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|  Cost-effectiveness of endoscopic versus open harvest of a short saphenous vein segment for coronary artery bypass grafting |  |
| A post hoc health economic evaluation of a randomised controlled trial |  |
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 Endoscopic vein harvesting







 Open vein harvesting

# Preface

This manuscript was written by Lars Oddershede during the fourth semester of the Medical Market Access branch of the education Master of Science in Medicine with Industrial Specialization at the Department of Health Science and Technology, Aalborg University. When completed, the manuscript will be submitted to The Journal of Thoracic and Cardiovascular Surgery, [European Journal of Cardio-Thoracic Surgery](http://ejcts.ctsnetjournals.org/) or Interactive CardioVascular and Thoracic Surgery.

I wish to thank Barbara Brocki who helped me with numerous practical issues and my supervisors, Lars Ehlers and Jan Jesper Andreasen, who gave excellent theoretical advice throughout the semester.

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Lars Oddershede

Cost-effectiveness of endoscopic versus open harvest of a short saphenous vein segment for coronary artery bypass grafting

A post hoc health economic evaluation of a randomised controlled trial

# Abstract

Background

A short saphenous vein segment is commonly used as a conduit for coronary artery bypass grafting (CABG), and clinicians must decide whether to obtain it by performing a traditional open vein harvest (OVH) or by performing an endoscopic vein harvest (EVH). We conducted a post hoc cost-utility analysis (CUA), based on a published study and from the Danish healthcare system´s viewpoint, to investigate whether EVH is cost-effective when compared to OVH.

### Methods

The economic analysis was performed using a 35 day follow-up period and in accordance with international guidelines. We constructed four cost-levels as the current literature is inconclusive as to which resource consumptions differ significantly between EVH and OVH. Outcomes were assessed by performing a quality of life conversion of patients´ postoperative pain, satisfaction with cosmetic results and observational data on mobility. We performed bias corrected bootstrap analyses on 5,000 re-samples to calculate the incremental cost-effectiveness ratio (ICER) and to construct cost-effectiveness acceptability curves (CEACs). Results were tested against a willingness-to-pay (WTP) threshold of £ 30,000/quality adjusted life-years (QALY).

### Results

When costs and outcomes within the first 35 days were compared, the ICER was £ 64,482/QALY but <1 % cost-effective at a WTP of £ 30,000/QALY. Adding costs of treatments of surgical wound infections of the leg, which were already initiated at 35 days postoperatively, the ICER dropped to £ 38,876/QALY, and EVH became approximately 2 % cost-effective at a WTP of £ 30,000/QALY. If mobility was excluded from the measurement of outcome, EVH was <1 % cost-effective at a WTP of £ 30,000/QALY.

### Conclusion

We conclude that, within the first five weeks postoperatively, EVH is not a cost-effective method for harvesting a short saphenous vein segment during CABG, when compared to OVH.

Keywords: Cost-effectiveness analysis, cost-utility analysis, CABG, endoscopic procedures, endoscopic vein harvest, open vein harvest, traditional vein harvest.

# Introduction

Although advances are being made in the use of arterial conduits for coronary artery bypass graft (CABG) surgery, the saphenous vein remains the most commonly used [1-3]. When compared to the traditional open vein harvest (OVH), the endoscopic vein harvest (EVH) has been preferred as the increased patient satisfaction and the short term reduction in leg wound morbidity are well documented [1-11]. Despite a vast number of randomised controlled trials (RCTs), reviews and meta-analyses comparing OVH with EVH only one cost-effectiveness analysis has been performed, using observational data [12]. Therefore, this study aims to evaluate the cost-utility of EVH compared to OVH for harvesting a short saphenous vein segment, by using patient-level data from a published RCT. This study is based upon the findings of a study by Andreasen et al who compared EVH to OVH in 132 non-consecutive patients, conducted in accordance with the CONSORT statement and with approval from the regional ethical committee [5]. For a more thorough description of the study by Andreasen et al than the one given in the methods section, please read the original article.

