# Risk adjustment in coronary bypass grafting: how EuroSCORE is related to cost, health related quality of life, and cost-effectiveness.

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# ABSTRACT

The aim of this study was to evaluate how EuroSCORE predicts short and long term cost and outcomes of CABG patients. We analysed the predictive power of EuroSCORE on various cost and outcome measures and evaluated which factors - in addition to the original EuroSCORE - affected the measures. We evaluated how patients' risk scores affected QALYs gained and cost per QALY gained. We assessed also the bias in cost and QALY estimates that are due to the fact that HRQoL information is usually available for specific patients that do not represent the total patient population.

We studied prospectively first-time consecutive coronary bypass patients operated in Helsinki University Hospital between 09122000 -21122001. The patient level risk score data was collected preoperatively from almost every patient. HRQoL was measured with 15D. It is a generic, standardized, self administrated instrument that can be used both as a profile and as a single index score measure. The patient level cost data on surgery hospital admission was based on cost accounting system of Helsinki University Hospital, which is derived "bottom-up approach" and is as such very accurate. In addition, with unique identification numbers various register data were linked in the data base. This allows us to follow patients for five years.

We evaluated the performance of the risk system using various multivariate analysis methods. Since our analysis is based before and after comparison many important assumptions should be made in order to evaluate the incremental cost effectiveness (CE) ratio (=Δ cost/ Δ QALY). Thus we calculated CE ratio by five cost and two QALY specifications.

According to the results EuroSCORE associated quite well with costs, various mortality indicators and life expectancy but not with HRQoL. In addition variables included in EuroSCORE, also pervious year cost and diabetes were significant additional "risk factors". We found that change in HRQoL was heavily dependent on preoperative HRQoL status. CE ratio was crucially depending on measurement of QALYs and specially on the assumptions on the effects of treatment on life expectancy. If the operation affects more on life expectancy of high risk patients than low risk patients, the cost per QALY difference between EuroSCORE groups will convergence. The cost per QALY figures derived from selected samples will overestimate positive results.


Keywords: Bypass surgery, EuroSCORE, Cost, HRQoL, QALY

## Introduction

Meaningful comparison within health care require risk adjustment -accounting for patient associated factors before comparing health care spending, resource utilisation across different patients, treatments, providers, regions, countries or populations. In addition, risk stratification models can be used to estimate need for resources, proper informed consent and quality monitoring. During the last decades several models to calculate mortality risk before the surgery have been developed. For heart surgery, several studies have indicated that EuroSCORE[1] (the European System for Cardiac Operative Risk Evaluation (1,2) ) performs better than other commonly used preoperative risk scores (3) . During the recent years EuroSCORE has been routinely been used in many countries. For example, since 2006 in Great Britain cardiac surgical results (adjusted using EuroSCORE) for individual surgical units and some cases for surgeons have been published on web. In Finland, since 2005 the collection of EuroSCORE for CABG patients has been included in the National discharge register.

EUROscore was originally developed using multinational database of 19 030 patients between the years 1995 and 1999. The 30 day mortality was as an outcome measure. Later several studies had analysed predictive power of EuroSCORE on cost and length of stay of surgery as well as specific postoperative complications(4,5). However, very seldom the risk factors have been evaluated with respect health related quality of life (HRQoL) (6,7) (8).

It has been increasingly recognised that measures of health outcomes should take in account both reduced mortality (i.e. increase of life expectancy) and quality aspects of life. This can be done by evaluating interventions in terms of QALYs (Quality-adjusted life years) gained, which combines within a single measure both changes in quantity and quality of life. In order to calculate QALYs we need to know the effects in terms of HRQoLs. So far, the data on HRQoL are not routinely available, although the feasibility of such data collection has been indicated (9). However, in future this may change since some countries have started to collect such data (10,11)

The main aim of this study is to evaluate how EuroSCORE predicts short and long term costs and outcomes of CABG patients. Firstly, we analyse the predictive power of EuroSCORE on various cost and outcome measures and evaluate which factors - in addition to the original EuroSCORE - affect the measures. Secondly, we evaluate how patients risk score affects QALYs gained and cost per QALY gained. We assess also the bias in cost and QALY estimates that are due to the fact that HRQoL information is usually available only for specific patients that do not necessarily represent the total patient population.

## Material

First-time consecutive 0912200-12212001 coronary by pass patients operated in Helsinki University Hospital were studied prospectively. The patient level risk score data was collected preoperatively from almost every patient. In addition, other data (such as length of hospital stay and ICU length of stay) were collected postoperatively.

[1] The scoring system identifies three group of risk factors (patient-related, cardiac and operation related) with their weights (additive % predicted mortality) see ( http://www.euroscore.org/)

HRQoL was measured with 15D. It is a generic, standardized, self administrated instrument that can be used both as a profile and single index score measure. It includes 15 dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity) (12-14). The valuation system of the 15D is based on an application of the multiattribute utility theory. A set of utility or preference weights, elicited from the general public through a valuation procedure is used in an additive aggregation formula to generate the 15-D score (single index number) over all the dimensions. The maximum score is 1 (no problems on any dimensions) and the minimum score is 0 (being dead). A change of $\geq 0.03$ in 15D was interpreted as minimum clinically significant change.

A questionnaire including on demographic information (family back ground, education) and 15D questionnaire was given to before the operation to for every patient. The 15D questionnaire was mailed also three months and one year after the surgery to the patients. The later questionnaire includes also questions concerning use and cost of health care services after the surgery. In addition, various register data were linked in the data base with unique identification numbers. This allows following patients five years. The register data included data on hospital discharge register, Finnish Death register, registers of Social Insurance Institute and data from the Finnish Hospital Benchmarking project. Using this data costs of hospital care (all inpatient care, outpatient visits of specialist hospital care) and costs of prescribed medicines by the previous year and subsequent five years after the operation were calculated.

Our data included also other risk score systems (Cleveland (15), Northern New England(16) , CABDEAL (17), but EuroSCORE performed against cost and outcome indicators either better or at least equivalently as the others.

The patient level cost data on surgery at hospital admission was based on cost accounting system of HUS, which is derived "bottom-up approach" and is as such very accurate. The utilisation information of (other than surgery admission) hospital inpatient care was converted into costs using Finnish standard costs for different types of health care services (18). The somatic and other acute hospital inpatient admissions were first grouped according to the Finnish version of the NordDRG i.e. Nordic Diagnosis Related Groups. Each admission was then converted into costs using average costs per inpatient day specific to each DRG groups. The outpatient visits in tertiary hospitals were converted using average cost per visits specific to each speciality and type (emergency /elective) of visit. All costs were converted to 2001 prices using the municipal health care price index. The costs of prescribed medicines were based on information on actual reimbursement at prevailing prices. Since questionnaire included information on cost and utilisation after one year of operation, we were able to estimate those cost that were not included in registries.

