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Cost-effectiveness of laparoscopic hysterectomy with morcellation compared to abdominal hysterectomy for presumed fibroids

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Abstract

Study objective—Hysterectomy for presumed leiomyomata is one of the most common surgical procedures performed in non-pregnant women in the United States. Laparoscopic hysterectomy (LH) with morcellation is an appealing alternative to abdominal hysterectomy (AH), but may result in dissemination of malignant cells and worse outcomes in the setting of an occult leiomyosarcoma. We sought to evaluate the cost-effectiveness of LH versus AH.

Study Design—Decision-analytic model of 100,000 women in the United States assessing the incremental cost-effectiveness ratio (ICER) in $/QALY gained.

Design Classification—Canadian Task Force Classification III

Setting—U.S. hospitals.

Patients—Adult premenopausal women undergoing LH or AH for presumed benign leiomyomata.

Interventions—We developed a decision-analytic model from a provider perspective across five-years, comparing the cost-effectiveness of LH to AH in terms of dollar (2014 USD) per quality adjusted life-year (QALY) gained. The model included average total direct medical costs and utilities associated with the procedures, complications, and clinical outcomes. Baseline estimates and ranges for cost and probability data were drawn from the existing literature.

Measurements and Main Results—Estimated overall deaths were lower in LH vs AH (98 vs 103). Death due to leiomyosarcoma was more common in LH vs AH (86 vs 71). Base-case

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assumptions estimated that average per person costs were lower in LH vs AH - a savings of $2,193 ($24,181 vs $26,374). Over five years, women in LH group experienced 4.99 QALY, versus women in AH group with 4.91 QALY (incremental gain of 0.085 QALYs). LH dominated AH in base-case estimates - LH being both less expensive and yielding greater QALY gains. The ICER was sensitive to operative costs for LH and AH. Varying operative costs of AH yielded an ICER of $87,651/QALY gained (minimum) to AH being dominated (maximum). Probabilistic sensitivity analyses, in which all input parameters and costs were varied simultaneously, demonstrated a relatively robust model. The AH approach was dominated 68.9% of the time. 17.4% of simulations fell above the willingness-to-pay threshold of $50,000/QALY gained.

Conclusions—When considering total direct hospital costs, complications, and morbidity, LH was less costly and yielded more QALYs gained versus AH. Driven by the rarity of occult leiomyosarcoma and the reduced incidence of intra- and postoperative complications, LH with morcellation may be a more cost-effective and less invasive alternative to AH and should remain an option for women needing hysterectomy for leiomyomata.

Introduction

Hysterectomy for presumed leiomyomata (fibroids) is one of the most common surgical procedures performed in non-pregnant women in the United States, with over 200,000 performed annually [1]. Surgeons increasingly employ less invasive laparoscopic techniques for both supracervical and total hysterectomies, shortening hospital stay and recuperation time [2,3]. In laparoscopic procedures, when the uterus is too large to be removed intact vaginally, the specimen must be cut into smaller pieces for removal via the smaller abdominal incisions. This dissection of solid tissue, so-called morcellation, may result in unintentional intra-abdominal spread of tissue fragments [4,5]. In the setting of previously undiagnosed leiomyosarcoma, morecellation may result in dissemination of malignant cells. The consequences of morcellation in the context of occult malignancy has sparked a heated debate regarding the risks associated with laparoscopic hysterectomy and morcellation [6].

The prevalence of occult leiomyosarcoma among women undergoing hysterectomy for presumed fibroids is not precisely known, but available reports indicate it is extremely rare [5,7–9], and difficult to distinguish from benign disease preoperatively [10]. For women with large fibroids, the benefits of a laparoscopic approach to hysterectomy—lower overall mortality, fewer intraand postoperative complications, improved quality of life, and lower cost—must be weighed against the uncommon risk of morcellation of an occult malignancy [3,10,11]. With governing bodies and hospital systems struggling with how to best address this clinical problem, additional insights into both the health and economic consequences of laparoscopic and abdominal hysterectomies are critically needed.