# Methods

This post hoc cost-utility analysis (CUA) was approved by The Danish Data Protection Agency (J.no. 2008-58-0028). The analysis was constructed from the Danish healthcare system´s viewpoint and based on a study by Andreasen et al which was performed between April 2004 and June 2007 at Aalborg Hospital, Denmark. The 132 patients enrolled in the study were followed to examine whether leg wound morbidity was reduced after EVH compared to OVH until the mandatory follow-up 30 days postoperatively. However, the median time from the surgery to the “day 30 follow-up” was 35 days (range: 21-49days) this study therefore refers to the follow-up as “day 35” and will use all the information available until this point for the base case analysis. The preoperative baseline characteristics for the two groups are shown in Table 1 and as seen, no significant differences were found between the two groups. The study was conducted in accordance with international

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| **Table 1** |  |  |  |
| Preoperative baseline demographic and clinical characteristics |
| **Variable** | **EVH (n=66)** | **OVH (n=63)** | ***P*-value** |
| Age (year), mean ± SD | 65±10 | 65±8 | 0.94 |
| Male, n (%) | 59 (89) | 52 (83) | 0.26 |
| Obesity (BMI>30 kg/m²), n (%) | 13 (20) | 17 (27) | 0.33 |
| Diabetes mellitus, n (%) | 7 (11) | 9 (14) | 0.53 |
| Logistic EuroSCORE, mean ± SD  | 3.5±3.4 | 3.5±3.0 | 0.89 |
| Smokers, n (%) | 9 (14) | 16 (25) | 0.09 |
| Hypercholesterolemia, n (%) | 49 (74) | 48 (76) | 0.80 |
| History of intermittent claudication, n (%) | 2 (3) | 3 (5) | 0.61 |
| Hemoglobin (mmol/l), mean ± SD | 8.8±0.7 | 8.7±0.8 | 0.48 |
| Creatinine (μmol/l), mean ± SD | 92±32 | 97±64 | 0.54 |
| Albumin (g/l), mean ± SD | 44±3.8 | 43±4.0 | 0.70 |
| Preoperative acetylsalicylic acid, n (%) | 44 (67) | 33 (52) | 0.10 |
| Preoperative clopidogrel, n (%) | 9 (14) | 10 (16) | 0.72 |
| Preoperative steroid, n (%) | 2 (3) | 1 (2) | 0.59 |
| BMI, Body Mass Index; EuroSCORE, European system for cardiac operative risk evaluation; diabetes mellitus = treatment with either insulin or oral agents; smoking = active at admission; preoperative acetylsalicylic acid and preoperative clopidogrel = intake of within 7 days prior to surgery |

guidelines and based on best available evidence. [13]

## Resource consumption and costs

With regards to the estimation of costs, all current meta-analysis, systematic review and literature checks have found that mean length of hospital stay (LOS) is decreased with the use of EVH, and all found that mean operation time is increased by using EVH, however not all found the difference to be significant [2-4, 6, 9, 10]. Because LOS and duration of surgery are two costs which carry great importance for the analysis, we therefore constructed 4 cost-scenarios where costs were added in layers, as it is somewhat uncertain whether the consumption of resources from these two factors definitely can be contributed to the choice of vein harvest method. The corresponding analyses of the incremental cost-effectiveness ratios (ICERs) were denominated ICER 1 & 5 for the first cost-level, ICER 2 & 6 for the second, ICER 3 & 7 for the third and ICER 4 & 8 for the fourth, as shown in Table 3. For the first cost-level, ICER 1 & 5, we excluded both the LOS and the duration of surgery.

 In the second cost-level, ICER 2 & 6, we added LOS to the cost analysis. This was chosen because 4 studies concluded that LOS was significantly reduced when minimal invasive vein harvest (MIVH) is used instead of OVH [2, 4, 6, 10], and only one recent study by Markar et al did not find the reduction to be significant [3]. If patients´ initial admission extended beyond 35 days, the remaining part for the admission was censored and for this analysis 5 patients had their initial admission censored. 3 out of the 5 patients who had their admissions censored beyond day 35 later died during their initial admission from non-cardiac or vein harvest related conditions. The censoring was performed for two reasons. Firstly, the extended initial admission did not have anything to do with the leg wounds. Secondly, it was done to give an intentional conservative estimate on costs resulting from admission in the OVH group. When admissions beyond 35 days were censored, the mean difference between EVH and OVH was -1.01 (95 % CI: -3.44 to 1.43), which corresponds to others findings [2, 6], and if we did not censor admissions beyond 35 days the mean difference would have been -2.83 (95 % CI: -7.01 to 1.35), potentially biasing results toward EVH.