We analysed the cost of i) surgery admission; ii) whole first hospitalisation; iii) first year and ;iv) five years. Outcome was analysed by mortality indices and by survival of five years and change in HRQoL score between before and after operation.

Figure 1 describes the total number of CABG patients in study period and the data used in this study. The main analysis was performed using the whole sample (n=925) which includes all patients of whom we had register data well as preoperative risk data. The HRQoL data include all 606 patients of whom we had preoperative 15D scores and scores after three months or patients died within three months. The HRQoL data was clearly selected (Table 1). This was verified by a logit regression using the "whole sample" on the probability to be included in HRQoL sample. It indicated that in HRQoL sample costs, 5 year mortality, EuroSCORE status (EuroSCORE 7 or over) and the share of females was lower compared to whole sample.

Table 1 and Figure 1 about here

# Methods

## Performance of EuroSCORE

The performance of the risk system was evaluated using various multivariate analysis methods. The analysis was started by including risk score into model as bivariate dummy variables and as a one continuous variable. Since the continuous specification performed in most cases better the modelling was extended using this specification. In the modelling of cost two extensions for the models was made. Firstly, two measures of mortality in model were included. The first was a dummy variable for death in the follow-up period, which reflects the fact that cost of those patients died in surgery are higher than those survived and more generally that cost of health care are concentrated to proximity to death (19,20). The second variable described the survival time and takes into account that cost are higher for those who lived longer. It is included in the estimation of five years costs.

In the second extensions also other significant potential risk variables were included. As potential risk variables two clinical factors that are excluded from EuroSCORE model were considered: diabetes with insulin and a body mass index (BMI). BMI was specified in two alternative ways: 28-30 and over 30. However, BMI does not become significant in any models and thus it is not reported in tables. In addition, total health care cost (hospital care and prescribed medicines) of the previous year was treated as a potential risk variable, since the variable has in many studies found to be a good predictor for current cost (21). It may take into account more widely all cost related to co-morbidity than the specific clinical factors included in the EuroSCORE measure.

Cost variation was modelled using a generalised linear model (GLM, gamma distribution with log link). GLM was compared with a traditional OLS by calculating the mean square error (MSE) for comparing the predictive power of the alternative specifications. The comparison was made using EuroSCORE as a continuous variable. In all cases MSE criterion favours GLM over OLS. The better performance of GLM was most clear in one and five year costs. In tables marginal effects are reported since they are more informative than coefficients of a GLM model. The predictive accuracy was measured in terms of $R^2$ and mean absolute error (MAD) (22)[2]. The latter is single summary measure of predictive accuracy that does not square the prediction errors and so, is not sensitive to large costs. The smaller the prediction error the better the model is performing. However, it is not expressed on a standardised scale, so comparison across studies is not possible.

The evaluation of risk score system on survival was done in a similar way as costs. Survival was analysed using cox-regression. The predictive power was measured by the area under the receiver

[2] MAD =(Σ| $c_i$-^$c_i$| )/n, where $c_i$ is actual cost for patient i, ^c predicted cost for patient i and n is sample size. The "deviation" in MAD denotes the sane quantity as "error " in phrase "mean squared error " (MSE) and the measures are related:MAD ~=0.8*MSE (32)

operator characteristics (ROC) curve after logit regression on 30 day, 90 day, one year and 5 year mortality. The discriminative power of ROC curve is excellent if the area is >0.80, very good if >0.75 and good if >0.70. In addition the calibration of the logit models were assessed by the Hosmer-Lemeshow goodness of fit statistics. For the test, the predicted risk of an individual patient was rank-ordered into 9 [3]groups of equal size, based on their predicted probability. A p>0.05 indicates acceptable calibration of the model.

The analysis of change in 15D was made applying traditional OLS.

## *Cost of QALY gained*

The cost effectiveness analysis (CE) aims to evaluate the incremental ratio:

CE=$\Delta$ cost/ $\Delta$ QALY

Since our analysis is based on before and after comparisons many important assumptions should be made. For measuring costs we need to define how to measure the change in cost due to operation. Usually only the cost of operation is used as a measure. However, a significant amount of patients has transferred to another department in the hospital or even to another hospital for further rehabilitation (at the end of surgery admission), and it can be justified that also this should be included in the analysis. In addition, one can argue, that at least a considerable part of other cost during the first year after the surgery must be included in the costs due to operation. But the inclusion of the later years health care cost is not so straightforward. There is no consensus among economic analysts about whether survivors' medical costs should be included in analysis (23-25). The question is more problematic in a non randomised study in which there are no way to separate what part of cost and QALY development is due to the operation. Metzler has made a strong case for including future cost in economic evaluation particularly, if an intervention increases length of life (26). It is customary subtracts any medical savings that are due to effectiveness in treating the original disease. Nyman 2004 argues that inclusion of unrelated medical care (i.e. care to treat an other disease) should be included in the numerator only when the utility from the survival medical care is included in nominator (25).

In this study the medical costs of following four years (i.e. the costs of second, third, forth and fifth year after operation) were treated by two alternative ways. Firstly, they were included totally. This can be seen as a maximum cost and is based on assumption that all patients have been died if the operation has not been performed. In the second alternative tries to take into account the fact that operation may reduce future treatment cost. This calculation is based on the difference in annual cost of the four following years against pervious year costs before operation. Thus it is assumed that without treatment the cost has been the same as they were one year before the operation. This calculation is based on assumption that operation has not affected to survival.

Figure 2 about here

Also measurement of QALY gains need several assumptions which can be illustrated by Figure 2 adapted from Williams 1985 and Castelli 2007 (27,28). It plots an individual's health status,

[3] It is recommended that 10 groups will be the best possible amount of groups. However, in this case only 9 equal size risk groups could be formed.

measured on the vertical axis using a scale where 1 indicates full health and 0 deaths, against time. The health stream without operation is the lowest curve h(ng) with patient dying at time $t^0$ . At time t operation is performed. Treatment initially reduces health but health soon improves health and life is extended to $t^g$ as described in the highest curve H(g). There is a risk that treatment will kill the patient before he is able to enjoy the improvement associated with treatment. Hence the expected health stream, conditional on surviving treatment, is shown by dotted line ah(g) .Usually in before and after comparisons it is assumed that the difference in HRQoL after and before the treatment will prevail the rest of life. It is thus assumed that the treatment do not affect to life expectancy (life expectancy will be $t^0$ in figure 2). If the treatment increases life expectancy the assumption underestimates the QALY gains (the area under H (g) curve from $t^0$ to $t^g$). The value of this area depends on the difference of the life expectancies between patients operated and not operated. If treatment is lifesaving (i.e. all patients will died very soon if they are not operated) the health effects will be the whole area under H (g) curve from t to $t^g$.

