

Economic Evaluation of Endoscopic vs Open Vein Harvesting

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Economic Evaluation of Endoscopic vs Open Vein Harvesting

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ABSTRACT

BACKGROUND Endoscopic vein harvesting is an alternative to open vein harvesting during coronary artery bypass grafting. Although endoscopic vein harvesting includes significant clinical benefits, few long-term cost-effectiveness studies have been performed, limiting its use in the United Kingdom. In this study, we assessed the cost-effectiveness of endoscopic vein harvesting compared with open vein harvesting from the United Kingdom's National Health Service perspective.

METHODS A Markov model was developed to estimate the cost-effectiveness of endoscopic vein harvesting vs open vein harvesting by investigating the incremental lifetime costs per quality-adjusted life-year gained. A scoping literature review was conducted to inform the development of the model. One-way and probabilistic sensitivity analyses examined the robustness of the results.

RESULTS Compared with open vein harvesting, endoscopic vein harvesting leads to cost savings of £68.46 and qualityadjusted life-year gains of 0.206 per patient over a lifetime perspective. Thus, endoscopic vein harvesting is a dominant treatment option over open vein harvesting (net monetary benefit: £6248.46). In the scenario analysis, which accounted for a high-risk population with respect to leg wound infections, the net monetary benefit was £7341.47. The probabilistic sensitivity analysis showed that endoscopic vein harvesting has a 62.3% probability of being cost-effective at a threshold of £30,000 per quality-adjusted life-year, highlighting uncertainties resulting from follow-up event rates.

CONCLUSIONS Endoscopic vein harvesting is a cost-effective method of harvesting a saphenous vein graft. Further clinical data beyond 5 years of follow-up are required to confirm the long-term cost-effectiveness.

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oronary artery bypass grafting (CABG) is among the most commonly performed cardiac procedures in the United Kingdom.¹ In most cases, a saphenous vein graft is used as conduit apart from the left internal mammary artery graft.²⁻⁴ The saphenous vein is harvested using an open or an endoscopic technique. Open vein harvesting (OVH) involves a long incision along the medial part of the lower leg or thigh.⁵ As a result of this large incision, OVH is often associated with wound healing complications, including infections and postoperative pain, leading to an increased length of stay and additional need for support in the community care setting. Endoscopic vein harvesting (EVH) is a minimally invasive procedure involving 1 or several small incisions, \sim 3 to 4 cm in length. It was first introduced in the mid-1990s. Advantages of EVH include reduced leg wound

complications, increased patient satisfaction, and improved cosmetic outcomes. $^{\rm 6}$

Despite the promising benefits for the patient, adoption rates for EVH have remained ~50% in the United Kingdom and other European countries.^{7,8} Partly, this may be due to concerns regarding vein graft quality after a publication by Lopes and colleagues⁹ reporting inferior graft quality for EVH veins compared with OVH veins, resulting in an increase in long-term ischemic events. However, in more recent investigations, such as the Randomized Endo-Vein Graft Perspective (REGROUP) trial, a causal effect on major

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adverse cardiac outcomes (MACE) could not be validated (no differences in intermediate-term results in respect to cardiovascular events were reported).^{6,8} Additionally, perceived higher costs for EVH are a concern among health care practitioners in the United Kingdom.¹⁰

However, to determine the economic implications of EVH, the investment costs and costs further down the treatment pathway should be considered and put alongside the health benefits. For this, an economic evaluation (comparative analysis) can be applied to identify the most efficient alternative. Specifically in the United Kingdom's National Health Service (NHS), costs per quality-adjusted life-year (QALY) gained are an important criterion in decision-making processes for the adoption of new health technologies.¹¹

To date, only few economic evaluations on EVH have been published, delivering different conclusions on the cost-effectiveness of EVH,^{6,12-15} while focusing only on a short-term analytic horizon. To enable more precise and informed decision making on the adoption of EVH as standard of care in the United Kingdom,^{10,12} our study assessed the cost-effectiveness of EVH compared with OVH from the NHS perspective over a long-term analytic horizon by following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.

MATERIAL AND METHODS

MODEL. We developed a Markov model using Excel 2010 (Microsoft) (Figure 1), which entailed 6 health states: CABG, asymptomatic state, leg wound infection,

myocardial infarction, repeat revascularization, and death representing clinical scenarios over a lifetime. Health states were based on the REGROUP trial² and were validated by 2 clinicians specialized in the field of CABG.