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| **Table 2** |  |  |  |
| Duration of surgery explained by:  |
| **Variable** | **β (95 % CI)** | **SE** | ***P*-value** |
| EVH (dummy) | 5.57 (-15.19 to 26.32) | 10.49 | 0.596 |
| No. of anastomoses | 33.69 (20.89 to 46.48) | 6.46 | <0.001 |
| Male (dummy) | 1.56 (-28.73 to 31.85) | 15.30 | 0.919 |
| Euroscore | -1.51 (-5.97 to 2.94) | 2.25 | 0.503 |
| CABGECC (dummy) | 10.50 (-14.75 to 35.76) | 12.76 | 0.412 |
| Constant | 111.62 (60.33 to 162.91) | 25.91 | <0.001 |
| Number of observations 129; R-squared 0.2447; P < 0.0001  |
| β, Coefficient. SE, Standard Error. ECC, extracorporeal circulation. |

 To the third cost-level, ICER 3 & 7, costs from the duration of surgery were added as results regarding this were more heterogenic than the ones on LOS. A study by Cheng et al concluded that total time in surgery was significantly increased when using EVH [2]. In a study by Allen et al the significance of the result depended on whether only RCT´s were analysed or if nonrandomised data was included [4], and two studies did not find the difference to be significant [3, 9]. In the study by Andreasen et al the EVH group had a mean duration of surgery, which was 15.67 minutes longer than the OVH group; however, the EVH group had a slightly higher number of anastomoses, and a slightly larger percentage of on-pump surgeries, i.e. CABG performed with the use of extracorporeal circulation (ECC) [5]. These intraoperative findings were not statistically significant, but may have contributed to a slightly increased duration of surgery and we therefore performed econometric modelling to assess how much of the time difference could be explained by the endoscopic harvesting procedure. The explained variable was duration of surgery and the explanatory variables were: use of EVH, number of anastomoses, male, Euroscore and use of ECC; results are seen in Table 2. The R-squared showed that the model explained 24.5 % of the variation in the duration of surgery. The coefficient of the EVH dummy variable was not significant; however, we found it to be the best available estimate of how much the duration of surgery increased by using EVH as opposed to OVH. We therefore corrected the duration of surgery from a mean difference of 15.67 minutes to a mean difference of 5.57 minutes by subtracting 10.1 minutes from each patient in the EVH, thereby leaving the standard error unchanged. [14]

In the fourth cost-level, ICER 4 & 8, we included all costs of initiated treatments for surgical wound infections (SWIs) of the leg at

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| **Table 3** |  |  |  |  |
| Resources consumed |  |  |  |  |
|  | **EVH group\***  | **OVH group\***  | **Mean difference (95% CI)** | **Price [reference]** |
| **Included in analysis ICER 1 & 5** | **n=66** | **n=63** |  |  |
| Disposable endoscopic equipment | 1.00±0.00 | - | 1.00 (1.00 to 1.00) | £ 535.84 [LC] |
| Readmission due to leg-SWIs\*\* (days) | 0 | 0.06±0.06 | -0.06 (-0.19 to 0.06) | £ 384.71 [15] |
| Surgical revision, in general anesthesia | 0 | 0.03±0.03 | -0.03 (-0.09 to 0.03) | £ 500.64 [LC] |
| Revisons without general anesthesia | 0 | 0.02±0.02 | -0.02 (-0.05 to 0.01) | £ 235.29 |
| V.A.C. machine (days) | 0 | 0.06±0.06 | -0.06 (-0.19 to 0.06) | £ 44.12 [LC] |
| Orthopedic assessments in hospital | 0 | 0.03±0.03 | -0.03 (-0.09 to 0.03) | £ 91.88 [16] |
| Visits to GP | 0.03±0.02 | 0.70±0.36 | -0.67 (-1.37 to 0.04) | £ 29.85 [17, 18] |
| Visits to outpatient clinic | 0 | 0.05±0.04 | -0.05 (-0.12 to 0.02) | £ 139.41 [16] |
| Visits by home care nurse | 0 | 0.48±0.27 | -0.48 (-1.00 to 0.05) | £ 26.50 [LC] |
| Dressings used at post-discharge visits | 0 | 1.19±0.56 | -1.19 (-2.28 to -0.11) | £ 12.57 [LC] |
| Post-discharge antibiotic treatment | 0,02±0,02 | 0.10±0.04 | -0.08 (-0.16 to 0.00) | £ 49.27 [19] |
| **Added in analysis ICER 2 & 6** |  |  |  |  |
| Initial admission (days) | 11.52±0.71 | 12.52±1.00 | -1.01 (-3.44 to 1.43) | £ 384.71 [15] |
| **Added in analysis ICER 3 & 7** |  |  |  |  |
| Surgery time (minutes) | 221.73±7.49 | 216.16±8.77 | 5.57 (-17.18 to 28.33) | £ 13.83 [12] |
| **Changed from previous to analysis 4 & 8** |  |  |  |  |
| Readmission due to leg-SWIs\*\* (days) | 0 | 0.19±0.19 | -0.19 (-0.56 to 0.18) | £ 384.71 [15] |
| Surgical revision, in general anesthesia | 0 | 0.05±0.05 | -0.05 (-0.14 to 0.04) | £ 500.64 [LC] |
| Revisons without general anesthesia | 0 | 0.03±0.03 | -0.03 (-0.09 to 0.03) | £ 235.29 |
| V.A.C. machine (days) | 0 | 0.16±0.16 | -0.16 (-0.47 to 0.15) | £ 44.12 [LC] |
| Visits to outpatient clinic | 0 | 0.08±0.06 | -0.08 (-0.19 to 0.03) | £ 139.41 [16] |
| LC, locally collected; SWIs, surgical wound infections; V.A.C., vacuum assisted closure; GP, general practitioner. |
| \*Values are means ±Standard Error. \*\* Due to leg wound complications |  |