Δ QALY was calculated by two alternative assumptions of life expectancy difference. First (QALY1) is based on a traditional way by assuming that life expectancy difference is minimal. This is based on the difference in the area under ah(g) and h(ng). The difference in HRQoL after operation ($q^*$) and before operation ($q^0$) is assumed to prevail whole life. The expected increase in QALYs from operation at time t is:

$$a\ q^*-q^0$$

,where a is the probability of surviving from treatment. The preoperative 15D score is used as measure of $q^0$ and 15D score after three months as a measure of $q^*$. Survival probabilities (a) were estimated using a logit model for three months mortality, where independent variable is patients EuroSCORE status. QALY gain is based on change in HRQoL and patients five years survival. For those who survived after five years we estimated the gains for rest of life using patients' age and gender specific expected life years from life tables of whole population (Statistics of Finland). Thus we assumed that health gains by operation lasted until end of life. We present also the figures for first five years of which are based on observed actual survival. Since we do not have HRQoL data for whole sample we use means for HRQoL sample by risk score groups for those patient with missing data in whole sample. The expected discounted health gains from treatment for patient i were calculated using formula:

$$(a_k\ q^*_i-q^0_i)\ \ ((1-e^{-rLi})/r)$$

where r is discount rate, $a_k$ expected survival of in each EuroSCORE category patients (k), Li the expected life-expectancy of individual i. 3 % discount rate was used for QALY changes in future years.

The second measurement (QALY2) is based on assumption that without operation all patients have died. In this case health gains are the area under ah(g) curve in figure 2. It is based on discounted value of $a_k * q^*_i$ and patients five year survival. Since health status (stock) is deteriorating with age we include a year factor (-0.002). It is based on cross-sectional effect of age on preoperative 15d status. In addition, we take into account the days that the patient has been in hospital inpatient care during the five year follow-up. It is assumed that in those days patient's 15D status has been 0.5.

CE figures were calculated by dividing cost of treatment admission (COST1), whole first hospital stay (COST2), first year (COST3), and first year cost and cost difference of following four years (COST4) by QALY1 and total discounted five years cost (COST5) by QALY2. Sensitivity analysis was performed using varying discount rates, using upper and lower 95 % confidence intervals for the mean differences in costs and QALYs. In addition, figures derived from whole sample were compared to figures calculated HRQoL sample.

# Results

## *Cost*

Figure 3, Table 2 and Table 3 about here.

The effects of EuroSCORE on time spent in the intensive care unit seem to be stronger than on cost of surgery admission. The risks score is less related to length of stay of operative admission (Figure 3). The risk system explains about 18 % of cost variation in surgery admission and explanatory power increases to 21 % when death and diabetes with insulin were included in the model (Table 2). The effect of risk score on costs decreases somewhat when additional variables were included in the mode . The death during the hospital stay increases the cost over €7000 and patients with diabetes (insulin) were about € 4000 more costly than other patients. When cost are analysed during the whole hospitalisation the effects of risk scores and diabetes increases compared to the model of the cost of surgery admission. The increase is most clear in mortality, which may indicate that severe patients that are going to die are moved to another department or hospital.

Figure 4. about here

The surgery admission amounts about 70-80 % of total one year health care cost of those patients who were alive after one year and filled the questionnaire (Figure 4). The share was highest among low score patients and lowest among those whose risk score was 7 or higher. Patients with risk score higher than 4 had much greater cost related to additional use of hospital care either by additional hospital days immediately after operating admission or later in the year as new hospitalisations or use of outpatient services of hospitals. Prescribed medicines as well as other use of outpatient services were divided rather evenly according to risk score groups. The health care cost (outpatient visits in primary care as well as OTC medicines) of which information from registers was not available were only 2-4 % of total one year costs.

Risk score alone was associated with one year total cost of health care about the same degree ( $R^2$ =0.17) as in shorter term cost estimates (Table 4). The inclusion of other significant variables to the model increased again the explanatory power by 3 percent points. Severe diabetes increased first year cost by € 7600. Contrary to shorter time cost estimates now also previous year cost became significant: an increase of them by € 1000 increased the one year cost by €700.

Figure 5. about here

About 80 % of five year cost was devoted to hospital care (Figure 5). The share of hospital care was highest (87 % among patients with risk score over 7 and lowest (25 %) among patients with risk score 0. The cost of surgery admission alone consist considerable (about 48 %) amount of the five year costs. However, after the first year about 50 % of costs are devoted to use of prescribed medicines. The five year costs are related to mortality and survival time in two ways as expected. The mortality as such increased costs by € 26000. On the other hand, an increase of life expectancy by 1 day increased cost by € 8 i.e. an increased survival by one year will increase the cost by €3100. The EuroSCORE status together with mortality and survival explained 13 % of variation of five years costs. The explanatory power increased to 26 % when diabetes status (effect €13 000) and pervious year health care was included in the models (Table 2). Their inclusion decreases the effects of mortality and survival time.

## Outcomes

Figure 6, Figure 7 and Table 4 about here

The average change between three months 15D and postoperative 15D score was 0.041 ( +/- 0.008) among those who survived the follow-up. Most of improvement occurred during the first three months and by the one year follow-up the 15D score somewhat decreased. After three months 35 % ( 32 % after one year ) of patients had clinically significant (>0.003) increase in 15D. Clinical improvement was evident in 46 .0% ( 40.3 % one after one year) of patients with risk score 0, 41.3 % (39.4% ) with risk score 1, 38.0% (38.0 % ) with risk score 2, 39.1 % (37. 6 %) with risk score 3, 37.0 % (36.1%) with risk score 4, 21. 2 % (19.3 %) with risk score 5, 33.8 % (29.4 % ) with risk score 6, 32.1 % (23.2 %) with risk score 7 and 11.7 % (16.0 %) with risk score over 7.

