From the New England Society for Vascular Surgery

Cost-effectiveness in the contemporary management of critical limb ischemia with tissue loss

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Background: **The care of patients with critical limb ischemia (CLI) and tissue loss is notoriously challenging and expensive. We evaluated the cost-effectiveness of various management strategies to identify those that would optimize value to patients.**
Methods: **A probabilistic Markov model was used to create a detailed simulation of patient-oriented outcomes, including clinical events, wound healing, functional outcomes, and quality-adjusted life-years (QALYs) after various management strategies in a CLI patient cohort during a 10-year period. Direct and indirect cost estimates for these strategies were obtained using transition cost-accounting methodology. Incremental cost-effectiveness ratios (ICERs), in 2009 U.S. dollars per QALYs, were calculated compared with the most conservative management strategy of local wound care with amputation as needed.**
Results: **With an ICER of $47,735/QALY, an initial surgical bypass with subsequent endovascular revision(s) as needed was the most cost-effective alternative to local wound care alone. Endovascular-first management strategies achieved comparable clinical outcomes but at higher cost (ICERs ≥$101,702/QALY); however, endovascular management did become cost-effective when the initial foot wound closure rate was >37% or when procedural costs were decreased by >42%. Primary amputation was dominated (less effectiveness and more costly than wound care alone).**
Conclusions: **Contemporary clinical effectiveness and cost estimates show an initial surgical bypass is the most cost-effective alternative to local wound care alone for CLI with tissue loss and can be supported even in a cost-averse health care environment. (J Vasc Surg 2012;56:1015-24.)**

Given the unsustainable rate of growth of U.S. health care costs and the increasingly important effect it is having on the overall U.S. economy,[1] ensuring the provision of cost-effective care stands among the foremost priorities for U.S. clinicians.[2,3] This priority should be especially poignant for vascular surgeons who care for patients with critical limb ischemia (CLI) and tissue loss, for several reasons. First, care for these patients is costly, laborious, and will not infrequently result in limb loss despite intensive efforts to avoid it.[4] Second, the U.S. population is increasingly elderly and/or diabetic, two characteristics that are strongly associated with CLI.[5] Finally, management of the ischemic limb is done in the context of systemic comorbidities that typically limit survival of the CLI patient population to ~50% at 5 years.[6]

The challenges present in the management of patients with CLI may lead to pessimism about the utility of limb salvage efforts. Even some within the field of vascular surgery have wondered whether aggressive revascularization and efforts to save the limb are worthwhile and whether primary amputation would be a better option for many patients.[7-9] To date, however, any statement on the relative cost-effectiveness of various CLI management strategies would have been conjecture, because no formal cost-effectiveness analysis comparing revascularization strategies has been published in the past 15 years.[10]

In this report, we describe our efforts to quantify the cost-effectiveness of various contemporary CLI management strategies. Specifically, the primary goal was to estimate incremental cost-effectiveness ratios for competing management strategies for CLI with tissue loss. We also sought to further understand the relationship between costs and effectiveness and to create a robust computer model to accurately simulate the 10-year outcomes of CLI management.

METHODS

Management strategies. The primary objective of this study was to compare the long-term costs and effectiveness of various management strategies used in contemporary clinical practice in the U.S. for previously ambulatory, independently living patients presenting with CLI and tissue loss in the context of a salvageable foot (ie, Rutherford category 5 limb ischemia[11]). The comparison assumed the availability of vein (saphenous or other) for conduit and

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Table I. Summary of the strategies modeled

Strategy	*Management summary*	*Initial intervention*	*Subsequent interventions other than wound care*
1	Local wound care	Local wound care alone	Major amputation as indicated
2	Primary amputation	Major amputation	None
3	Bypass with surgical revision(s)	Surgical bypass	Up to five surgical procedures as needed to maintain or restore patency; major amputation as indicated
4	Bypass with endovascular revisions	Surgical bypass	Up to five endovascular interventions as needed to maintain or restore patency; major amputation as indicated
5	Purely endovascular	Endovascular intervention	Up to five additional endovascular interventions as needed to maintain or restore patency; major amputation as indicated
6	Endovascular, bypass for failure	Endovascular intervention	Surgical bypass for failure of endovascular intervention to alleviate CLI; up to four additional surgical procedures to maintain or restore patency; major amputation as indicated

CLI, Critical limb ischemia.

anatomy that could be treated with surgical bypass or an endovascular intervention. A computerized Markov model simulation quantified the cost-effectiveness of these management strategies.[12-14] Six contemporary strategies for managing CLI with tissue loss were evaluated (Table I), and their respective benefits were categorized according to the patient-oriented outcomes of ambulatory status, independent living status, and state of wound healing (Fig 1).

Strategy 1: A conservative strategy of local wound care with major amputation was used as the baseline comparator strategy. Patients were subject to the possibility of spontaneous wound healing, with or without recurrence, the possibility of requiring major amputation, and the possibility of death due to coronary, cerebrovascular, or other causes.

Strategy 2: Patients underwent primary amputation at the initiation of the model and were subject to the possibility of impaired stump wound healing and the possibility of death (periprocedural or other).

The remaining four limb salvage strategies began with an index revascularization procedure, followed by wound care, and the possibility of requiring reintervention to maintain or restore patency, the possibility of requiring major amputation, and the possibility of periprocedural death or death from another cause (Fig 1).