35 days postoperatively. This analysis was constructed because a study by Swenne et al showed that following CABG 73 % of SWIs of the leg are diagnosed within the first 30 days postoperatively and the remaining 27 % between days 31 to 60 postoperatively [20]. This implies that costs due to SWIs will occur, to some extent, after 35 days postoperatively.

The mean (±SE) resource consumption, and corresponding unit price for each cost-level are given in Table 3. All unit prices shown are 2011 values in Danish Crowns (DKK) which was subsequently converted to Great British Pounds (GBP) using the exchange rate £ 1 GBP = 8.5 DKK. Some unit prices for medical equipment were 2009 values and therefore we subsequently converted them to 2011 prices by multiplying 2009 values with 1.09 which the retail price index for medical products, appliances and equipment increased with during the period [21]. As the unit price for a minute of cardiothoracic theatre time we used the price reported by Rao et al, which was $ 21.78 United States Dollars (USD), and converted it to GBP using an exchange rate of $ 1 USD = £ 0.6164 GBP. Subsequently we converted this 2007 unit price of cardiothoracic theatre time to a 2011 value by multiplying it with 1.03 which the retail price index for hospital treatments increased with during the period [21]. When calculating unit costs for the medical staff we used average total annual incomes, including all benefits, from Odense Hospital, Denmark, under the assumption that a year contained 1400 effective hours of work [22, 23]. However, reports have shown that healthcare assistants spend 56 % of their time (1077 hours per year) at recipients´ home and we assumed that this factor was the same for visiting homecare nurses and that an average visit was 30 minutes [23-25]. With the exception of use of disposable endoscopic equipment, all information was available at a patient-level. The use of disposable endoscopic equipment was therefore estimated post hoc and we assumed that one unit had been used for all patients in the EVH group. Unit prices for general practitioner (GP) visits were calculated by multiplying GP service fees with two, as GPs receive approximately half their pay from capitation and half from service fees [17, 18].

Capital expenditures were discounted at 5 % and the annuity method was used to find the annual cost for 5 years and the costs were subsequently divided onto 300 patients per year [13]. An initial investment of £ 53,000 (undiscounted) was made in The Guidant VasoView® 6 Endoscopic Harvesting System (Guidant Corporation, CA, USA), making it £ 45.16 per patient when discounted. The surgeon (JJA), who performed all EVH in the study, initially completed 30 EVH cases before the trial began to overcome the learning curve. Vein harvest times were collected for all 30 cases and compared to the mean OVH time in the study and the additional time spend in surgery was used to estimate the cost of learning the procedure in conjunction with travelling expenses to courses on EVH and its corresponding time consumption. The cost of learning the procedure reached an estimated £ 5,200 (undiscounted) and £ 4.32 per patient when discounted.

## Outcomes measurement

The study by Andreasen et al was not originally designed for a health economic evaluation and as a result patients were not asked to score their quality of life (Qol). Therefore, to estimate patient outcome the authors performed a Qol conversion using patients VAS score of pain located to the harvest site and their grading of the cosmetic result. Patients were asked to score their current pain-level at day 5, and at day 35 they were asked to rate their satisfaction with the cosmetic result and their average pain-level between day 6 and day 35. For all analyses, ICER 1-8, the VAS scores of pain were converted to answers on the EuroQol-5Dimension (EQ-5D) questionnaire regarding pain/discomfort, and cosmetic scores to EQ-5D answers regarding anxiety/depression, and consequently assigned a Qol score from the Danish Time Trade-Off (TTO) for EQ-5D [26]. VAS scores of 0-3 were interpreted as the health state “no pain or discomfort”, VAS scores of 4-8 as the health state “moderate pain or discomfort” and VAS scores of 9-10 as