A hypothetical cohort of 10,000 patients entered the model through the health state CABG. In line with the baseline age of the REGROUP trial (66.4 years), we assumed an age of 66 years for all patients entering the model (rounded value to simplify calculations).² The first cycle was 6 weeks long, followed by 35 (annually occurring) cycles. Data addressing the mean follow-up period of 2.78 (SD, 4.7) years were rounded to 3.0 (SD, 5.0) years due to their alignment with the cumulative incidence curves and to simplify calculations. A description of the model components is provided subsequently.

DATA. We identified suitable data inputs for the model by conducting a scoping literature review in PubMed. To determine treatment effects, transition probabilities, costs, and health utilities, we searched for clinical trials, systematic reviews, meta-analyses, and economic evaluations on EVH/OVH in participants aged >18 years, published after 2000, and available in English full text. Additionally, only articles addressing saphenous vein harvesting (OVH or open-tunnel EVH) were included.

TREATMENT EFFECTS. Treatment effects describe possible consequences after the operation. Leg wound infections may occur shortly after the surgical procedure and are experienced once by a certain proportion of the

TABLE 1 Transition Probabilities				
	Expected Value			
Transition Probability (from to)	OVH Group	EVH Group (95% CI)	Distribution	
P (CABG wound infection) only in first cycle	0.0314 ²	0.014 (0.0061-0.0317) $\alpha = 8, \beta = 568^2$	Beta	
P (CABG death)	0.0189 ¹⁷	0.0162 (0.0108-0.0191) α = 86, β = 5223 ¹⁷	Beta	
P (CABG myocardial infarction)	0.0108 ¹⁷	0.0074 (0.0044-0.0135) α = 18, β = 2405 ¹⁷	Beta	
P (asymptomatic death)	Life table	Life table	Fixed	
P (asymptomatic myocardial infarction) until year 3	0.0165 ²	0.013 (0.0078-0.0214) $\alpha = 23, \beta = 553^{2,17}$	Beta	
P (asymptomatic repeat revascularization) until year 3	0.0207 ²	0.0182 (0.0112-0.0296) α = 12, β = 576^2	Beta	
P (asymptomatic myocardial infarction) after year 3	0.0076 ^{2,8}	0.0093 α = 5, β = 529 ^{2,8}	Beta	
P (asymptomatic repeat revascularization) after year 3	0.0199 ^{2,8}	0.013 α = 7, β = 525 ^{2,8}	Beta	
P (myocardial infarction repeat revascularization)	0.124 ¹⁴	0.09841 (0.0738-0.124) ²	Uniform	
P (myocardial infarction myocardial infarction)	0.0323 ²	0.0123 α = 1, β = 27 ²	Beta	
P (repeat revascularization repeat revascularization)	0.1143 ²	$0.0323 \alpha = 3, \beta = 31^2$	Beta	
CABG, coronary artery bypass grafting; EVH, endoscopic vein harvesting; OVH, open vein harvesting; P, probability.				

cohort only during the first cycle (transition to a different state after the first cycle).^{2,16} Clinical and postoperative events, such as the harvesting time, antibiotics treatment (outpatient care), and hospital length of stay, were mapped and included in the health state CABG. Event probabilities and relative risks were drawn from previous studies.^{2,17,18}

TRANSITION PROBABILITIES. Transition probabilities were primarily derived from the REGROUP trial.² Probabilities for myocardial infarction and death in the first cycle were retrieved from Li and colleagues.¹⁷ The baseline mortality risk was drawn from United Kingdom interim life tables and linked to the population characteristics of the REGROUP trial.^{2,19} For patients experiencing other health states besides CABG, asymptomatic state, and leg wound infection, a higher hazard ratio for all-cause mortality was used.^{5,20} The estimated hazard ratio for all-cause mortality was identical for patients allocated to repeat revascularization and myocardial infarction.¹⁴ Because

TABLE 2 Unit Costs per Health State		
Health States	Unit Costs, £	
Endoscopic vein harvesting	2198.32 ^a	
Open vein harvesting	1603.64 ^b	
Repeat revascularization	6210.72 ²³	
Myocardial infarction	5969.04 ²³	
Leg wound infection		
Endoscopic vein harvesting	1530.69 ²⁰	
Open vein harvesting	3609.17 ²⁰	
^a Supplemental Table 1; ^b Supplemental Table 2.		

of the uncertainty of transition probabilities between the health states of myocardial infarction and repeat revascularization, probabilities of Oddershede and Andreasen¹⁴ were used for the OVH cohort.