In this study, we evaluated the cost-effectiveness of laparoscopic hysterectomy with morcellation for removal of presumed fibroids as compared to abdominal hysterectomy. We estimated the total per person direct hospital costs associated with both procedures and the anticipated associated intraoperative and postoperative complications from existing literature. Our primary outcome was the incremental cost-effectiveness per quality adjusted life year (QALY) gained.

Methods

We developed a decision-tree model (Figure 1), constructed using Excel™ 2010 (Microsoft Corp, Redmond, WA, USA) and TreePlan™ (TreePlan Software, San Francisco, California) to simulate costs, outcomes, and incremental cost-effectiveness ratios (ICERs) comparing laparoscopic hysterectomy with morcellation (LH) to abdominal hysterectomy (AH). AH is considered the base case scenario, with LH evaluated as the alternative. An ICER in which the alternative (LH) is less expensive and more effective (more QALYs gained) compared to AH would be interpreted as "dominant" [12]. Costs and outcomes were evaluated across a 5-year time horizon. This study was considered exempt from review by the Institutional Review Board at the University of North Carolina at Chapel Hill, as it involved synthesis and analysis of existing published data.

Mortality, complications, and quality of life

Assumptions regarding anticipated clinical events and associated QALYs are presented elsewhere [13]. Briefly, we simulated a hypothetical cohort of 100,000 adult premenopausal (i.e., still menstruating) women undergoing either LH or AH for presumed benign leiomyomata. This hypothetical cohort is limited to women with a uterus large enough that it would either require laparotomy or laparoscopy with morcellation. Women who could have intact removal through the vagina are not included as they are not the focus of this investigation. We examined frequency of transfusion, wound infection, venous thromboembolism (VTE), incisional hernia, vaginal cuff dehiscence, overall mortality, and complications associated with occult leiomyosarcoma. All women were at risk for surgical complications associated with hysterectomy, represented as unique and independent health states in the model. The base-case estimates and ranges for mortality, probabilities of complications, and utilities were determined by literature review (Table 1). We derived leiomyoscarcama estimates, weighting high-quality more recent studies with larger sample size that used pathologic diagnostic criteria. The base case estimate for leiomoysarcoma risk (6/5084; 0.0012) was derived using mean estimates of leiomoysarcoma rates from the four highest-quality studies – 0.0008[9], 0.0007 [7], 0.0009 [5], 0.0023[8]. The range that was used in one-way and probabilistic sensitivity analyses use the lowest and highest reported rate of occult disease among studies with a sample size greater than 1000, ranging from 0.0007[7] to 0.0049 [14], a range inclusive of the most recent FDA estimate[6].

In terms of sarcoma-related mortality, the estimates from death from sarcoma were taken from SEER based 5-year mortality reporting on LMS outcomes in the United States and varied depending on if a woman underwent TAH or TLH based on the presumed up-staging of disease due to dissemination during morcellation. We assumed that women with metastatic disease would be identified preoperatively and would not be included in this hypothetical cohort. Survival of women with distant metastases is likely driven by the metastatic disease, so morcellation would not change their stage nor impact overall survival, meaning the post-operative prognosis would not vary for women with preoperative stage IV disease. We assumed that occult LMS in a woman undergoing TAH is represented by International Federation of Gynecology and Obstetrics stage I or stage II diagnosis (confined to the pelvis) and that morcellation (TLH), with its theoretical dissemination of cancer cells,

would, at worst lend the same poor prognosis as spontaneous cancer metastasis, a stage III diagnosis (extra-pelvic disease). Therefore, the probability of death following sarcoma after TAH was set as 5 year death rate of stage I–II (weighted average) disease (0.59), and the probability of death following sarcoma after TLH was set at 5 year death rate of stage III disease: 0.72[15]. Thus all women with occult LMS who underwent TLH were given a worse prognosis than those undergoing TAH. The survival was not calculated annually, as the best population-estimates available are traditional 5-year rates. We also examined more recent observational studies of LMS cohorts, including 315 patients treated from 1982 – 2010 [16–18]. These were similar to the population-based SEER estimates and therefore the estimates were not changed. We assumed that patients with LMS received adjuvant chemotherapy regimens (gemcitabine and carboplatin).

Health utility estimates were derived for each health state, accounting for the average duration that an individual would remain in that state.