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| **Table 4** |  |  |  |
| Qol conversion of VAS and cosmetic scores |
|  | EVH  | OVH  | Qol change  |
| **ICER 1-8** | n=66 | n=61/63 |  |
| *Pain, day 5* |  |  |  |
| No. scoring 0-3 on a VAS | 65 | 58 | 0 |
| No. scoring 4-8 on a VAS | 1 | 3 | -0.062 |
| No. scoring 9-10 on a VAS | 0 | 0 | -0.396 |
| *Mean pain, day 6-35* | n=66 | n=62/63 |  |
| No. scoring 0-3 on a VAS | 65 | 56 | 0 |
| No. scoring 4-8 on a VAS | 1 | 6 | -0.062 |
| No. scoring 9-10 on a VAS | 0 | 0 | -0.396 |
| *Cosmetic score, day 35* | n=66 | n=62/63 |  |
| No. scoring "unacceptable" | 0 | 2 | -0.068 |
| **ICER 5-8\*** |  |  |  |
| *Mobility, day 2* |  |  |  |
| No. scoring 10-7 on a VAS | 57 | 0 | 0 |
| No. scoring 6-2 on a VAS | 9 | 63 | -0.053 |
| No. scoring 1-0 on a VAS | 0 | 0 | -0.411 |
| *Mobility, day 35* |  |  |  |
| No. scoring 10-7 on a VAS | 66 | 63 | 0 |
| No. scoring 6-2 on a VAS | 0 | 0 | -0.053 |
| No. scoring 1-0 on a VAS | 0 | 0 | -0.411 |
| \*not patient level data |  |  |  |

the health state “extreme pain or discomfort” [27-29]. The patients judged the cosmetic results on a scale graduated as follows: unacceptable = 1, not satisfied = 2, satisfied = 3, very satisfied = 4 and extremely satisfied = 5. For all analyses, ICER 1-8, the patients who felt the cosmetic result of the vein harvest was “unacceptable” were assigned the health state “moderately anxious or depressed”[29].

No information regarding patients’ mobility was collected. However, it seems evident that endoscopic harvesting of the vein increases patients’ postoperative mobility [2, 8]. Therefore, the analysis denominated ICER 5-8 attempts to include the variability in mobility scores by assigning patients the mean mobility score measured in a RCT by Kiaii et al [8]. In their study mobility was judged by patients at discharge and at 6 weeks postoperatively using a horizontal VAS of 0 to 10 where 0 was “unable to walk” and 10 was “excellent mobilisation”. For EVH the mean mobility score (±SD) was 8.8 (±0.8) at discharge and 9.8 (±0.5) at 6 weeks, whereas for OVH the mean mobility score was 6.4 (±1.3) at discharge and 7.0 (±3.5) at 6 weeks. Mobility VAS scores of 10-7 were interpreted as the health state “no problems in walking about”, mobility VAS scores of 6-2 as the health state “some problems in walking about” and mobility VAS scores of 1-0 as the health state “confined to bed” [29]. The conversion rate for EVH to OVH was 14 % (9 of 66 patients) it was assumed that these patients had the same reduction in Qol as the OVH patients, regarding mobility for the sensitivity analysis. The assumptions made for the Qol conversion are summarised in Table 4.

 To calculate the incremental Quality Adjusted Life-Years (QALYs) associated with the EVH and OVH procedures we assumed that the Qol changed in a linear manner between two measurements, however, there was one exception. On day 35, patients were asked to score their average pain-level between day 6 and day 35, and consequently we used these VAS score as the average of the timeframe between day 6 and day 35. Although cosmetic results could be considered permanent, we assumed patients had learned to live with their results 35 days postoperatively, that leg wound pain subsided 35 days postoperatively and that any restriction in mobility had nothing to do with the leg wound beyond 35 days postoperatively. Assumptions were made to give intentional conservative estimates on the QALY payoff from the EVH procedure.