The most important positive changes in 15D occurred in moving, breathing and vitality (Figure 6). Risk score was not very clearly associated with changes in HRQoL. The change was highest among those who had risk score 0 and clearly positive also among patients with score under four (Figure 7). The explanatory power score system was very low (Table 4) and increased considerably when initial 15D score was included into model. The effect of initial 15D score was negative indicating that operation gained most of those patients whose initial health status was worse. The change in HRQoL was smaller among patients who had higher health care cost the in pervious year.

The EuroSCORE model had very good discriminatory ability against most of mortality indicators (Table 5). Only in five years mortality the area under ROC curve was under 80. In all except one year mortality also Hosmer-Lemeshow test showed good calibration. In most cases the extended model performed somewhat better than the restricted model. Previous years costs and diabetes with insulin (five years mortality) seemed, in addition to risk score, to be important factor explaining mortality. The both variables were also significant predictors for 5 years survival (Table 5) in whole sample but not in HRQoL sample.

In whole sample the patients with EuroSCORE 7 or more had the highest hazard rate and they distinguished clearly from other patients (Table 6). The five year mortality in this group was 40 %. Patients with risk score 6 or 7 had rather high hazard, which was also higher than patients with lower risk scores. Only one person who had EuroSCORE 0 died within five years. A comparison of hazard rates between whole sample and HRQoL sample indicates again the selection of less severe patients to the HRQoL group.

Table 5 and Table 6 about here

## Cost per QALY gained

All incremental cost measures increased with risk scores (Table 7). In the lowest risk score groups annual costs even decreased when they were compared with the cost before operation. The estimated QALY gains were positive in the five lowest EuroSCORE groups, when calculation was based on assumption of no effects in life expectancy (QALY1). However, if an extreme effect of life expectancy is assumed (i.e. without operation all patients have died) the QALY gains were rather high even in the highest risk score groups (Table 8). The cost per QALY gained were depending on both the cost and QALY measures. The average incremental cost per QALY varied between 60 000 - 85 000 when only change in quality components of life is assumed and reduced about one tenth when extreme effect of life expectancy is assumed. The CE increases heavily with risk score level. In the extreme assumption of life expectancy the cost per QALY gained has been rather low even among patients owing high risk scores (Table 9). Sensitivity analysis indicated that the measurement of QALY was the most critical (Table 10). In addition, the CE figures derived from HRQoL sample were 40 % lower compared to respective figures derived from whole sample (Figure 8 ). The difference was due to two reasons: the selection HRQoL sample l underestimated cost and overestimated QALY gains. Only in COST5/QALY2 the difference between the two samples was small.

Table 7, Table 8, Table 9, Table 10 and Figure 8 about here

# CONCLUSIONS /DISCUSSION

Compared to earlier studies on relationship between EURОscore and hospital cost of cardiac surgery our result ($R^2$ =0.19) was similar with studies by Pintor et al. (29) ( $R^2$ =0.22 ), and Sokolovic et al. (30) ($R^2$ =0.19) and Nielson et al. (31) (0.22) but we found stronger relationship than Hekmat et al. (4) ($R^2$ =0.05). In addition, in our study EuroSCORE predicts to some extent also one year and even five years costs. The prediction of cost can be somewhat improved by including two additional postoperative variables (previous year cost and diabetes with insulin).

EuroSCORE model, initially designed to predict 30-day mortality, predicted satisfactory also one year mortality and even five years survival. Again the two variables improved the predictions. However, risk stratification model does not predict much the changes in HRQoL. As in previous Finnish study(7) a significant difference in change in HRQoL between low-risk and high risk patients was found a recent Croatian study (6) using a small sample (111) indicated opposite: patients with high operative risk (EuroSCORE ≥6) were likely to experience significant improvement in a greater number of health domains (using SF 36 scores) compared to patients with low and medium risks (EuroSCORE <6). However, the results are not comparable because they used a different HRQoL measure, which were used only as a profile measures. The Finnish experience indicates that EuroSCORE does separate patients into 2 -3 groups according changes in HRQoL but do not perform well as a predictive model for the changes. For example, initial HRQol status predicts HRQoL changes much better than EuroSCORE.

According to our calculation average cost per QALY was among patients with risk score less than 2 always less than \$30 000 or \$75 000 which has sometimes been used as maximum that society is willing to pay for extra QALY. However CE ratio is crucially depending on measurement of QALYs and specially the assumptions on the effects of treatment on life expectancy. If the operation affects more on life expectancy of high risk patients than low risk patients the CE difference between risk score groups will convergence.

Nowadays it is widely accepted that measures of outcome and even the output of health should be based on QALYs. Usually the effects of treatment have been estimated using the difference in HRQoL before and after treatment. It is suggested that this kind of data enables to make comparison between providers, regions, countries or years. However, our study indicates clear challenges for routine collection of outcome data. Although we managed to get HRQoL data about 65 % of patients, the sample was clearly selective affecting crucially to the CE ratios. For example, average CE ratio (COST1/QALY1) will decrease from € 60 000 to € 38 000 (40 %) when it is estimated form HRQoL sample instead of whole sample. This will indicate that many previous studies based on patient reported changes in HRQol have overestimated much the real health gains of treatments and thus also the COST per QALY gained.

Our study indicates that a routine collection of risk scores together with register based measurement of cost and outcomes give much information for operation plantings. Specific attention should be paid for high risk groups, because HRQoL changes are rather modest among patients with EuroSCORE over seven, which have extended ICU stay, high mortality and costs.

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# Figure 1. Description of samples

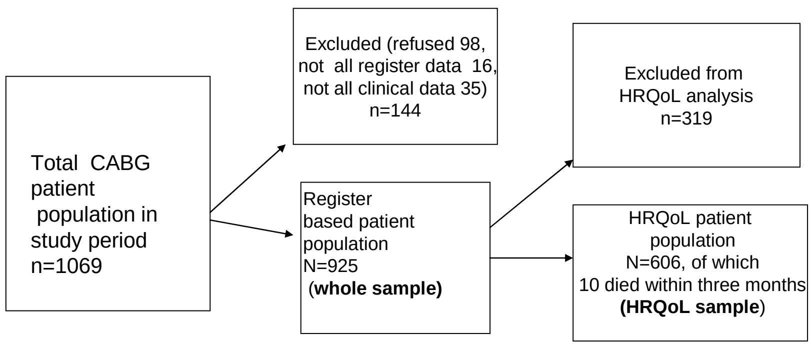

Figure 2. Health profile with and without treatment (CABG)