Strategy 3: Patients underwent an initial infrainguinal surgical bypass with a vein conduit and were then subject to the need for up to five additional surgical procedures to maintain or restore patency.

Strategy 4: Patients underwent an initial infrainguinal surgical bypass with a vein conduit and were then subject to the need for up to five endovascular interventions to maintain or restore patency of the vein graft.

Strategy 5: Patients underwent an initial endovascular intervention and were then subject to the need for up to five additional endovascular interventions.

Strategy 6: Patients underwent an initial endovascular intervention; if this failed, a surgical bypass was performed and up to four additional surgical procedures to maintain or restore patency.

The base-case scenario assumed that no foot wound in these patients was closed during the initial hospitalization.

Estimates of clinical and utility parameters. The selection of estimates for the clinical event and utility parameters of this model has been previously described.[5] In brief, previously published limb salvage literature was comprehensively reviewed, with emphasis given to studies specifically focused on clinical trials and observational studies of high methodologic quality that focused on patients with CLI and tissue loss. Uncertainty in the estimates of various parameters was accounted for using a probabilistic model structure; thus, the parameters used in a given simulation varied randomly within a predetermined distribution that was thought to best represent the degree of uncertainty associated with various parameter estimates. Additional deterministic sensitivity analyses were used to vary preselected parameters over a range of possible values to better understand the relationship between parameters and to identify threshold parameter values beyond which certain study findings would change. Selected parameters used in the model are presented in Table II.

Estimates of cost parameters. Consistent with recommended guidelines,[14] a societal perspective was considered in the base-case analysis. Accordingly, inpatient and outpatient costs accumulated by patients with Rutherford 5 CLI were considered. A thorough literature review revealed that most publications reporting inpatient cost estimates were of insufficient quality for contemporary cost-effectiveness evaluation because they were published >10 years ago or were based on administrative/claims databases, which do provide data on large numbers of patients but provide payments or charges, not costs, and lack precision in identifying specific patient

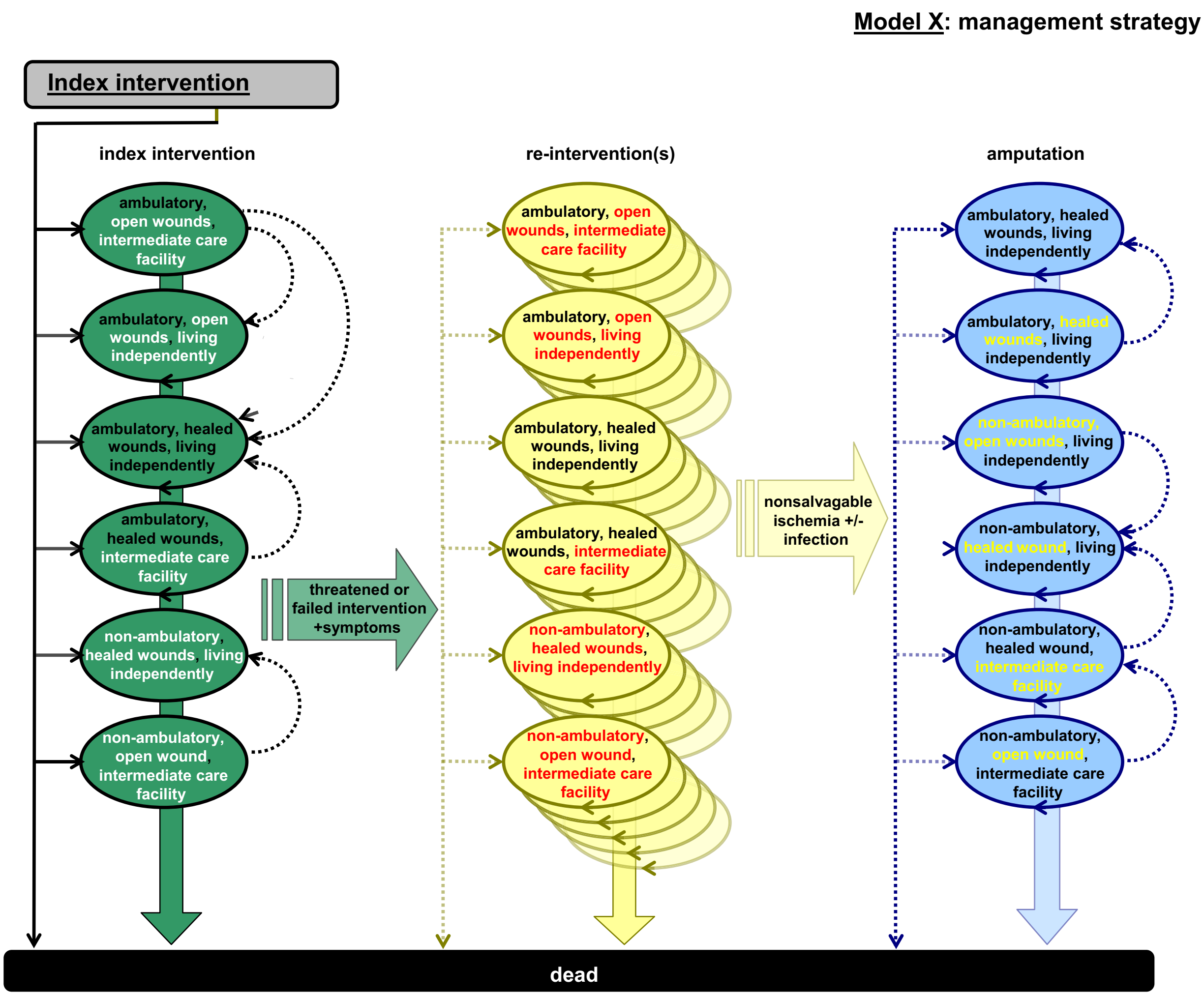

Fig 1. Schematic diagram demonstrates an overview of the patient-oriented clinical states modeled in the computer simulation for critical limb ischemia (CLI) management strategies 3 to 6.