## Analysis

 The data were analysed by the intention-to-treat method. The groups´ preoperative baseline characteristics were compared using t-tests for continuous variables and chi-squared tests for categorical variables. Mean costs and effects where estimated by performing 5,000 bootstrap re-samples and 95 % confidence intervals (CI), for mean differences, were calculated using ±2\*bootstrap standard error [30]. ICERs were calculated for all analyses based on 5,000 bootstrap re-samples [31]. Cost-effectiveness acceptability curves (CEACs) were based on a dataset which contained the mean difference in costs and QALYs between the bootstrap re-samples of the EVH group and the OVH group. CEACs were interpreted using a willingness-to-pay (WTP) threshold of £ 30,000/QALY. For all analyses, bias corrected means were calculated during the bootstrap process. Econometric modelling was performed to estimate how much of the increased duration of surgery, in the EVH group compared to the OVH group, could be attributed the harvesting method [14, 32]. All calculations and analyses of data were performed in Stata version 11.1 (StataCorp, College Station, Texas, USA) and CEACs were drawn in Graph version 4.3 (General Public License product).

# Results

Table 5 shows the mean costs per person, with the corresponding bootstrap SE, for each type of resource used. The main costs in the EVH group were the disposable endoscopic kit and the surgery time, whereas costs due to treatment of SWIs of the leg and initial investments were of minor importance. In the OVH group an extra day´s initial admission and miscellaneous treatments of SWIs of the leg carried the greatest costs. Regarding outcome, the analyses ICER 1-4 did not include the Qol influence of mobility, as this had not been measured in the study by Andreasen et al, and found a mean difference of 5.30E-4 QALY (95 % CI: 5.10E-4 to 5.50E-4). The analyses denominated ICER 5-8 included mean mobility scores from Kiaii et al and found a mean difference of 2.724E-3 QALY (95 % CI: 2.717E-3 to 2.731E-3), as seen in Table 6. In the analyses denominated ICER 1 & 5, where costs from hospital stay and surgery time were excluded, the mean difference in cost was £ 477.45 (95 % CI: 475.61 to 479.29). ICERs therefore varied depending on whether the costs from the first cost-level were compared to outcomes without mobility, ICER 1 £ 900,858/QALY, or including mobility, ICER 5 £ 175,277/QALY. When adding costs from the hospital, as done in the second cost-level, the mean difference in cost changed to £ 99.39 (95 % CI: 85.95 to 112.83) as this cost was greatest in the OVH group. ICER 2 and ICER 6 therefore became £ 187,523/QALY and £ 36,486/QALY respectively. In the third cost-level we added cost of surgery time to the analysis and the mean difference in cost increased to £ 175.65 (95 % CI: 161.57 to 189.73) as this study estimated that 5.57 minutes, out of the 15.67 minutes which the duration of surgery was increased by, could be explained by the use of EVH in the econometric model presented in Table 2. Resulting from the increased mean difference in cost, ICER 3 and ICER 7 increased to £ 331,413/QALY and £ 64,482/QALY respectively. When costs of treatments of SWIs of the leg initiated at 35 days postoperatively were included to the fourth cost-level the mean difference in cost declined to £ 105.90 (95 % CI: 91.54 to 120.26) as only patients from the OVH group had additional treatments initiated at this point. As OVH costs rose, ICER 4 and ICER 8

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| **Table 5** |  |  |
| Mean costs and outcomes (±bootstrap SE) |  |
|  | **EVH group (mean±SE)** | **OVH group (mean±SE)** |
| **Included in analysis ICER 1 & 5** | **n=66** | **n=63** |
| Inital invesment in EVH equipment\* | £ 45.16±0.00 | - |
| Intial training of staff in EVH-method\* | £ 4.32±0.00 | - |
| Disposable endoscopic equipment | £ 535.84±0.00 | - |
| Readmission due to leg-SWIs | 0 | £ 24.43±24.25 |
| Wound revisions | 0 | £ 19.63±16.13 |
| VAC rent  | 0 | £ 2.80±2.78 |
| Orthopedic assessments in hospital | 0 |  £ 2.92±2.85 |
| Visits to GP | £ 0.90±0.63 | £ 20.85±10.66 |
| Visits to outpatient clinic | 0 | £ 6.64±4.81 |
| Visits by home care nurse | 0 | £ 12.62±7.16 |
| Dressings used at post-discharge visits | 0 | £ 14.96±6.93 |
| Post-discharge antibiotic treatment | £ 1.01±1.01 | £ 4.41±2.02 |
| **Added in analysis ICER 2 & 6** |  |  |
| Initial admission | £ 4,429.95±273.54 | £ 4,817.98±380.80 |
| **Added in analysis ICER 3 & 7** |  |  |
| Surgery time  | £ 3,066.11±101.96 | £ 2,989.03±119.79 |
| **Changed from previous to analysis ICER 4 & 8** |  |  |
| Readmission due to leg-SWIs | 0 | £ 73.28±72.74 |
| Wound revisions | 0 | £ 31.31±31.08 |
| VAC rent | 0 | £ 7.00±6.95 |
| Visits to outpatient clinic | 0 | £ 11.06±7.82 |
| **Outcomes for analysis ICER 1-4** |  |  |
| QALY payoff | 0.09581±7.73E¯⁵ | 0.09528±2.05E¯⁴ |
| **Outcomes for analysis ICER 5-8** |  |  |
| QALY payoff\*\* | 0.09546±1.31E¯⁴ | 0.09274±2.05E¯⁴ |
| SWIs, surgical wound infections. V.A.C., vacuum assisted closure. GP general practitioner |
| \*discounted at 5%, divided on 300 patients/year for 5 years. \*\* Qol payoff for mobility added, still 35 day followup |