Cost inputs

We used a provider perspective and included direct medical costs associated with surgical procedures, intraoperative or postoperative complications, and cancer-related care, as reported in the literature (Table 1). For women with leiomyosarcoma, we included costs associated with cancer-directed treatment and/or palliative care, as reported in the literature. The costs that we report are direct medical costs or reimbursed medical costs in US dollars for care delivered, as opposed to prices charged. We chose this approach to costing because prices charged vary substantially across hospitals and settings, may not be generalizable to all patients, and may not be indicative of actual resources required to deliver services. Because we employed the provider perspective, indirect, non-medical costs (such as patient transportation costs) were not relevant and were not included in our analysis.

All costs (in 2014 USD) were derived from published literature. Costs collected prior to 2014 were inflated using historical consumer price index data for urban consumers, medical care expenditure category [19]. Procedural costs for abdominal and laparoscopic hysterectomies were derived from retrospective cohort analyses [20,21], and a randomized clinical trial [22]. In this case, surgical procedural costs were derived from micro-costing approaches and included operative expenses, supplies, equipment and instruments, and physician and staff costs. Operative expenses were derived using accounting ledgers, where costs were associated with operative time (staffing costs) using an institutional time-based linear algorithm. Both of the retrospective trials were conducted in the US. By contrast, the randomized clinical trial was conducted in Sweden, and in that setting, the procedural costs, including equipment and OR-related staffing expenses, were considerably less than those reported by the US-based trials. Accordingly, we used the Swedish estimates as the low-end of the cost range for procedure-associated costs.

Costs for surgery-related complications were derived from several sources. Transfusion costs included total direct hospital costs for laboratory services, staff labor, and materials[23,24]. Total direct hospital costs for management of surgical site infections were derived from patient-level micro-costing approach based on supplies and staff-time [25], and ICD-9 diagnosis codes for postoperative surgical site infections in gynecologic surgical

procedures [26]. Total direct hospital costs for hernia repair were based on a retrospective analysis of patients who underwent repair for a ventral hernia[27]. Estimates included average total direct hospital cost associated with length of stay, operating room time, time in intensive care units, resuscitation, and any costs associated with related readmissions. We were unable to identify costs associated with repair of vaginal cuff dehiscence and therefore assumed that the costs would be similar to those of hernia repair, based on the invasiveness of treatment and spectrum of clinical complications.

Published hospital cost data were not available for VTE or leiomyosarcoma therapy and associated end-of-life care. The best available studies rely on reimbursement, which is related to hospital costs, but not identical. However, we conducted sensitivity analyses to assess the impact of these cost inputs on overall model-projected cost and cost-effectiveness estimates. Costs for VTE were based on a retrospective cohort analysis of reimbursed costs from administrative insurance claims databases in large US private health care plans [28], and a retrospective analysis from a national database of hospital claims evaluating provider payments and reimbursements for cost of hospitalization [29]. Chemotherapy costs were derived from Medicare reimbursements processed from ICD-9 diagnosis codes and procedural codes (CPT and HCPCS codes) for the treatment of leiomyosarcoma assuming six one-month cycles of concurrent docetaxel and gemcitabine, and included drug costs and costs associated with drug-related toxicities (neuropathy and neutropenia), weighted probabilistically based on the likelihood that such toxicities occur[30]. In addition to drug and toxicity management costs, cancer care costs included physician visits, all infusion and related /treatment charges, and the costs of standard pretreatment medications. We assumed that patients who did not respond to the first six-month cycle of chemotherapy would incur costs associated with a second six-month cycle and eventually end-of-life care. Costs associated with end-of-life care were based on reimbursements from Medicaid administrative claims data among beneficiaries who died after a cancer diagnosis compared to a matched cohort of beneficiaries who died of other causes, using reimbursed costs specific to gynecologic cancer patients[31].

Base case analysis

We used base case cost and utility estimates to compare differences between AH and LH. We subtracted the base case AH costs from LH costs and base case AH utilities from LH utilities, and then divided the cost difference (incremental cost) by the difference in utilities (incremental effectiveness) to yield the base case ICER.