populations.[15] We therefore endeavored to obtain accurate estimates of the costs of managing patients with Rutherford 5 CLI that were representative of contemporary vascular surgery practice in U.S. medical centers through a patient-level transaction cost-accounting system (see Appendix B [online only] for details).

Estimates of relevant outpatient costs were obtained from the published literature (Table II).[5] In brief, important outpatient costs included the cost of wound care, limb prosthesis purchase and maintenance, short-term rehabilitation stays in a nursing facility, and long-term stays in nursing homes. We did not include the effect of lost workdays for patients because the advanced age and degree of baseline morbidity associated with CLI typically precludes employment in these patients.

A computer simulation was used to create a probabilistic Markov model that recreated the above-described clinical events, patient-oriented outcomes, utilities, and costs resulting from various management strategies. Simulations for each management strategy were performed for 1000 hypothetical cohorts, each with 1000 patients. A 10-year time horizon was chosen with Markov cycles of 1 year in duration. All modeling and analysis was performed using Excel 2003 software (Microsoft Corp, Redmond, Wash) with additional programming in Visual Basic for Application (Microsoft Corp). Reported clinical or utility values represent the median value of the 1000 simulations.

All cost values reported are in 2009 U.S. dollars (USD) and represent a median value, unless otherwise noted. Utilities and cost values were discounted at the recommended 3.5% annual rate.[16] Cost-effectiveness was quantified using incremental cost-effectiveness ratios (ICERs) in USD per quality-adjusted life-years (QALY) and cost-effectiveness acceptability curves.

To explore other outcomes that may provide meaningful value to patients not expressed in QALYs, two alternative measures of cost-effectiveness were also considered: (1) the cost per salvaged limb-year, calculated as the ratio of the

Table II. Important parameters included in the model[a]

Parameter	*Point estimate*	*Range[b]*
Clinical events		
Annual (baseline) mortality, %	11.70	9.3-14.1
Excess mortality rate associated with		
Major amputation, %	3.90	2.1-5.7
Surgical bypass, %	2.60	1.4-3.8
Endovascular intervention, %	2.60	1.4-3.8
Annual rate of major amputation during year 1 after		
Local wound care, %	38.00	27.9-48.1
Surgical bypass, %	10.80	8.4-13.2
Endovascular intervention, %	12.20	6.9-17.5
Annual rate of major amputation during years 2-10 after		
Local wound care, %	38.00	27.9-48.1
Surgical bypass, %	2.60	2.0-3.0
Endovascular intervention, %	2.60	2.0-3.0
Wound healing at 1 year after		
Local wound care, %	41.00	24.8-57.2
Surgical bypass, %	95.00	90.0-100.0
Endovascular intervention, %	60.30	53.6-67.0
Probability of reintervention (endovascular or surgical) after		
Surgical bypass, %	22.70	20.5-24.9
Endovascular intervention, %	26.00	23.8-28.2
Probability of initial discharge to rehabilitation facility after		
Local wound care, %	0	0
Major amputation, %	100	100
Surgical bypass, %	28.70	26.3-31.1
Endovascular intervention, %	28.70	26.3-31.1
Probability of ambulation after		
Major amputation, %	55.50	52.4-58.6
Surgical bypass, %	97.10	95.5-98.7
Endovascular intervention, %	97.10	95.5-98.7
Probability of living independently after discharge		
Surgical bypass, %	98.60	97.7-99.5
Endovascular intervention, %	98.60	97.7-99.5
Major amputation, %	92.00	86.5-97.5
Utilities associated with wounds		
Unhealed (persistent/recurrent) foot wound or unhealed amputation stump wound after		
Local wound care, %	0.42	0.28-0.52
Primary amputation, %	0.48	0.30-0.58
Surgical bypass, %	0.5	0.57-0.67
Endovascular intervention, %	0.5	0.59-0.69
Healed wound after		
Local wound care, %	0.64	0.59-0.69
Primary amputation, %	0.54	0.32-0.65
Surgical bypass, %	0.62	0.54-0.70
Endovascular intervention, %	0.62	0.54-0.70
Outpatient costs		
Local wound care, per year, $	21,029	19,036-25,715
Inpatient rehabilitation and/or home health nursing, $	12,048	$1364-44,895
Residence in a nursing home, per year, $	67,878	35,235-83,898
Limb prosthesis		
Initial purchase, $	10,000	6,057-14,573
Yearly maintenance, $	750	513-995

[a]See the review by Barshes et al[5] for more details.
[b]The full range of values used in the probabilistic model was determined by various distributions which included beta, gamma, and triangular. The ranges listed here are the 95% confidence level equivalent for clinical event probabilities and utilities and the actual range (minimum and maximum) for cost values.

costs of limb salvage efforts to the duration of time for which the limb is salvaged; and (2) the cost per functional limb-year, calculated as the ratio of costs of providing any functioning limb—whether that be through salvage of the autogenous limb or through postamputation ambulation using a limb prosthesis—to the duration of time during which the patient has a functional autogenous or prosthetic limb.