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| **Table 6** |  |  |  |
| Main results  |  |  |  |
| **Analysis**  | **Mean difference in costs (95%CI)** | **Mean difference in effects (95%CI)** | **ICER** |
| ICER 1 | £ 477.45 (475.61 to 479.29) | 0.000530 (0.000510 to 0.000550) | 900,858 |
| ICER 2 | £ 99.39 (85.95 to 112.83) | 0.000530 (0.000510 to 0.000550) | 187,523 |
| ICER 3 | £ 175.65 (161.57 to 189.73) | 0.000530 (0.000510 to 0.000550) | 331,413 |
| ICER 4 | £ 105.90 (91.54 to 120.26) | 0.000530 (0.000510 to 0.000550) | 199,807 |
| ICER 5 | £ 477.45 (475.61 to 479.29) | 0.002724 (0.002717 to 0.002731) | 175,277 |
| ICER 6 | £ 99.39 (85.95 to 112.83) | 0.002724 (0.002717 to 0.002731) | 36,486 |
| ICER 7 | £ 175.65 (161.57 to 189.73) | 0.002724 (0.002717 to 0.002731) | 64,482 |
| ICER 8 | £ 105.90 (91.54 to 120.26) | 0.002724 (0.002717 to 0.002731) | 38,876 |
|  |  |  |  |

**Figure 1: CEACs for analyses without mobility**



**Figure 2: CEACs for analyses with mobility**



fell to £ 199,807/QALY and £ 38,876/QALY respectively.

Figure 1 shows the CEACs from the 4 analyses where mobility was not included, that is ICER 1-4. It is seen in Figure 1 that in all four analyses EVH is <1% cost-effective at a WTP of £ 30,000/QALY when mobility is not included in the analyses. Figure 2 shows the CEACs for the analyses which did include mobility in its outcome measurement, that ICER 5-8. In ICER 5 & 7 EVH was <1% cost-effective at a WTP of £ 30,000/QALY. However, when costs from treatments of SWIs of the leg initiated at 35 days postoperatively were included in ICER 8, EVH was estimated to be cost-effective in 1 % of the cases at a WTP of £ 30,000/QALY.

# Discussion

As it has been suggested that both the LOS and the duration of surgery may not be significantly different between EVH and OVH [3, 9], and that 27 % of all SWIs of the leg are diagnosed after 30 days postoperatively [20], we constructed four cost-levels where costs attributable to these factors were added in layers. When comparing our experimental data on outcomes with the four cost-levels in ICER 1-4, the EVH method was <1 % cost-effective at a WTP of £ 30,000/QALY. In ICER 5-8 we converted mean mobility score from a study by Kiaii et al to Qol outcomes and assigned these to the patients to estimate how sensitive the results were to this omission in the original study by Andreasen et al. In both ICER 5 and ICER 7 the EVH method remained <1 % cost-effective at a WTP of £ 30,000/QALY. However, in ICER 6 and ICER 8 the EVH method was 2 % and 1 % cost-effective at a WTP of £ 30,000/QALY, respectively.