Sensitivity analyses

We performed one-way, deterministic sensitivity analyses for parameters identified as major drivers of the ICER outcome, holding all else constant. We conducted a probabilistic sensitivity analysis (PSA) using Monte Carlo simulations (1000 trials) for the ICER outcome (Crystal Ball version 11.1.2.3 [Oracle, Redwood Shores, CA, USA]). In this process, probability distributions are assigned based upon expected ranges for all input parameters (probabilities, utilities, and costs) and then values for each parameter are drawn randomly from within these distributions to generate our outcome of interest [3233]. Table 1 details the distributions that we used in the PSA. For example, for an input parameter with a

triangular distribution, with each simulation, the value of that point estimate may be anywhere within the pre-defined parameter range, with values closer to the base case being more likely to be drawn than those towards the tail (minimum and maximum). In this way, we vary the inputs across the parameter range in 1000 distinct scenarios, and in doing so, examine the uncertainty around all ranges. The probabilistic sensitivity analysis allows for natural stochasticity due to chance as well as uncertainty in the value of input parameters that may arise across diverse studies and samples.

The range of probability parameters are detailed elsewhere[13]. In brief, all probabilities were selected using literature review of primary data, with preference to higher quality and more recent studies that appropriately reflect advances in the field. Table 1 details the base case parameter values employed as well as relevant ranges selected for sensitivity analyses. Probabilities and utility estimates assumed triangular distributions. Given limited reports on utilities for the health states in our model, all utilities were varied by 20% above and below the base-case estimate. We assumed a gamma distribution for costs considering the base-case estimate evaluated over the literature-informed range[12]. Gamma distributions were selected for utilities in that this distribution is constrained to be positive and fully continuous.

Because total direct hospital cost data were not available for VTE or leiomyosarcoma-related costs (chemotherapy and/or end-of-life care), we conducted extensive a priori individual one-way sensitivity analyses with these cost inputs, varying base case estimates by +/− 40%.

In an alternative scenario, we modeled the effect of patients with progressive leiomyosarcoma dying in year two of the model, rather than surviving to year five. In this analysis, patients with leiomyosarcoma who did not respond to the initial six-month course of chemotherapy no longer contributed QALYs to the model beyond year two. These women still received a second course of chemo and end-of-life care. This represents a more conservative scenario that would tend to favor AH, as more women in the LH arm may have progressive leiomyosarcoma.

Results

In our model of 100,000 premenopausal women undergoing hysterectomy for presumed leiomyomata, we estimated that overall deaths were lower in LH vs AH (98 vs 103). However, death due to leiomyosarcoma was more common in LH vs AH (86 vs 71). Using base-case assumptions, we estimated average per person costs as lower in LH compared to AH, resulting in a savings of $2,193 for LH patients ($24,181 vs $26,374) (Table 2). Over five years, women in the LH group experienced 4.99 QALY, compared to women in the AH group with 4.91 QALY, for an incremental gain of 0.085 QALYs. As such, LH dominated AH in base-case estimates, with LH being both less expensive and yielding greater QALY gains.

Sensitivity analyses

In one-way sensitivity analyses, we estimated the potential range of ICERs across the probable range of input parameters (Table 3). The ICER was especially sensitive to operative costs and the estimated quality-of-life decrement associated with AH. Using the minimum ($7,268) and maximum ($35,584) estimate for LH operative costs, the ICER comparing LH to AH varied from AH being dominated (negative ICER) to LH resulting in $120,259/QALY gained, which is above the commonly accepted $50,000/QALY gained threshold, indicating that we would not adopt LH over AH. Univariate analyses that varied operative costs of AH between minimum ($12,281) and maximum ($32,648) yielded an ICER of $87,651/QALY gained when evaluated at the minimum AH operative cost, to AH being dominated at the maximum AH operative cost. These analyses suggest that the ICER is very sensitive to the operating costs of LH and AH. Varying the utility estimate for the health-related quality of life associated with undergoing AH (0.72, 1.0) continued to demonstrate that LH dominated AH across the predefined range of utilities for this parameter.