RESULTS

Base-case scenario: clinical outcomes and health utilities. The strategy of local wound care (strategy 1) resulted in expectedly poor limb salvage rates of 27.0% at 5 years and 9.8% at 10 years. Of the patients surviving at 5 years, 73.9% had undergone a major amputation, 13.2% had a persistent or recurrent ulcer or foot wound, and 12.9% had healed. At 5 and 10 years, 18.2% and 22.4% of patients, respectively, lived in a nursing home. This strategy produced a mean of 2.287 QALYs per patient.

Primary amputation (strategy 2) obviously resulted in no limb salvage. The percentage of surviving patients that remained ambulatory with a prosthetic limb was 72% at 5 and 10 years, and overall 24.6% of patients remained ambulatory at 5 and 10 years. The strategy of primary amputation produced a mean of 2.178 QALYs per patient.

Strategies 3 and 4, which featured an initial surgical bypass, both resulted in limb salvage rates of 79.2% at 5 years and 69.9% at 10 years. Revision or reintervention was required in 16.8% of patients in both groups. Of these, 76.7% underwent one revision, 19.0% underwent two revisions, 3.6% underwent three revisions, and 0.06% underwent four. At 5 and 10 years, 92% and 90% of living patients remained ambulatory, and 6.1% and 8.4% of patients lived in nursing homes. Both strategies produced a mean of 2.556 QALYs per patient.

Strategies 5 and 6, which featured an initial endovascular intervention, resulted in limb salvage rates of 79.4% to 79.6% at 5 years and 70.0% at 10 years. In strategy 5, which was purely endovascular, a repeat endovascular intervention was required in 25.6% of patients, comprising one repeat intervention in 78.3%, two repeat interventions in 17.1%, three repeat interventions in 3.7%, and four repeat interventions in 0.9%. In strategy 6, endovascular with bypass for failure, 25.6% of patients underwent surgical revision. As with surgical bypass strategies, the percentage of surviving patients that remained ambulatory in strategies 5 and 6 was 92% and 90% at 5 and 10

Table III. The costs, benefits, and incremental cost-effectiveness ratios (*ICERs*) of various contemporary management strategies for Rutherford category 5 critical limb ischemia (CLI)

Strategy	*Management*	*Cost, $* *(2009 used)*	*Benefit* *(QALYs)*	*Compared with strategy 1* *Incremental cost, $*	*Incremental benefit*	*ICER, $*
Strategy 1	Local wound care	68,736	2.280	. . .	. . .	. . .
Strategy 4	Bypass with endovascular revisions	81,920	2.556	13,184	0.276	47,738
Strategy 3	Bypass with surgical revisions	84,961	2.556	16,225	0.276	58,749
Strategy 6	Endovascular, bypass for failure	88,306	2.472	19,570	0.192	101,702
Strategy 5	Purely endovascular	89,040	2.448	20,304	0.168	121,010
Strategy 2	Primary amputation	78,958	2.178	10,222	−0.102	Dominated

QALYs, Quality adjusted life-years.

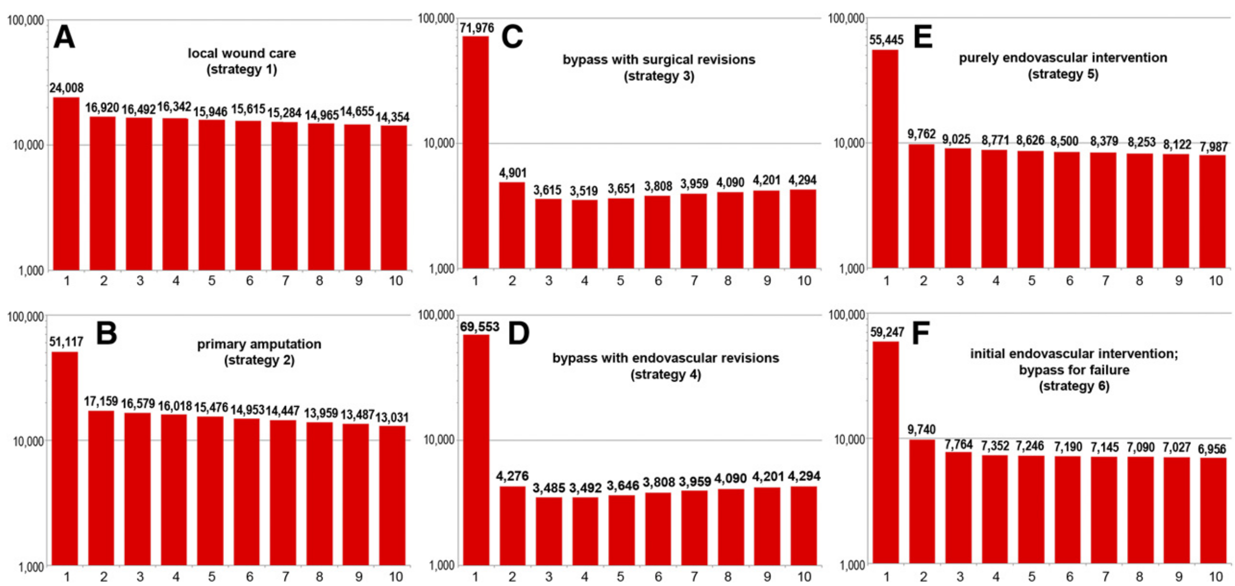

Fig 2. The annual costs per living patient are demonstrated during the 10-year interval after the initiation of various management strategies: **(A)** strategy 1 (local wound care); **(B)** strategy 2 (primary amputation); **(C)** strategy 3 (surgical bypass with surgical revision); **(D)** strategy 4 (surgical bypass with endovascular revision); **(E)** strategy 5 (purely endovascular intervention); and **(F)** strategy 6 (endovascular intervention, surgical bypass for failure).