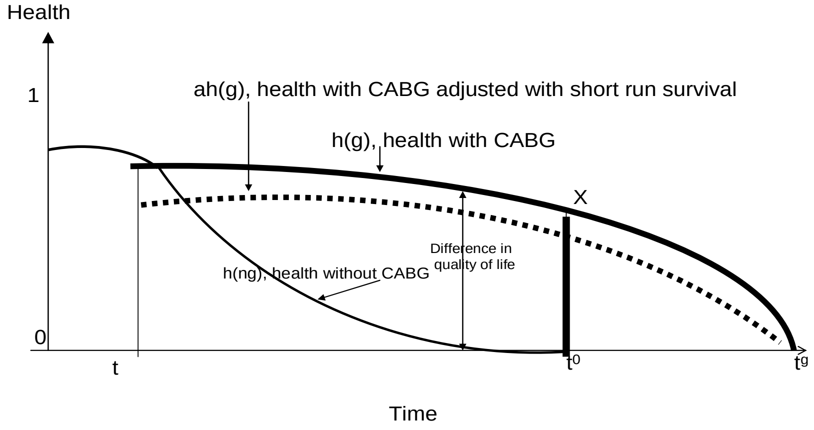


**Figure 3. The relative cost of surgery admission and length of stay in operation admission and in intensive care unit according to EuroSCORE level (Indices 100 = average in whole sample) .**

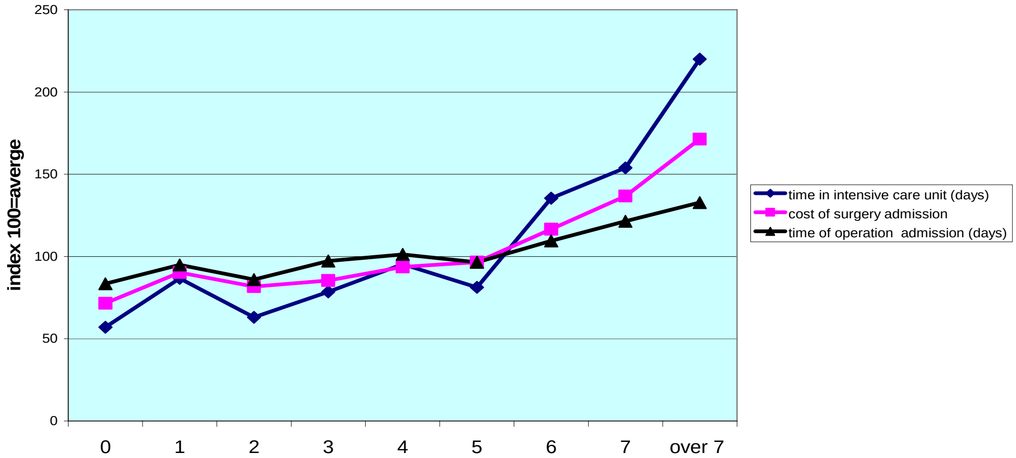

**Figure 4. The composition of the first year cost according to EuroSCORE status of patients. Based on those alive patients who filled the follow-up questionnaire (N=533)**

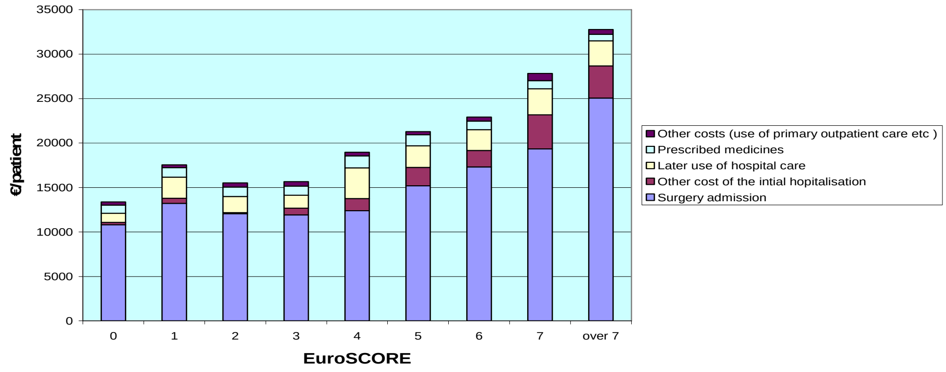


**Figure 5. Five years cost of hospital care (including outpatient visits in specialist care) and prescribed medicines according to EuroSCORE status of patients. Based on alive patients after five years (N=788)**

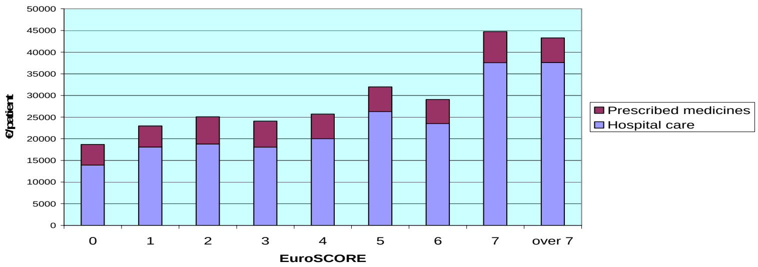


**Figure 6. The 15 dimensions and mean 15D score of health before, 3 and 12 months after by CABG (HRQol sample deaths included)**

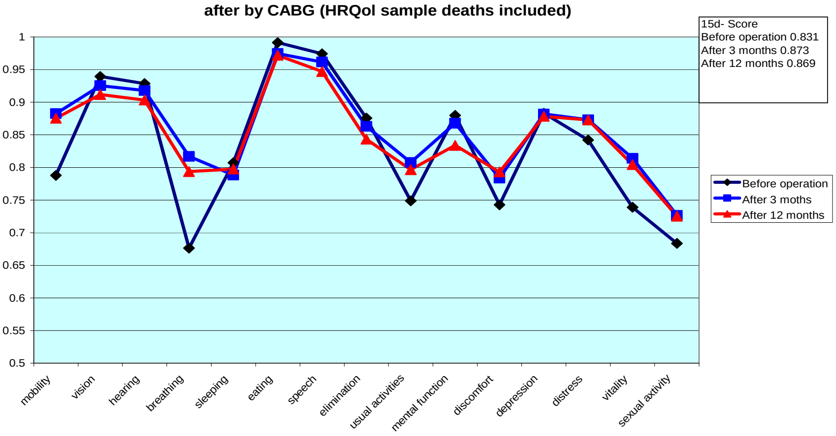

**Figure 7. The average change (and its confidence intervals) of 15D score between three months after and before CABG operation according to EuroSCORE status of patients, HRQol sample death excluded**