The identified hazard ratio for recurrent MACE of the REGROUP trial was applied to estimate the transition probability for the EVH cohort.² Furthermore, we assumed that the risk for experiencing a myocardial infarction was similar in the case of asymptomatic state, leg wound infection, and repeat revascularization. Transition probabilities remained stable from year 4 onward due to the lack of long-term data. Table 1 lists the transition probabilities used.^{2,8,14,17}

COSTS. This study was conducted from a health care payer perspective (NHS). Costs are presented in 2020£. Data on resource consumption was primarily obtained from Krishnamoorthy and colleagues²¹ and validated by 3 clinical experts in the field of OVH/EVH. Resource unit costs were derived from national sources.²² Costs on repeat revascularization and myocardial infarction, as follow-up events of CABG, were derived from Danese and colleagues.²³ For leg wound infection, average costs per case (EVH/OVH) were derived from Luckraz and colleagues.²⁰ Table 2 provides an overview of the unit costs per health state.^{20,23} Supplemental Tables 1-4 provide additional details regarding the cost components per procedure.

HEALTH-RELATED QUALITY OF LIFE. To determine the health-related quality of life (utilities), we used patient-level data from the REGROUP trial,² collected through the Seattle Angina Questionnaire at baseline, 6 weeks and 1 year, and converted them to the European Quality of Life Scale²⁴ to generate the mean utility

	Expected Value (95% CI)			
Health-Related Quality-of-Life Estimates	OVH Group	EVH Group	Distribution	
Baseline	0.7772 (0.6453 to 0.9068) ^{2,24}	0.7772 (0.6519 to 0.9001) ^{2,24}	Normal	
6 weeks postoperative	0.8754 (0.7645 to 0.9757) ^{2,24}	0.8788 (0.7696 to 0.9762) ^{2,24}	Normal	
1 year postoperative	0.9078 (0.8061 to 0.9859) ^{2,24}	0.9031 (0.8074 to 0.9799) ^{2,24}	Normal	
Health-related quality-of-life decrements used in health state				
Temporary reduction				
Leg wound infection	Reduction of 11% ^{27,28}	Reduction of 11% ^{27,28}	Fixed	
Myocardial infarction	-0.148 (-0.186 to -0.109) ^{14,29}	-0.148 (-0.186 to -0.109) ^{14,29}	Lognormal	
Repeat revascularization (CABG)	-0.09 (-0.12 to -0.07) ^{14,30}	-0.09 (-0.12 to -0.07) ^{14,30}	Lognormal	
Repeat revascularization	$-0.04 (-0.05 \text{ to } -0.03)^{14,30}$	$-0.04 (-0.05 \text{ to } -0.03)^{14,30}$	Lognormal	
Annual reduction	-0.0008 (-0.001 to -0.0006) ^{14,26}	-0.0008 (-0.001 to -0.0006) ^{14,26}	Lognormal	

values for the asymptomatic state. Following previous studies,^{25,26} an annual utility decrement of 0.0008 per year was used. For leg wound infection, we used the utility reduction of surgical site infections in the United Kingdom at 30 days postoperatively.²⁷ For all other health states, health-related quality of life decrements stated by Oddershede and Andreasen¹⁴ were used. Table 3 summarizes all health-related quality of life estimates.^{2,14,24,26-30}

ECONOMIC ANALYSIS. To determine the costeffectiveness of EVH, we conducted a cost-utility analysis. The previously described data inputs for costs and effects related to both treatment options were used to calculate the incremental cost-effectiveness ratio (ICER) by applying a discount rate of 3.5%.^{11,31}

BASE CASE ANALYSIS. We estimated total lifetime QALYs and costs for EVH and OVH, followed by a computation of the ICER. The National Institute for Health and Clinical Excellence threshold of £30,000 per QALY was