years, respectively, and 6.5% and 8.7%, respectively, of patients lived in a nursing home. Strategy 5 produced 2.448 QALYs and strategy 6 produced 2.472 QALYs.

Patient survival was similar across all models, with mean survival rates of 51.4% for primary amputation, 51.5% and 51.6% for endovascular-first and surgery-first strategies, and 52.3% at 5 years. The 10-year survival rate was 27.4% to 28.0%.

Costs and cost-effectiveness. The median costs of the hospitalizations associated with various index procedures, obtained from the single-center review with activity-based cost allocation,[17] were $44,634 for infrainguinal bypass, $26,509 for endovascular intervention, $28,701 for major amputation, $28,039 for surgical revision of a vein graft, $13,137 for endovascular intervention of a vein graft, and $17,751 for minor amputation and foot debridement.

These costs were incorporated into the simulation model, which then estimated the long-term (10-year) costs associated with various strategies (Table III). The strategy of local wound care alone (strategy 1) was associated with the lowest total cost, with a mean total 10-year cost of $68,736. The endovascular-first strategies had the highest costs, at $89,040 for strategy 5 and $88,306 for strategy 6. The long-term cost associated with primary amputation (strategy 2) was $78,958 and was comparable to costs for the surgery-first strategies of $84,961 for strategy 3 and $81,920 for strategy 4.

Fig 2 demonstrates the annual per capita costs for all six strategies, showing that local wound care (strategy 1; Fig 2, *A*) had the lowest initial cost of $24,008 during year 1, but costs during subsequent years were $14,354 to $16,920 per year. In contrast, strategies 3 and 4 (Fig 2, *C* and *D*) had the highest initial costs—$71,976 and $69,553, respectively, during year 1—but the lowest subsequent annual costs (range, $3485-$4901). The year-1 costs of $55,445 and $59,247 for the endovascular-first strategies (5 and 6), respectively (Fig 2, *E* and *F*), were somewhat less than the costs of the surgery-first

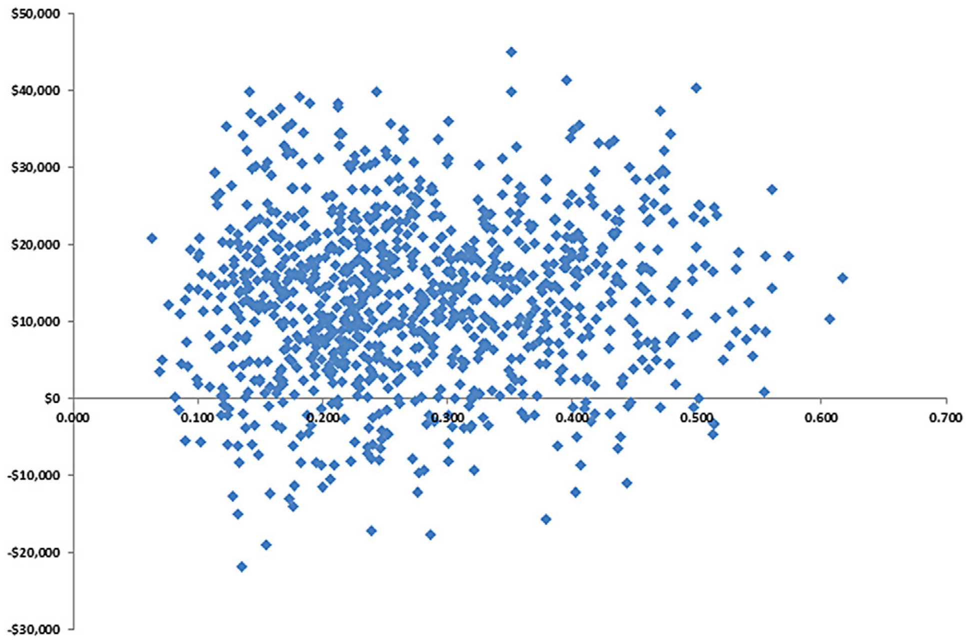

Fig 3. The incremental costs (in 2009 U.S. dollars) and incremental benefits (quality-adjusted life-years) are demonstrated for strategy 4 (surgical bypass with endovascular revision) compared with strategy 1 (local wound care with amputation as indicated).

strategies (3 and 4) but had higher subsequent annual costs of $7987 to $9762 for strategy 5 and $6956 to $9740 for strategy 6 due to the higher rates of reintervention and continuing wound care needs. Primary amputation (strategy 2; Fig. 2, *B*) had a year-1 cost of $51,117—intermediate between surgical bypass and local wound care—but the subsequent annual costs (range, $14,354-$16,920) were higher than those of the endovascular-first strategies.