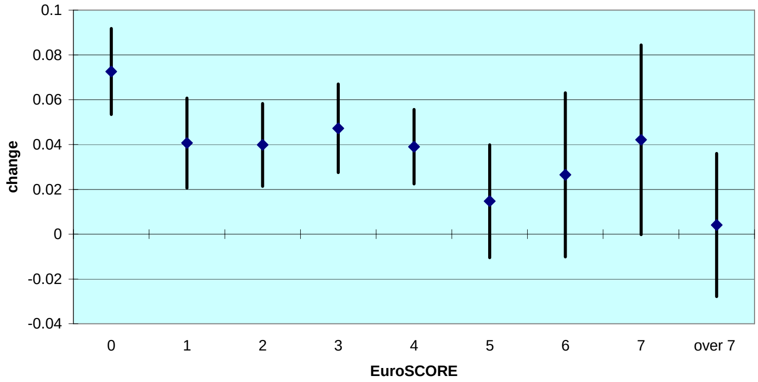


**Figure 8. A comparison of C/E estimates calculated from whole and HRQoL sample**

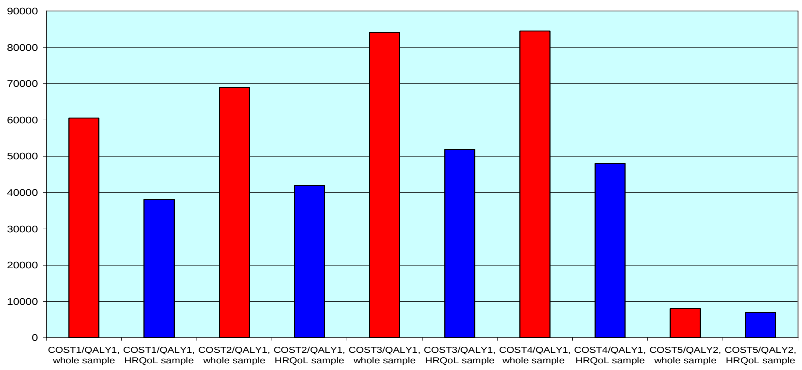


Table 1 Patient characteristic

| Variable | Whole Sample (n= 925) | | HRQol sample (n=606) | |
|---|---|---|---|---|
| | Mean (%) | SD | Mean (%) | SD |
| Age | 64.9 | 9.98 | 64.1 | 9.39 |
| Share of females (%) | 26.8 | 44.3 | 23.7 | 42.6 |
| Average EuroSCORE | 3.77 | 3.03 | 3.33 | 2.59 |
| Cost of surgery admission | 14451 | 11096 | 12603 | 7815 |
| Cost of hospital stay | 16468 | 16762 | 13874 | 9556 |
| One year cost | 20101 | 16762 | 17172 | 10963 |
| Five year cost | 30285 | 26442 | 26960 | 20494 |
| Cost of previous year | 3229 | 2315 | 3160 | 2156 |
| 30 day mortality | 0.035 | 0.186 | 0.014 | 0.12 |
| One year mortality | 0.06 | 0.24 | 0.026 | 0.16 |
| Five year mortality | 0.148 | 0.36 | 0.10 | 0.29 |
| Diabetes with insulin (%) | 0.0832 | 0.276 | 0.054 | 0.23 |

Table 2. GLM estimation on cost of opertion admission and whole hospitalisation, marginal effects of coefficients (constant not reported), loglikelyhood and measures of predictive accuracy of models

| | Cost of operation admission | | | | | | | | cost of whole hospitalisation | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dummy specification of riskscore | | Continous spefification of riskscore | | | | | | Dummy specification of riskscore | | Continous spefification of riskscore | | | | | |
| | Restricted specification | | Restricted specification | | Resticted specificatin +death | | Extended specification | | Restricted specification | | Restricted specification | | Resticted specificatin +death | | Extended specification | |
| | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value |
| EuroSCORE | | | 1122 | 11.2 | 1048 | 10.38 | 1028 | 10.47 | | | 1549 | 12.02 | 1393 | 11.15 | 1356 | 11.19 |
| EuroSCORE , O reference value | | | | | | | | | | | | | | | | |
| 1 | 3555 | 2.9 | | | | | | | 4510 | 2.6 | | | | | | |
| 2 | 1954 | 1.8 | | | | | | | 2661 | 1.7 | | | | | | |
| 3 | 2625 | 2.4 | | | | | | | 4435 | 2.8 | | | | | | |
| 4 | 4187 | 3.3 | | | | | | | 6521 | 3.6 | | | | | | |
| 5 | 4720 | 3.6 | | | | | | | 7491 | 4.0 | | | | | | |
| 6 | 8481 | 4.8 | | | | | | | 12375 | 5.3 | | | | | | |
| 7 | 12228 | 5.5 | | | | | | | 18438 | 6.6 | | | | | | |
| over 7 | 17825 | 8.3 | | | | | | | 27663 | 10.5 | | | | | | |
| Death during the follow up (1 if death) | | | | | 7891 | 2.35 | 7313 | 2.26 | | | | | 19018.7 | 4.4 | 17701 | 4.3 |
| Diabetes insulin (1 if user) | | | | | | | 4239 | 3.5 | | | | | | | 6015 | 3.92 |
| Previous years cost/€1000 | | | | | | | | | | | | | | | | |
| log likelyhood | -13929 | | -9752 | | -9747 | | -9748 | | -9857 | | -9858 | | 14047 | | -14047 | |
| $R^2$ | 0.14 | | 0.18 | | 0.20 | | 0.21 | | 0.16 | | 0.17 | | 0.20 | | 0.23 | |
| MAD | 5762 | | 5655 | | 5558 | | 5531 | | 7373 | | 7265 | | 7101 | | 7040 | |