Because we had to rely on reimbursement instead of total direct hospital costs for VTE, leiomyosarcoma treatment, and end-of-life care, we conducted one-way sensitivity analyses for the inputs, extending the range +/−40% of base case. Results suggest that the ICER outcome was not sensitive to these costs; AH remained dominated across the wide range of costs for each parameter.

Probabilistic sensitivity analyses, in which all input parameters and costs were varied simultaneously, demonstrates a relatively robust model. Each draw results in a new incremental cost and incremental effectiveness of LH compared with AH. Resulting point estimates (Figure 2) represent the ICERs of the 1000 draws executed through Montel Carlo simulations. The AH approach is dominated (i.e., the strategy is both less effective and more costly compared with LH) 68.9% of the time. The remaining 31.1% of simulations lie in the “tradeoff” zone in which LH is both more effective and more costly than AH; 17.4% of simulations fell above the willingness-to-pay threshold of $50,000/QALY gained.

The base-case ICERs continued to demonstrate LH dominating AH when women with leiomyosarcoma died in year two of the model, rather than living at reduced quality-of-life for years three to five.

Discussion

In our base case analysis, we found that LH dominated AH. When considering the total direct medical costs associated with each procedure, resulting complications, and morbidity, LH was less costly and yielded more QALYs gained compared to AH. Despite the potential risks associated with dissemination of malignant tissue during the morcellation process, the rarity of preoperatively undiagnosed leiomyosarcoma and the reduced intra- and postoperative complication rates suggest that on a population level, across the probable range of inputs, LH is likely a more cost-effective alternative compared to AH. Probabilistic sensitivity analyses demonstrate robust model performance with simultaneous and random draws from the probable range of complication probabilities, estimated utilities, and

associated costs. In simulations, the majority of ICER outcomes were negative; that is, compared to AH, LH was less costly and marginally more effective in terms of QALYs gained.

The incremental QALYs gained were minimal comparing LH to AH. This suggests that despite the less-invasive laparoscopic approach, LH is associated with only moderate benefits in terms of QALYs once the risk of leiomyosarcoma is considered. This limited variability in QALYs is likely driven by the fact that most women proceed through the model without experiencing any complication. Women in the LH group who do not experience complications are modeled as having a health-related quality-of-life of 1 (maximum utility) throughout the five-year model time horizon. Conversely, women in the AH group who do not sustain complications, the majority of women, experience decreased health-related quality-of-life associated with recovery from an open surgical procedure (0.9) for the six-month period immediately following surgery [34]. However, even in a sensitivity analysis adopting the more conservative assumption that women undergoing AH do not have any health-related quality-of-life decrement postoperatively, the ICER for LH continued to dominate AH.

Importantly, perceived utility of a given health state, and thus the estimated QALY resulting from occupying that health state, may vary according to age, income status, and other socioeconomic factors. Granular detail specifying this level variation within this particular patient population is not currently available, and therefore, aggregate health utility estimates may mask some of the demographic and socioeconomic variation in these values. We attempted to mitigate this limitation by varying all utility estimates by 20% above and below the base-case estimate. However, future studies should seek to explore sub-population specific variation in health related quality of life reporting.

Women undergoing AH were more likely to experience an immediate (i.e., transfusion) and/or longer-term (i.e., hernia) complication. Vaginal cuff dehiscence was the only complication that was more common among women undergoing LH[35–37], perhaps attributable to electrosurgical rather than sharp colpotomy or inadequate tissue inclusion during cuff closure[38,39]. The consequences of vaginal cuff dehiscence are highly variable, depending on the degree of evisceration. We did not explicitly model the variability of dehiscence complications, but rather focus on its average morbidity and costs.