Considering long-term costs and benefits in the estimation of ICERs, we found that bypass with endovascular revisions (strategy 4) was associated with an ICER of $47,738 and was the most cost-effective alternative to local wound care alone. Fig. 3 is a scatterplot, or cost-effectiveness plane, that displays the ICERs of each of the 1000 trials. As illustrated, surgical bypass with endovascular revision (strategy 4) provided incremental benefit (ie, more QALYs) vs local wound care. This strategy actually provided cost savings (higher benefits at lower costs) in 10.8% of trials. Bypass with surgical revision (strategy 3) yielded an ICER of $58,749, comparable to that of bypass with endovascular revision (strategy 4). The ICERs associated with the two endovascular-first strategies (strategies 5 and 6) were higher, at $121,010 and $101,702, respectively. Finally, primary amputation was dominated; that is, it was both more costly and provided less benefit than local wound care.

A cost-effectiveness acceptability curve demonstrating the relationship between the willingness-to-pay threshold and the probability that various management strategies are cost-effective is presented in Fig 4. The probability of surgical bypass with endovascular revisions (strategy 4) being a more cost-effective approach than conservative management (strategy 1) was 25.9% at a willingness-to-pay threshold of $25,000/QALY, 48.7% at a threshold of $50,000/QALY, 75.7% at a threshold of $100,000/QALY, and 90.2% at threshold of $200,000/QALY.

Alternative end points. The findings were largely similar when the two alternative measures of benefit or "value" to patients were considered. First, compared with local wound care alone, the costs per year of limb preservation were lowest for the surgery-first strategies 3 and 4 ($8640 and $7021/limb-year, respectively) and slightly higher for endovascular-first strategies 5 and 6 ($10,752 and $10,399/limb-year, respectively). Similarly, the cost per functional limb-year (ie, ambulation on a functioning limb after limb preservation or on a limb prosthesis after major amputation) was lower for the surgery-first strategies 3 and 4 ($6934 and $5634/functioning limb-year, respectively) than the endovascular-first strategies 5 and 6 ($8660 and $8350, respectively) compared with local wound care alone. Primary amputation cost $15,527/functional limb-year compared with local wound care and was the highest cost of all management strategies assessed.

Deterministic sensitivity analyses. Several deterministic sensitivity analyses were performed. First, the effects of costs related to endovascular and surgical procedures were examined. With all other parameters remaining unchanged, the ICER of the endovascular-first strategies did not decrease below the ICER of the bypass-first strategies until endovascular procedural costs were decreased by ≥42%; specifically, from $26,509 to ≤$15,640. We also considered the possibility that the frequency of hospitalization increased more after surgical bypass than after the other

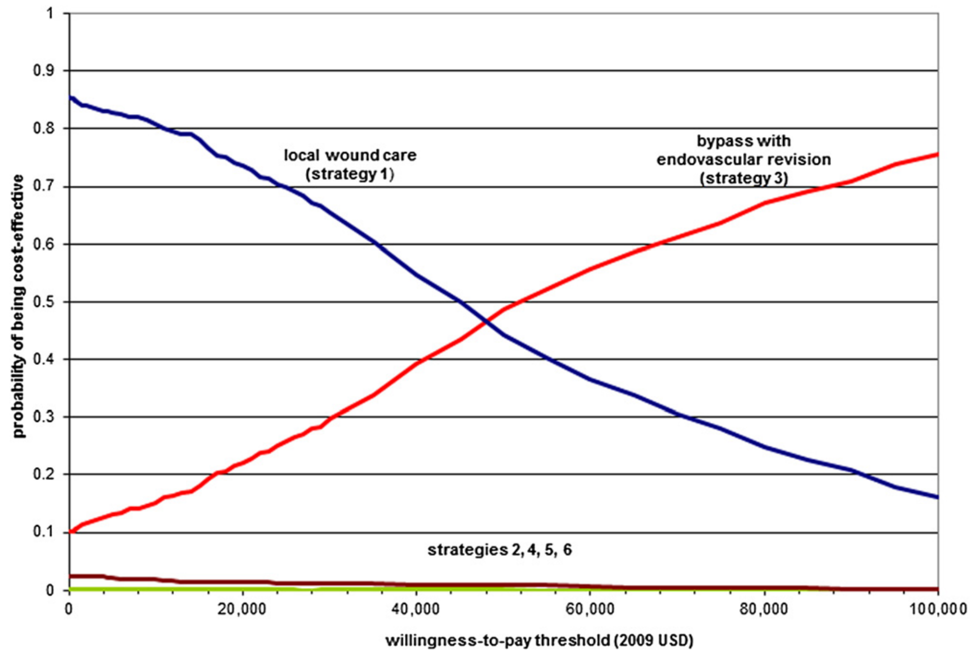

Fig 4. Cost-effectiveness acceptability curves are shown for critical limb ischemia (CLI) management strategies compared with strategy 1 (local wound care). The probability of strategy 4 (surgical bypass with endovascular revision) being a cost-effective alternative increases as the willingness-to-pay threshold in U.S. dollars (*USD*) surpasses \$39,255 per quality-adjusted life-year.

strategies by simulating an additional \$20,000 of accumulated inpatient hospital costs during the first year after surgical bypass. Even with this additional cost, bypass with endovascular revision (strategy 4) remained the most cost-effective alternative to local wound care, but the corresponding ICER increased to \$119,060/QALY.