Table 3. GLM estimation on one and five years costs, marginal effects of coefficients (constant not reported), loglikelyhood and measures of predictive accuracy of models

| | one year cost | | | | | | | | five year cost | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dummy specification of riskscore | | Continous spefification of riskscore | | | | | | Dummy specification of riskscore | | Continous spefification of riskscore | | | | | |
| | Restricted specification | | Restricted specification | | Restricted specification +death | | Extended specification | | Restricted specification | | Restricted specification | | Resrticted specification +death | | Extended specification | |
| | marginal effects | z-value | coeff. | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value |
| EuroSCORE | | | 1776 | 12 | 1594 | 10.74 | 1540 | 11.44 | | | 2543 | 9.46 | 2137 | 8.07 | 2118 | 9.14 |
| EuroSCORE , O reference value | 5963 | 3.02 | | | | | | | 7519 | 2.30 | | | | | | |
| 1 | 4773 | 2.54 | | | | | | | 10183 | 3.12 | | | | | | |
| 2 | 5721 | 3.12 | | | | | | | 9895 | 3.18 | | | | | | |
| 3 | 9166 | 4.39 | | | | | | | 17483 | 4.81 | | | | | | |
| 4 | 10590 | 4.9 | | | | | | | 25837 | 6.49 | | | | | | |
| 5 | 14497 | 5.48 | | | | | | | 23423 | 5.20 | | | | | | |
| 6 | 21653 | 6.9 | | | | | | | 36604 | 6.73 | | | | | | |
| 7 | 31512 | 10.8 | | | | | | | 38878 | 8.47 | | | | | | |
| over 7 | | | | | | | | | | | | | | | | |
| Death during the follow up (1 if death) | | | | | 9322 | 4.11 | 7290 | 3.59 | | | | | 25780 | 4.83 | 18120 | 4.11 |
| Days lived in follow-up | | | | | | | | | | | | | 8.5 | 2.63 | 7.7 | 2.72 |
| Diabetes insulin (1 if user) | | | | | | | 7646 | 4.49 | | | | | | | 13068 | 4.6 |
| Previous years cost/€1000 | | | | | | | 696 | 4.01 | | | | | | | 1909 | 5.94 |
| log likelyhood | -14339 | | -14339 | | -9731 | | -9691 | | -10434 | | -10438 | | -10427 | | -10405 | |
| $R^2$ | 0.15 | | 0.17 | | 0.17 | | 0.21 | | 0.10 | | 0.10 | | 0.13 | | 0.26 | |
| MAD | 8945 | | 8798 | | 8648 | | 8460 | | 14913 | | 14929 | | 14306 | | 13378.5 | |

Table 4. OLS estimation on change in 15D score (after 90 days year and before operation) and logit model for 90 day mortality

| | OLS FOR 15D (HRQoL sample) | | | | | | logit for 90 day mortality (whole sample) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dummy specification of riskscore | | Continous spefification of riskscore | | | | Dummy specification of riskscore | | Continous spefification of riskscore | | | |
| | Restricted specification | | Restricted specification | | Extended specification | | Restricted specification | | Restricted specification | | Extended specification | |
| | coeff. | t-value | coeff. | t-value | coeff. | t-value | marginal effects | z-value | marginal effects | z-value | marginal effects | z-value |
| Constant | 0.073 | 7.15 | 0.053 | 8.27 | 0.428 | 14.03 | 0.062 | 5.93 | | | | |
| EUROscore | | | -0.005 | -3.23 | -0.007 | -4.91 | | | 0.008 | 7.87 | 0.008 | -4.82 |
| EUROscore , O reference value | | | | | | | | | | | | |
| 1 | -0.032 | -2.16 | | | | | | | | | | |
| 2 | -0.033 | -2.26 | | | | | 0.015 | 0.46 | | | | |
| 3 | -0.025 | -1.86 | | | | | 0.011 | 0.36 | | | | |
| 4 | -0.034 | -2.24 | | | | | 0.076 | 1.63 | | | | |
| 5 | -0.058 | -3.53 | | | | | 0.105 | 1.98 | | | | |
| 6 | -0.046 | -2.56 | | | | | 0.297 | 3.21 | | | | |
| 7 | -0.030 | -1.47 | | | | | 0.205 | 2.55 | | | | |
| over 7 | -0.069 | -3.6 | | | | | 0.410 | 3.94 | | | | |
| Preoperative 15 D score | | | | | -0.425 | -12.53 | | | | | | |
| Previous years cost/€1000 | | | | | -0.004 | -2.49 | | | | | 0.002 | 2.63 |
| $R^2$ /pseudo $R^2$ | 0.03 | | 0.02 | | 0.22 | | 0.19 | | 0.20 | | 0.21 | |

Table 5 Validity of EuroSCORE on different measures of mortality

| Mortality indicator | Model | Pseudo-$R^2$ | Hosmer-Lemeshow after logit model | | Area under ROC |
|---|---|---|---|---|---|
| | | | chi $^2$ | p | |
| 30 day mortality | Restricted model | 0.1638 | 8.29 | 0.3081 | 0.8178 |
| 90 day mortality | Restricted model | 0.1976 | 8.21 | 0.3144 | 0.8384 |
| | Extended (previous year cost) | 0.2124 | 9.29 | 0.2328 | 0.8483 |
| one year mortality | Restricted model | 0.1764 | 13.9 | 0.053 | 0.83 |
| | Extended (previous year cost) | 0.1888 | 14.39 | 0.0446 | 0.8388 |
| five year mortality | Restricted model | 0.1275 | 12.74 | 0.0787 | 0.7698 |
| | Extended (preivious year expenditure,diabets with insulin) | 0.1515 | 9.58 | 0.2136 | 0.7844 |

**Table 6. Estimation results of a cox regression model (five years follow-up)**

| EuroSCORE | Whole sample | | | | | | HRQoL sample | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Dummy specification of risk score | | Continous spefication of risk score | | | | Dummy specification of risk score | | Continous spefification of risk score | |
| | Restricted specification | | Restricted specification | | Extended specification | | Restricted specification | | Restricted specification | |
| | hazard ratio | z-value | hazard ratio | z-value | hazard ratio | z-value | hazard ratio | z-value | hazard ratio | z-value |
| EuroSCORE | | | 1.27 | 11.03 | 1.28 | 10.82 | | | 1.206 | 4.72 |
| EuroSCORE, O and 1 reference values | | | | | | | | | | |
| 2 | 3.9 | 2.22 | | | | | 5.3 | 2.43 | | |
| 3 | 6.4 | 3.30 | | | | | 4.5 | 2.23 | | |
| 4 | 9.9 | 4.13 | | | | | 8.6 | 3.33 | | |
| 5 | 10.3 | 4.20 | | | | | 6.4 | 2.62 | | |
| 6 | 20.0 | 5.47 | | | | | 12.5 | 3.79 | | |
| 7 | 22.3 | 5.62 | | | | | 14.5 | 3.78 | | |
| over 7 | 31.6 | 6.57 | | | | | 11.6 | 3.55 | | |
| Diabetes insulin (1 if user) | | | | | 1.77 | 2.41 | | | | |
| Previous years cost/€1000 | | | | | 1.08 | 3.87 | | | | |
| log likelyhood | -866 | | -874 | | -865 | | -351 | | -357 | |