## Results in context

Whether significant or not, all current meta-analysis, systematic reviews and literature checks found that EVH had a lower mean LOS and a higher mean duration of surgery [2-4, 6, 9, 10]. Therefore, ICER 7 is of interest as it reflects the findings of the clinical literature and can be compared to the findings in CUA by Rao et al. Their results suggested that the EVH was the most cost-effective option with an ICER of $ 19,859/QALY (approximately £ 12,241 at an exchange rate of $ 1 USD = £ 0.6164 GBP) and it was 95.6 % cost-effective at a WTP $ 50,000USD/QALY. In comparison, ICER 7 was £ 64,482/QALY, which is 5.3 times greater than the results reported by Rao et al; however, some of this difference can be attributed to differences in study designs. Rao et al reported an incremental cost of $ 459 (£ 283), which is 1.6 times greater than our findings, and an incremental effect of 0.0231 QALY over a 42 day-period, which is 8.5 times greater that our finding. The difference in the measurement of costs between the two studies can be explained mainly by the mean difference in duration of surgery. Where Rao et al used a mean difference of 15.26 minutes, we used a mean difference of 5.57 minutes. The 8.5 times greater QALY effect estimated by Rao et al can be explained by three things. Firstly, on a VAS scale of pain, Rao et al estimated leg wound pain at discharge to be 1.1 (SD±2) for EVH patients and 4.7 (SD±1.8) for OVH patients, whereas Andreasen et al found leg wound pain to be 0.52 (SD±1.04) for EVH patients and 0.87 (SD±1.22) for OVH patients at day 5 postoperatively. We argue that patients in the study used by Rao et al did not receive sufficient treatment for their pain or were not asked merely to score leg wound pain, which might cause the EVH effect on postoperative pain to be overestimated. Secondly, it seems that the study by Rao et al did not account for the fact that some EVH patients must be converted to OVH, thereby reducing their mobility related Qol in the same manner as the patients in the OVH group. Thirdly, we used a 35 days follow-up regarding outcomes, whereas Rao et al used a 42 days follow-up period, which may be better at capturing the full effect of using the EVH method. However, overestimating the pain related Qol gain in the EVH group, and ignoring the facts that some EVH must be converted to OVH, will potentially bias results toward the EVH method, and we feel that the inclusion of these factors in our study is a major strength.

The result of ICER 8 raises the question, whether a 35 days follow-up period is sufficient to obtain an unbiased estimate of the cost-effectiveness of EVH compared to OVH. In the fourth cost-level used for ICER 8 we included all costs of initiated treatments for SWIs of the leg at 35 days postoperatively, and as a result the ICER changed from £ 64,482/QALY to £ 38,876/QALY, and the EVH method became approximately 2 % cost-effective at a WTP of £ 30,000/QALY. In our opinion, this suggests that 35 days may not be a sufficient follow-up period to capture all relevant costs and outcomes of the two methods, and the follow-up period used in this study may, as a result, be viewed as a limitation of the study.

## Limitations

In general, performing a post hoc CUA is a limitation as the study by Andreasen et al was neither designed, nor powered for health economic evaluation. This causes limitations not only due to a follow-up period, which may possibly be too short, but also from sample size, cost and outcome measurements. Due to the sample size, most of the mean differences in resource consumption were not significantly different from 0. Therefore, interpretation of most results on costs must be done with caution, and especially ICER 8, where EVH was estimated 2 % cost-effective at a WTP of £ 30,000/QALY, since none of the costs added in the analysis were significantly different from 0. Because the study by Andreasen et al did not include results from an EQ-5D questionnaire, we resorted to a Qol conversion. Decision makers must therefore evaluate whether they find our conversion appropriate, especially the mobility-related Qol conversion, as we were unable to find references on how mobility, measured on a VAS, could be converted to EQ-5D answers.

Another limitation of this study includes the mixing of experimental data with observational data. When mean measures of used disposable endoscopic equipment and mobility are used, the calculated standard error will not reflect the true variation of data, causing the confidence interval to be biased for both costs and outcomes. However, excluding mobility merely for this reason would bias results far more, as it was seen in ICER 1-4.

A consequence of our strategy to evaluate cost-effectiveness within the first 35 days postoperatively was that we assumed that all patients were followed exactly until day 35 postoperatively. However, they were not; median time from the surgery follow-up was 35 days (range: 21-49days) and this could potentially bias our results.

In addition bootstrap analysis captures variation due to differences in quantities consumed in the two groups, but does not capture uncertainty which comes from varying unit prices in decision analytic modeling. However, this limitation will be addressed by performing sensitivity analyses on unit prices before submission of the manuscript.

## Future work

Recently, the medium- and long-term graft patency has become a major concern, as EVH has been associated with increased rates of vein graft failure and adverse clinical outcomes such as death, myocardial infarction or repeated revascularisation [3, 10, 33, 34]. Further research is therefore needed to establish the long-term cost-effectiveness of EVH.

# Conclusion

We conclude that, within the first five weeks postoperatively, EVH is not a cost-effective method for harvesting a short saphenous vein segment during CABG, when compared to OVH. The finding of our study is especially interesting as the long-term patency of EVH grafts is now also being questioned.

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