The wide range of reported reintervention rates after endovascular intervention[5] suggested uncertainty about the estimates for this parameter, and a conservative point estimate of 26% was used in the base-case model. To explore the effect of an increased reintervention rate after endovascular intervention, the effect of a 50% reintervention rate was examined. This increased the ICER of a purely endovascular intervention (strategy 5) to \$125,583 and the ICER of endovascular intervention with bypass for failure (strategy 6) to \$104,481.

The base-case model included the conservative assumption of a 0% wound closure rate during the index hospitalization. As might be expected, the ICER of all the limb salvage strategies decreased as the wound closure rate increased. In fact, the ICER of the endovascular-first strategies decreased at a faster rate than the ICER of the surgery-first strategies. As a result, the purely endovascular intervention (strategy 5) became a more cost-effective alternative to local wound care than surgery with endovascular revisions (strategy 4) once the initial wound closure rate increased >37%. The purely endovascular intervention became cost saving (ie, both more beneficial and less costly) than local wound care once the initial wound closure rate reached 51%, and surgical bypass with endovascular revisions became cost saving once the initial wound closure rate increased >71%.

Finally, cost perspective was changed to model the third-party payer perspective by considering only inpatient costs, interim stays in rehabilitation facilities, and purchase and maintenance costs for a limb prosthesis. The costs of wound care and residence in a nursing home were excluded. In this scenario, the ICERs of the bypass-first strategies increased (\$136,101 for strategy 3 and \$125,237 for strategy 4) and became slightly higher than those of the endovascular-first strategies (\$117,182 for strategy 5 and \$123,348 for strategy 6). Primary amputation remained dominated.

DISCUSSION

For the past 2 decades, U.S. clinicians have driven evidence-based care for patients with vascular diseases through the collaborative performance of high-quality randomized, controlled clinical trials[18-22] and multidisciplinary consensus statements on the management of vascular diseases.[23-26] More recently, U.S. clinicians who treat vascular disease have advocated for patient safety through the formation of regional quality-improvement initiatives and the analysis of risk-adjusted outcomes data.[27-29] The most pressing issue currently facing U.S. clinicians and U.S. health care in general is unsustainable increases in the per-capita costs of health care.[1,30] Thus, the foremost challenge for vascular clinicians is to find ways to maintain or further improve patient-oriented outcomes while minimizing monetary costs—in other words, optimizing the cost-effectiveness and "value" of the health care provided to patients.[2]

This study suggests that surgical bypass with endovascular revision(s) as needed is the most cost-effective alternative to local wound care for previously ambulatory, independently living patients who present with CLI and tissue loss. With an ICER of $47,738, this management strategy is well within the range of cost-effectiveness values traditionally accepted to represent an efficient use of resources in the U.S. ($50,000-$120,000/QALY)[3,31,32] and not far off the much more stringent £20,000/QALY (~$33,000/QALY) threshold suggested by the United Kingdom's National Institute for Health and Clinical Excellence for being considered cost-effective.[33] Endovascular-first intervention strategies did not prove to be cost-effective for patients presenting with CLI and tissue loss in our base-case scenario, but several possible scenarios (including a reduction of endovascular procedure costs and improvement in the postintervention wound healing rate) could make endovascular strategies a cost-effective management approach.

In contrast to what some authors have suggested,[7-9] primary amputation does not appear to be a cost-effective management option by standard measurements of cost per QALY or by the alternative measures of cost per benefit that we considered in this study. Indeed, primary amputation was dominated (ie, provided fewer benefits and required higher costs) by all of the management strategy options considered. Although there are valid indications for primary amputation in select patients (eg, foot wounds that cannot be salvaged or nonambulatory patients), this study suggests that expectant management with local wound care and major amputation as needed would be a more cost-effective management strategy for ambulatory, independently living patients with CLI and tissue loss.

This study has helped to identify certain cost drivers, which, if effectively targeted, may provide the opportunity to further improve the cost-effectiveness of limb salvage efforts. As mentioned, one such cost driver is the rate of wound healing after revascularization. The development of reliable strategies, techniques, or adjuncts to improve the wound healing rate after revascularization or to allow for the early closure of foot wounds[34] would improve the cost-effectiveness of all limb salvage and revascularization strategies, possibly to the point that these strategies would be dominant; that is, associated with improved outcomes and lower costs compared with local wound care alone.

Procedural costs may be another such cost driver. As the deterministic sensitivity analyses demonstrated, the cost-effectiveness of the various management strategies may vary somewhat in health care environments that have different absolute and relative costs but would be unlikely to change the ranking without large differences in these procedural costs. Nonetheless, similar analyses should be repeated across a variety of cost structures and operating environments, and each center should examine its own costs before generalizing the results of this study to its own practice.