TABLE 4 Univariate Sensitivity Analyses Variables Overview				
Variables	Lower Bound	Upper Bound		
Transition probabilities between health states, %	-10	+20		
EVH-related costs, % ^a	-10 and -20	+10 and +20		
Length of stay	-0.12 ³³	-1.08 ³³		
Cost of leg wound infections, %	- 25	+25		
QALYs after 6 weeks (EVH group), % ^{b,2}	-10	+10		
Repeat revascularization rate	0.0112 ²	0.0296 ²		
Myocardial infarction rate	0.0078 ²	0.0214 ²		

^aTo account for additional potential fixed costs (eg, generator, sterilization of reusable equipment) and to address overall changes in material costs; ^bTo account for, for example, reported leg pain. EVH, endoscopic vein harvesting; QALY, quality-adjusted life-year. applied, assessing the cost-effectiveness of EVH compared with OVH (if nondominant result).

SCENARIO ANALYSIS. A scenario analysis was conducted to assess the cost-effectiveness of EVH in a high-risk population for developing leg wound complications (eg, female sex, diabetes mellitus, increased body mass index, smoking). With a rising prevalence of diabetes and obesity, the risk rate for leg wound complications is expected to increase as well, which can be reduced by EVH.³² Therefore, adjusted transition probabilities from the health state of CABG to leg wound infection were applied to both cohorts, based on Luckraz and colleagues²⁰ (EVH, 0.04; OVH, 0.48), to assess the cost-effectiveness of EVH in this specific population.^{20,32}

SENSITIVITY ANALYSES. To assess the influence of parameter uncertainty, several sensitivity analyses were conducted. An overview of the conducted univariate sensitivity analyses can be found in Table 4.^{2,33} Additionally, a probabilistic sensitivity analysis was performed including 1000 simulations in Excel. A beta or normal distribution was generally administered.

RESULTS

BASE CASE ANALYSIS. The base case analysis showed that EVH is associated with a lifetime savings of £68.46 and QALY gains of 0.206 per patient, leading to a

TABLE 5 Results of the Base Case Analysis				
Intervention	Costs (£)	Utilities (QALYs)		
OVH	4215.82	14.197		
EVH (dominant)	4147.36	14.402		
EVH, endoscopic vein har quality-adjusted life-year.	vesting; OVH, open vein h	arvesting; QALY,		



FIGURE 2 Tornado diagram of net monetary benefit. Results of the 1-way sensitivity analyses. The centerline represents the base case analysis, the bars indicate the sensitivity of the result (net monetary benefit) to changes in selected variables (upper and lower limits of variability per variable are indicated in brackets) (EVH, endoscopic vein harvesting; LOS, length of stay; QALY, quality-adjusted life-year).

dominant ICER located in the southeast quadrant of the cost-effectiveness plane (dominant: less costly, more QALYs¹¹; net monetary benefit: £6248.46). The results of the base case analysis are summarized in Table 5.

SCENARIO ANALYSIS. In the scenario analysis, which looked at the cost-effectiveness of EVH in a high-risk population, lifetime cost savings of £1641.47 and QALY gains of 0.19 per patient were achieved with EVH, again resulting in a dominant ICER (net monetary benefit: £7341.47).

SENSITIVITY ANALYSES. The results of the 1-way sensitivity analyses (Figure 2) show that variations in the transition probabilities of myocardial infarction or repeat revascularization had the highest impact on the



cost-effectiveness of EVH. The related utility losses could turn EVH into the inferior alternative. Additionally, these 2 variables could be identified as the main drivers in relation to the costs (besides the cost directly linked to the endoscopic procedure). For further details, Supplemental Figures 1 and 2 show the impact of the variations per variable on costs and QALYs.

PROBABILISTIC SENSITIVITY ANALYSIS. The probabilistic sensitivity analysis demonstrated a centralized distribution, affecting all quadrants (Figure 3). The tightest cluster was found in the northeast quadrant of the cost-effectiveness plane. Overall, more than half of all simulations are below the National Institute for Health and Clinical Excellence threshold, suggesting EVH has a 62.3% probability of being cost-effective (Figure 4).

