with incremental cost-effectiveness ratio (plus sign) and uncertainty around the incremental cost-effectiveness ratio from 2000 bootstrap replicates in a univariate crude analysis of the eighty-seven patients treated with primary hip or knee arthroplasty.

### Statistical Methods

The primary analysis was a univariate analysis of incremental cost and effects. It was used because of the expectation of some degree of non-normality of the data, estimated by employing a nonparametric bootstrap procedure with 2000 bias-corrected bootstrap replicates of the arithmetic mean. Missing values resulting from incompleteness of data were, in accordance with the method described by Brunenberg et al.<sup>25</sup>, replaced with the mean value for the group in the univariate analysis of health-related quality of life and with regression imputation in the multivariate analysis. A total of 1.2% of the data points were imputed. The significance level was set at  $p < 0.05$  and tested with the nonparametric percentile method<sup>24</sup>.

### Uncertainty of Results Due to Choice of Model and Cost Estimate

#### Different Analysis Models

We performed multivariate analyses of incremental costs because this method can be superior to univariate analysis as a result of its ability to explain variation due to other causes<sup>24</sup>. Primary multivariate analysis of incremental costs (cost estimate A) and effects was performed by using ordinary least-square regression with 2000 bias-corrected and accelerated replicates of the incremental difference. We also performed secondary multivariate analyses of incremental costs with generalized linear models because these models seem to be ideal for handling the mean and variance functions on the original scale of skewed cost data<sup>24,26</sup>. Generalized linear model analyses were performed with a log link function and the following families: Gaussian, Poisson, Gamma, and inverse Gaussian/Wald. We

report only the generalized linear model link functions and families that passed all of the following tests: skewness/kurtosis test, heteroskedasticity test (Breusch-Pagan test), modified Park test (generalized linear models family test), Pregibon link test, modified Hosmer-Lemeshow test, and Pearson correlation test<sup>24</sup>. Differences between treatment groups were tested by using the nonparametric percentile method<sup>24</sup>. In the multivariate analyses, incremental cost was adjusted for any preoperative primary-care cost, health-related quality of life at baseline, sex, age, a diagnosis of osteoarthritis or not, a cemented implant or not, whether the patient was employed or not, and whether a hip or knee arthroplasty was performed. In the multivariate analyses of incremental effect, we adjusted for health-related quality of life at baseline together with sex, age, a diagnosis of osteoarthritis or not, a cemented implant or not, and whether a hip or knee arthroplasty was performed.

#### Different Cost Estimates

Analyses with an additional three cost estimates (cost estimates B, C, and D) were carried out to enhance the transferability of costs in different areas within or outside the hospital and to evaluate their consequences for the conclusion. Cost estimate B was the total average cost with exclusion of the average costs of hospital readmissions in the follow-up period and was estimated because our results could be heavily affected by some fortuitous readmissions in one of the randomization arms. Cost estimate C was the total average cost with exclusion of the average productivity loss and was estimated because productivity loss is considered to be a separate cost group<sup>22</sup>. Cost estimate D was the total average cost with exclusion of both the