Another important finding that merits discussion is the discrepancy between estimated ICERs of the limb salvage strategies when considering payer and societal perspectives. The societal perspective is all-encompassing and includes costs associated with a management strategy or health technology, regardless of the payer. This perspective is recommended in cost-effectiveness analysis because it is thought to be a more accurate representation of the true costs of health care.[14] The payer perspective, in contrast, considers only costs that might be paid by a particular payer. In this study, we performed a sensitivity analysis that simulated the payer perspective of Medicare part A or certain other nongovernmental third-party payers that might pay the costs of inpatient care, interim stays in rehabilitation facilities, and limb prostheses but not the costs of outpatient wound care and nursing home care. This change in payer perspective alone led to purely endovascular intervention (strategy 5) appearing to have cost savings compared with local wound care alone. The costs of outpatient wound care and nursing home costs would have to be borne by some payer—in many circumstances, the patient as an individual through out-of-pocket expenses or the taxpayers as a society—so the conclusions drawn from this payer perspective are clearly not the best representation of "value." Yet, this provides a clear example of how imperfect alignment between societal, payer, and patient interests may reinforce perverse incentives rather than optimizing the "value" of health care.[2] So, although deterministic sensitivity analyses from the institutional perspective are recommended, we strongly emphasize the recommended use of the societal payer perspective for the base-case scenario of future cost-effectiveness analyses in vascular surgery.[14]

The high degree of consistency between the clinical outcomes projected by the simulation model in this study and studies upon which the projections were based and others upon which it was not directly based suggest the model has internal and external validity. Specifically, 5-year limb salvage rates that are 79% and equivalent for endovascular and surgical strategies are comparable to the results of the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial and several high-quality observational studies that report long-term outcomes,[19,35-37] and projected 5-year survival rates of 51% to 52% for the various strategies are consistent with clinical trials and large clinical studies.[18,36-38] Although there are plentiful data on limb salvage and patient survival rates in the published literature, for example, much less data are available for health utilities before or after limb salvage efforts. Uncertainty can be accounted for in the model to some degree, but the potential for uncertainty or inaccuracy to nevertheless lead to biased ICER estimates does remain.

CONCLUSIONS

This study suggests that although endovascular-first and surgery-first strategies can both achieve comparable long-term limb salvage rates, surgical bypass (especially with endovascular revisions as needed) is the most cost-effective alternative to local wound care alone for the management of CLI with tissue loss. Primary amputation is as costly as bypass, yet it provides less benefit than local wound care and is thus dominated by these other management strategies. Vascular clinicians should weigh clinical benefits as well as costs in choosing management strategies, because providing cost-effective care is in the interest of not only patients and payers but also health care providers.

AUTHOR CONTRIBUTIONS

Conception and design: NB, MB
Analysis and interpretation: NB, JC, JC, MB
Data collection: NB, MB
Writing the article: NB, JC, JC, MB
Critical revision of the article: NB, MB
Final approval of the article: NB, MB
Statistical analysis: NB, JC, JC, MB
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Overall responsibility: NB, MB

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APPENDIX A

The Model to Optimize Healthcare Value in Ischemic Extremities 1 (MOVIE) Study Collaborators. The Brigham and Women's Hospital, Division of Vascular and Endovascular Surgery, Department of Surgery (Boston, Mass): Michael Belkin, MD; C. Keith Ozaki, MD; Louis L. Nguyen, MD, MPH, MBA; Matthew T. Menard, MD; James T. McPhee, MD; and Marcus E. Semel, MD, MPH.

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APPENDIX B (online only)

Methodology for obtaining cost estimates. To obtain inpatient hospitalization cost estimates, we first identified all patients undergoing index interventions for critical limb ischemia (CLI) with tissue loss, specifically, nonhealing ulcers, dry gangrene of toe(s) or foot, or nonhealing wounds after minor amputation, in the context of a salvageable foot (ie, Rutherford category 5 limb ischemia) through a comprehensive search of the operating room and endovascular suite registries at the Brigham and Women's Hospital, starting on January 1, 2009, and proceeding forward chronologically. Patients were included for analysis if the procedure performed included any of the following major interventions: (1) an initial infrainguinal surgical bypass with vein graft conduit, (2) an initial endovascular intervention (including angioplasty and selective stenting†) for infrainguinal arterial occlusive disease, or (3) primary major amputation, including amputations below, through or above the knee.

Once these patients were identified, the total costs (direct plus indirect costs‡) of their full inpatient hospital stays were obtained and categorized by index intervention. These direct and indirect costs[2] were calculated using our institution's transition cost accounting system (Eclipsys Solutions Corp, Boca Raton, Fla) to obtain individual patient-level activity-based estimates[17] of the total cost for inpatient hospitalizations. A median cost and cost distribution was then obtained based on the sample of patients undergoing various interventions.

In a similar fashion, the costs of the inpatient hospitalizations associated with the following secondary procedures were also calculated: (1) endovascular revision of a threatened, failing, or failed bypass graft, including percutaneous thrombectomy, angioplasty, and stenting; (2) surgical revision of a threatened, failing, or failed bypass graft, including thrombectomy and revision of the bypass graft; or (3) foot wound care-associated procedures, including debridement, skin grafting, and any amputations limited to the forefoot or midfoot such as toe amputations or transmetatarsal amputations. A total of 21,206 cost items associated with 86 patients with Rutherford category 5 limb ischemia were reviewed and used in cost calculations. The cost data were obtained under the approval of Brigham and Women's Hospital/Partners Human Research Committee Institutional Review Board (Protocol #2010-P-002227/1).

†In contrast to direct costs (costs that can be directly linked to an individual patient or particular unit of production), indirect costs include "overhead" and capital costs, which are more difficult to allocate among patients. Examples of such costs include hospital administration, housekeeping, the costs associated with the use of an operating room for an interval of time.

‡In the cost data from our institution, the total direct and indirect procedural costs for patients undergoing endovascular intervention represented 44% of the total cost of hospitalization, and the cost of stents represented just 5.6% of the total cost of hospitalization. Atherectomy devices, cryoplasty balloons, and reentry devices were not used at this center.