Total direct hospital cost data were drawn primarily from US-based studies. Operative costs for AH and LH, the major driver of ICER outcomes, were from studies conducted in the last five years. More recent cost estimates for some complications, including transfusion, surgical site infection, and VTE, were not available. However, these costs did nto dramatically influence ICER estimates in sensitivity analyses. There was variability in the method of ascertaining costs across studies, resulting in uncertainty regarding the estimated costs. Ideally, all costs, including those associated with the procedure and any follow-up interventions due to procedural complications, would be assessed using micro-costing techniques in which a cohort of patients was followed prospectively and all costs obtained using hospital data. However, this highly intensive approach was not feasible and was beyond the scope of this study. Nevertheless, in sensitivity analyses, we were able to address

the uncertainty associated with costs and found that despite varying reimbursement-derived costs by a generous +/−40% range and other costs according to the best available data, AH remained dominated by LH in the majority of simulations, demonstrating that these costs were not a major driver of our ICER outcome. Indeed, in extensive sensitivity analyses pursued in this study, the only costs that had a substantial influence on ICER outcomes were the procedural costs of LH and AH, which came from robust cohort and randomized trials using total direct hospital cost estimates. Assessment and inclusion of indirect costs were beyond the scope of this study due to our provider perspective. However, inclusion of indirect costs, such as time away from work (lost wages, lost productivity), would likely favor LH over AH given differences in expected recovery time.

Our original decision analysis and this cost-effectiveness analysis focused on laparoscopic hysterectomy. Data are mixed regarding cost robotically-assisted hysterectomy[40–42]. If the robotic platform indeed raises the cost of the operation, it would temper the benefit observed for laparoscopy in this cost analysis. That said, while clear advantages for laparoscopy over laparotomy in patient outcomes, there are no demonstrable advantages for robotic laparoscopy over conventional laparoscopy. In the context of this model, morcellation captures all procedures involving the cutting of uterine tissue to facilitate laparoscopic removal. Data are lacking regarding safety differences between various morcellation techniques, preventing stratification by type of morcellation. The few studies that suggest survival differences in patients with leiomyosarcoma comparing surgery with and without morcellation include a heterogeneous set of extraction modalities[11,43].

There are limited and highly variable data regarding the incidence of occult leiomyosarcoma in the setting of hysterectomy for presumed leiomyomata[5,7–9,14,44–48]. We modeled the increased risk of disease progression and mortality in the setting of morcellation with LH compared to AH. Even at the highest incidence estimate, the ICER for LH continued to dominate AH. Ongoing endeavors to develop improved containment tools during uterine extraction or improved diagnostics to distinguish between benign and malignant myomata could markedly reduce risk associated with tissue dissemination during morcellation. We chose to focus specifically on leiomyosarcoma because this is the malignancy which mimics large leiomyomata and our knowledge of the effect of morcellation on leiomyosarcoma (limited as it is) is better understood than the effect on other malignancies [49]. We did not model endometrial or cervical cancers explicitly, as these are distinct entities from leiomyosarcoma in that we have significantly better preoperative diagnostic testing for endometrial and cervical cancer. Furthermore, uteri with occult endometrial or cervical cancer can presumably be much more frequently be delivered intact through the vagina, avoiding morcellation altogether, and thus are less relevant to the model as designed here.

This cost-effectiveness analysis, and the clinical outcomes analysis that preceded it [13], are meant to inform policymakers, clinicians, and other decision makers in what has emerged as the most debated issue in gynecologic surgery. Like all medical procedures, a woman's decision to undergo laparoscopic or abdominal hysterectomy should include a thorough discussion of risks, and must consider patient-specific circumstances, values, preferences, and risk-aversion. Driven by the rarity of occult leiomyosarcoma and the reduced incidence of intra- and postoperative complications, LH with morcellation may be a more cost-

effective and less invasive alternative to AH and ought to remain an option for women needing hysterectomy for large fibroids.