COMMENT

This economic evaluation suggests that EVH is costeffective compared with OVH from the NHS perspective. In our study, EVH is associated with cost savings of £68.46 and QALY gains of 0.206 per patient. This is because lower costs further downstream in the treatment pathway outweigh the initial higher investment for the EVH equipment. Our findings are in line with the results from Oddershede and Andreasen,¹⁴ who found EVH to be cost-effective, with a dominant ICER of £8219 per QALY, and the findings by Luckraz and colleagues,²⁰ who identified cost savings of £856 per EVH patient. Similar to Rao and colleagues,¹² our study reveals that EVH is even more cost-effective in a high-risk population.

The discrepancy in cost savings compared with Oddershede and Andreasen¹⁴ can possibly be explained by the difference in the data used, as in contrast to their study, our study includes data from the REGROUP trial.^{2,8} Luckraz and colleagues²⁰ identified even higher cost savings compared with our base case analysis, but lower savings compared with our scenario analysis, where the same relative risk for leg wound infections was applied. This may be because our microcosting approach also accounted for costs of surgical equipment. Further, our study assesses the cumulative effect of clinical events further downstream over a patient's lifespan, not only leg wound infections, to deliver a complete picture of the economic impact of EVH vs OVH.

Our sensitivity analyses identified the noninferiority of repeat revascularization and myocardial infarction in the EVH cohort as highly relevant for defining EVH as the dominant vein harvesting method. Compared with the findings by Alexander and colleagues³⁴ from 2005, an increase in MACE among patients undergoing EVH was not reported in the recent REGROUP trial but rather an overall trend for decreased MACE in the EVH group.²

clinical outcomes between the 2 trials may be a result of immature technology and lack of clinical experience with EVH at the time of the 2005 trial. Not only have the features and handling of the endoscopic devices improved over the years, but it is also well established that the harvester's learning curve is an important aspect in the intraoperative outcomes of EVH.⁶ Consequently, regulations should be in place that allow EVH to be performed only by well-trained harvesters.

LIMITATIONS. The data on the occurrence of clinical events was derived from the REGROUP trial, in which 99.5% of the study population were male patients.² Thus, an underestimation of the likelihood for clinical events, as female sex constitutes a risk factor, cannot be excluded.²⁰ Further, generalizability of the data is limited, because the REGROUP trial was conducted in the United States. Also, nonsignificant event probabilities from the REGROUP trial were included (current best evidence), limiting the internal and external validity. Consequently, more data on the long-term effects would be beneficial to overcome uncertainties associated with the used probabilities.

Also, transferability of our results to other health care settings is uncertain, because several variables, including the reimbursement structure and costs for medical equipment, drugs, staff, and hospital days, differ between countries and may impact the costeffectiveness. Further studies in other settings would be needed to confirm our findings.

Extrapolation, a typical flaw of economic evaluations, became necessary to estimate lifetime costs and QALYs because the underlying data set only included information up to 4.7 years.⁸ Long-term data of the REGROUP trial are planned to be published and will provide more certainty.⁸

Further, no background costs were included. The derived cost data from Krishnamoorthy and colleagues²¹ did not include procedure-related costs. Also, stated costs in their study may be outdated. Therefore, clinical expertise was requested to validate the data, which may differ and represents the lowest evidence level.³⁵

Costs associated with leg wound infections were derived from a high-risk population,²⁰ potentially leading to an overestimation of costs. Consequently, there may be some uncertainty about whether the



same treatment pathway would be applied for the general population, potentially affecting the external validity. To overcome these limitations, an identification and cost data gathering of the typical treatment pathway for leg wound infections in the United Kingdom is recommended.

CONCLUSION. Our study suggests that EVH is a costeffective technique compared with OVH for harvesting a saphenous vein segment during CABG from the NHS perspective. This applies not only to a high-risk population but also to the general population in the United Kingdom undergoing this surgical intervention. As a result, EVH should be maintained and recommended as the standard of care within the NHS setting. Long-term clinical data >5 years of follow-up are required to make an even more precise costeffectiveness estimation of EVH.

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Cost Effectiveness of Endoscopic Vein Harvest for CABG

INVITED COMMENTARY:

Endoscopic vein harvest (EVH) of saphenous vein conduit for coronary revascularization has well-



documented benefits over open vein harvest, particu-

larly reduced wound complication rates and healing time.¹ Following initial descriptions of EVH techniques in the 1990s, there has been variable uptake worldwide. EVH has become the dominant technique in the United States and is now used in 80% to 90% of