Table 7.Estimates of incremental cost of CABG patients according to EuroSCORE status

| | Cost of operation admission | Cost of whole hospital stay (COST2) | Cost of first year ( | Annual cost differnce of following four years against one year before operation ( 3 % discount rate) | First year cost (COST3) and cost differnce in following four years | Cost of following four years (3 % discount rate) | Total five year cost (3 % discount rate) COST5 |
|---|---|---|---|---|---|---|---|
| EuroSCORE | COST 1 | COST2 | COST3 | ACC | COST4 (=COST3+ACC) | C4Y | COST5 (=COST3+C4Y) |
| 0 | 10342 | 10642 | 12914 | -4694 | 8220 | 5379 | 18293 |
| 1 | 13047 | 13812 | 17054 | -4166 | 12888 | 6177 | 23230 |
| 2 | 11814 | 12495 | 16218 | -2623 | 13595 | 8594 | 24812 |
| 3 | 12338 | 13787 | 16919 | -625 | 16294 | 7811 | 24730 |
| 4 | 13541 | 15278 | 19370 | 415 | 19785 | 10352 | 29723 |
| 5 | 13955 | 15987 | 20404 | 7238 | 27642 | 14914 | 35318 |
| 6 | 16850 | 19460 | 23078 | 310 | 23388 | 10477 | 33555 |
| 7 | 19756 | 23839 | 28164 | 5426 | 33590 | 14060 | 42224 |
| over 7 | 24762 | 31711 | 36437 | 4245 | 40682 | 9067 | 45504 |
| totally | 14451 | 16468 | 20101 | 86 | 20188 | 9192 | 29293 |

Table 8. Post and preoperative HRQoL, short run survival, life extepectancy and QALYs according to EuroSCORE status

| EuroSCORE | HRQoL (15D) | | | | Short run (3 months) survival | Averege life expectancy of the survived | QALY1 | | | | QALY2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | preopertive (N=596) | 3 months after opeation(n =596) | differnce between 3 months follow-up and preoprative (N=596) | 1 year after operation (n=570) | | | HRQoL sample | | whole sample | | HRQoL sample | Whole sample |
| | | | | | | | five years | whole life | five years | whole life | | |
| 0 | 0.828 | 0.901 | 0.073 | 0.897 | 0.994 | 26.483 | 0.310 | 1.211 | 0.265 | 1.039 | 4.084 | 4.070 |
| 1 | 0.831 | 0.872 | 0.041 | 0.871 | 0.991 | 24.846 | 0.151 | 0.544 | 0.150 | 0.564 | 3.924 | 3.959 |
| 2 | 0.844 | 0.884 | 0.040 | 0.889 | 0.987 | 20.856 | 0.127 | 0.394 | 0.128 | 0.413 | 3.950 | 3.944 |
| 3 | 0.838 | 0.886 | 0.047 | 0.886 | 0.981 | 17.436 | 0.148 | 0.494 | 0.138 | 0.444 | 3.895 | 3.827 |
| 4 | 0.852 | 0.891 | 0.039 | 0.873 | 0.974 | 14.920 | 0.081 | 0.246 | 0.092 | 0.272 | 3.727 | 3.569 |
| 5 | 0.831 | 0.846 | 0.015 | 0.842 | 0.963 | 14.397 | -0.068 | -0.086 | -0.033 | -0.030 | 3.546 | 3.494 |
| 6 | 0.820 | 0.846 | 0.027 | 0.846 | 0.948 | 13.106 | -0.039 | 0.009 | -0.062 | -0.064 | 3.453 | 3.423 |
| 7 | 0.745 | 0.787 | 0.042 | 0.779 | 0.928 | 12.064 | -0.012 | 0.002 | -0.058 | -0.109 | 3.039 | 2.932 |
| over 7 | 0.811 | 0.815 | 0.004 | 0.812 | 0.780 | 11.126 | -0.662 | -1.555 | -0.621 | -1.418 | 2.776 | 2.521 |
| totally | 0.830 | 0.871 | 0.041 | 0.868 | 0.956 | 18.287 | 0.073 | 0.331 | 0.042 | 0.239 | 3.745 | 3.634 |

Table 9 . Cost per QALY gained according to EuroSCORE status

| EUROSCORE | Cost of operation admissio n (COST 1)/QALY 1 | Cost of whole hospital stay (COST 2)/QALY | Cost of first year (COST 3)/ QALY1 | Cost of first year and cost differnce in four following years (COST4)/QAL | Cost of five years (COST 5)/QALY" |
|---|---|---|---|---|---|
| 0 | 9954 | 10243 | 12430 | 7912 | 4494 |
| 1 | 23144 | 24502 | 30252 | 22862 | 5868 |
| 2 | 28601 | 30249 | 39263 | 32913 | 6290 |
| 3 | 27780 | 31042 | 38093 | 36687 | 6462 |
| 4 | 49696 | 56073 | 71092 | 72615 | 8329 |
| 5 | a | a | a | a | 10109 |
| 6 | a | a | a | a | 9804 |
| 7 | a | a | a | a | 14403 |
| over 7 | a | a | a | a | 18052 |
| totally | 60496 | 68938 | 84149 | 84511 | 8061 |

Table 10 Sensitivity of cost of first year (COST3) per QALY1 estimates

| | Discount rate for QALY1 | | Cost estimate (QALY1 fixed) | | QALY1 estimate (COST 3 fixed ) | |
|---|---|---|---|---|---|---|
| EuroSCORE | not discounted | 5% discount rate | upper 95%l | lower 95% | upper 95%l | lower 95% |
| 0 | 8537 | 15488 | 13373 | 11488 | 9759 | 17114 |
| 1 | 20797 | 37521 | 35075 | 25428 | 20288 | 59445 |
| 2 | 28812 | 47170 | 43254 | 35272 | 26293 | 77490 |
| 3 | 27718 | 45868 | 42484 | 33703 | 24336 | 87625 |
| 4 | 53585 | 83971 | 82541 | 59643 | 42992 | 205225 |
| 5 | á | a | a | a | 139518 | a |
| 6 | a | a | a | a | 103794 | a |
| 7 | a | a | a | a | 264899 | a |
| over 7 | a | a | a | a | | |
| totally | 55011 | 108453 | 88677 | 79621 | 60406 | 138642 |