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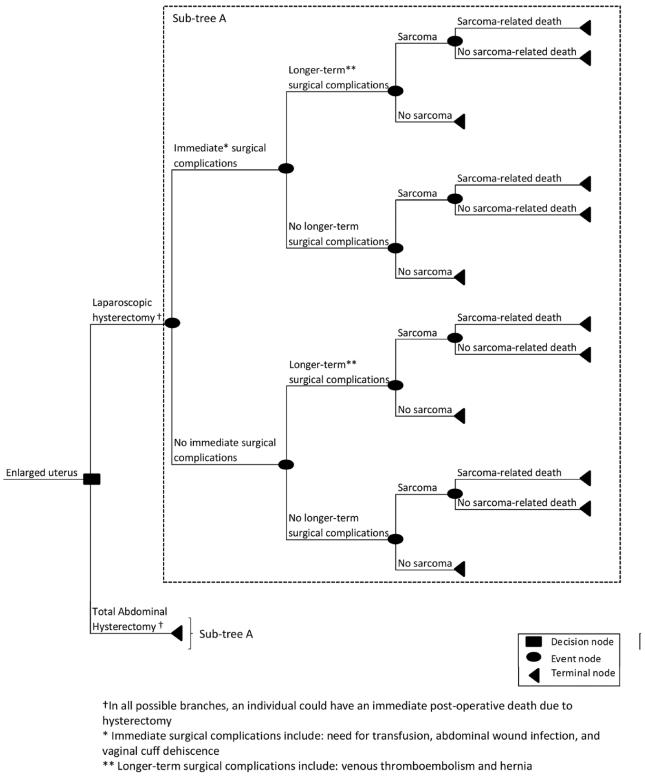

Figure 1. Decision Tree

Women requiring hysterectomy for an enlarged uterus could undergo laparoscopic or abdominal hysterectomy. In either approach, death could occur immediately after the procedure. Women who survive the procedure could experience immediate surgical complications (blood transfusion, wound infection, or vaginal cuff dehiscence) and/or longer term surgical complications (hernia and venous thromboembolism). Women who had occult leiomyosarcoma at the time of the procedure would undergo treatment, after which point they could recover or die (sarcoma-related death). (Reproduced with permission from reference 13)

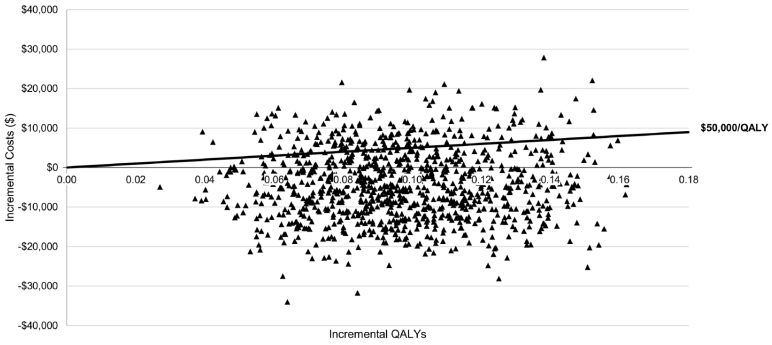

Figure 2. Laparoscopic vs. abdominal hysterectomy incremental cost-effectiveness plane

In the ICER plane, the horizontal axis represents the difference in QALY gained between LH and AH. The vertical axis represents the difference in cost. These differences are therefore the incremental effectiveness (QALY gained) and incremental costs (dollars) when comparing LH to AH. Each triangle represents an ICER corresponding to the outcome observed in the probabilistic sensitivity analysis. The dark solid line from the origin extending into the upper right quadrant represents the willingness-to-pay threshold of $50,000/QALY gained – any point falling above this line would exceed that threshold. Approximately 17% of all estimated ICER points fall above this line. Points that fall to the right of 0 on the x-axis and below 0 on the y-axis represent scenarios in which LH is both more effective and less costly than AH. This represents a dominant scenario. Approximately 68% of all estimated ICER points are cost savings where LH is dominant.

Table 1

Input probabilities, utilities, and costs

Parameter	Laparoscopic hysterectomy[1] Prob	[range]	Abdominal hysterectomy[1] Prob.	[range]	Refs (prob)	Utility[1]	[range][a]	Refs (utility)	Cost[2,b] ($)	[range]	Refs (cost)
Hysterectomy for fibroids (LH)	--	--	--	--	--	--	--	--	23,218	[7,268, 35,584]	20 – 22
Hysterectomy for fibroids (AH)	--	--	--	--	--	0.9	[0.72, 1.0]	34	21,889	[12,281, 32,648]	20,21,51
Transfusion	0.024	[0.013, 0.035]	0.047	[0.043, 0.047]	3,52,53	0.48	[0.38, 0.58]	54	3,254	[2,293, 4,445]	23,24
Surgical site infection	0.015	[0.00055, 0.015]	0.063	Not varied	3,52	0.607	[0.49, 0.73]	55	7,766	[5,934, 20,143]	25,26,56
Vaginal cuff dehiscence	0.0064	[0.0002, 0.0089]	0.0029	[0.0015, 0.006]	35 – 37	0.54	[0.43, 0.65]	55	39,601[c]	[26,647, 58904]	27
Venous thromboembolism	0.0069	[0.003, 0.009]	0.0084	[0.0072, 0.0084]	3,52,53,57,58	0.8	[0.64, 0.96]	59	15,086	[13,003, 23,241]	28,29
Hernia	0.0071	[0.0014, 0.09]	0.00880	[0.045, 0.098]	60 – 64	0.77	[0.62, 0.92]	65	39,601	[26,647, 58,904]	27
Occult leiomyosarcoma incidence	0.0012	[0.0007, 0.0049]	0.0012	[0.0007, 0.0049]	5,7–9,14	--	--	--	--	--	--
Procedure-related death	0.00012	[0.000096, 0.00012]	0.00032	[0.00032, 0.00038]	52,53,66	--	--	--	--	--	--
5-year mortality from leiomyosarcoma	0.72	Not varied	0.59	Not varied	15	--	--	--	--	--	--
Leiomyosarcoma (1st 6-month chemotherapy)	--	--	--	--	--	0.76	[0.61, 0.91]	67	43,179	[34,543, 51,815]	30
Leiomyosarcoma progression (2nd 6-month chemotherapy)	--	--	--	--	--	0.66	[0.53, 0.79]	67	43,179	[34,543, 51,815]	30
Leiomyosarcoma progression (palliative care)	--	--	--	--	--	0.71	[0.57, 0.85]	68	47,967	[38,374, 57,560]	31

AH, abdominal hysterectomy; LH, laparoscopic hysterectomy; prob, probability; Refs, references

[a] Range based on +/− 20% of base-case utility. If +20% exceeded 1.0, the utility was assigned a value of 1.0

[b] Costs inflated to 2014 US dollars using historical consumer price index for urban consumers, medical care expenditure category

[c] Cost data not available for vaginal cuff dehiscence. Assumed to be identical to cost for hernia repair.

[1] Triangular distribution;

[2] Gamma distribution

Table 2

Base-case cost-effectiveness of laparoscopic vs abdominal hysterectomy

	Total direct costs (per person)	Total QALYs* (per person)	Incremental costs	Incremental effectiveness (QALYs)	ICER ($/QALY gained)
Laparoscopic hysterectomy	$24,181	4.99	−$2,192	0.085	dominates
Abdominal hysterectomy	$26,374	4.91	--	--	--

QALY, Quality-adjusted life-year

* QALYs evaluated over 5-year model period

Table 3

One-way sensitivity analyses

Parameter	Minimum input	ICER ($/QALY gained)	Maximum input	ICER ($/QALY gained)
Operative cost (LH)	$7,268	dominates	$35,584	120,259
Operative cost (AH)	$12,281	87,651	$32,648	dominates
Utility associated with hysterectomy for fibroids (AH)	0.72	dominates	1.0	dominates

AH, abdominal hysterectomy; ICER, incremental cost-effectiveness ratio; LH, laparoscopic hysterectomy; QALY, quality-adjusted life-year Dominates indicates a negative ICER, in which LH is both less expensive and more effective compared to AH

Notes: This table depicts one-way sensitivity analyses in which each parameter (left column) was varied was varied in turn according to pre-specified ranges, holding all else constant. The table presents the sensitivity analysis outcomes, in rank-order, of the parameters that had the most significant effect on our outcome (ICER). For example, the estimated operative costs of LH were the biggest driver: when this input parameter was set to the low-end of the estimated range ($7,268), LH dominates AH – it is both less expensive and yields more QALYs. However, when the cost of LH is instead set to the high-end of the estimated range ($35,584), the $/QALY comparing LH to AH is $120,259/QALY. “Operative costs” were derived from micro-costing approaches and included operative expenses, supplies, equipment and instruments, and physician and staff costs. The process of varying inputs between their low and high range, holding all else constant, was then repeated for all parameters; the three most influential are presented here.