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Laparoscopic hysterectomy with morcellation versus abdominal hysterectomy for presumed fibroids in premenopausal women: a decision analysis

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Abstract

Objective—To model outcomes in laparoscopic hysterectomy with morcellation compared to abdominal hysterectomy for the presumed fibroid uterus, examining short-and long-term complications, as well as mortality.

Study Design—A decision tree was constructed to compare outcomes for a hypothetical cohort of 100,000 premenopausal women undergoing hysterectomy for presumed fibroids over a 5-year time horizon. Parameter and quality of life utility estimates were determined from published literature for postoperative complications, leiomyosarcoma incidence, death related to leiomyomsarcoma, and procedure-related death.

Results—The decision analysis predicted fewer overall deaths with laparoscopic hysterectomy compared to abdominal hysterectomy (98 vs. 103 per 100,000). While there were more deaths from leiomyosarcoma following laparoscopic hysterectomy (86 vs. 71 per 100,000), there were more hysterectomy-related deaths with abdominal hysterectomy (32 vs. 12 per 100,000). The laparoscopic group had lower rates of transfusion (2,400 vs. 4,700 per 100,000), wound infection (1,500 vs 6,300 per 100,000), venous thromboembolism (690 vs. 840 per 100,000) and incisional hernia (710 vs. 8,800 per 100,000), but a higher rate of vaginal cuff dehiscence (640 vs. 290 per 100,000). Laparoscopic hysterectomy resulted in more quality-adjusted life years (499,171 vs. 490,711 over five years).

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Conclusion—The risk of leiomyosarcoma morcellation is balanced by procedure-related complications associated with laparotomy, including death. This analysis provides patients and surgeons with estimates of risk and benefit, upon which patient-centered decisions can be made.

Keywords

Abdominal Hysterectomy; Laparoscopic Hysterectomy; Morcellation; Uterine fibroids

Introduction

Hysterectomy is the most common procedure performed in non-pregnant women in the United States, with leiomyomata (fibroids) the indication for a significant proportion of these.[1] Surgeons are increasingly employing laparoscopy for hysterectomy.[2] For all laparoscopic supracervical hysterectomies and total laparoscopic hysterectomies where the specimen is too large to be removed intact vaginally, the uterus must be morcellated—i.e. cut into pieces which will fit through small incisions. If morcellation is not contained in a retrieval bag, tissue may be unintentionally left behind, which can lead to spread of benign or malignant tissue.[3,4]

Morcellation has come under scrutiny regarding the risk of disseminating occult leiomyosarcoma, highlighted by a recent Food and Drug Administration safety notification.[5] Unlike other gynecologic malignancies, leiomyosarcoma is difficult to distinguish from benign disease preoperatively and bears a poor prognosis.[6] Retrospective studies suggest a worse prognosis with morcellation of leiomyosarcoma compared to intact removal of the uterus.[7,8]

Laparoscopic hysterectomy affords shorter hospital stay and convalescence compared to abdominal hysterectomy. In addition, laparoscopic hysterectomy is associated with less pain, lower blood loss, and lower rates of wound infection, incisional hernia, and venous thromboembolism.[9] On the other hand, abdominal hysterectomy avoids the risk of morcellating leiomyosarcoma. To provide physicians with better estimates of health outcomes when considering these surgical approaches, we conducted a decision analysis comparing laparoscopic hysterectomy to abdominal hysterectomy for the management of the enlarged uterus with presumed benign leiomyomata in premenopausal women, examining mortality, surgical complications, and quality of life.

Materials and Methods

We constructed a decision tree to compare outcomes of laparoscopic hysterectomy with morcellation to abdominal hysterectomy for women with an enlarged uterus due to presumed benign leiomyomata (Figure 1). We assessed a hypothetical cohort of 100,000 premenopausal women, as approximately 200,000 hysterectomies are performed for leiomyomata annually in the United States.[1] It made clinical sense that roughly half of those could involve uteri large enough to require morcellation if considered for laparoscopic hysterectomy. The decision tree model was constructed using Excel ™ 2010 (Microsoft Corp, Redmond, Washington) and TreePlan ™ (TreePlan Software, San Francisco, California).

Women undergoing both laparoscopic and abdominal hysterectomy were at risk for potential surgical complications, each represented as unique and independent health states in the model. Morbidity and mortality outcomes were evaluated over 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 analysis of existing published data. S.W., S.R., and M.S. were responsible for analyzing data.

Base-case estimates and ranges for each parameter, as well as transition probabilities governing movement between branches in the decision tree, were determined by published literature review (Table 1). In selecting estimates, preference was given to higher quality studies and more recent publications, reflecting advances in surgical practice. Surgical complications in the model included transfusion, abdominal wound infection, vaginal cuff dehiscence, venous thromboembolism, incisional hernia, leiomyosarcoma, death from leiomyosarcoma, and death from hysterectomy. Febrile episodes and vaginal cuff infections were considered but felt better represented by identifiable and more objective diagnoses, wound infection and cuff dehiscence. Major visceral and vascular adverse events were not included as they are rare and not significantly different between laparoscopic and abdominal hysterectomy.[10]

Mortality rates due to hysterectomy were reflected in the literature as a short-term outcome and were not categorized by a specific cause (e.g. fatal embolic event). Excluding older studies conducted when safety and prophylactic measures (e.g. infection, venous thromboembolism) were different from modern practice,[11,12] estimates of 0.00012 (laparoscopic hysterectomy) and 0.00032 (abdominal hysterectomy) were derived from three larger and more recent series.[13-15]

In terms of occult malignancy, we focused on leiomyosarcoma in particular as it mimics benign myomatous disease. Other more rare uterine mesenchymal tumors have diverse biologic behavior and the impact of morcellation on these tumors is unknown. Cerivical cancer is almost always a known preoperative diagnosis, and the risk of tissue dissemination appears to be less serious with endometrial cancer.[16] Ten sources were considered regarding the incidence of leiomyosarcoma among women undergoing hysterectomy for presumed fibroids (Table 2).[4, 17-25] Quality and the degree to which the study population mirrored that for our decision analysis was evaluated based on year of publication, menopausal status, number of subjects, geographical location, and pathologic criteria used to determine leiomosarcoma diagnosis. An estimate of 0.0012 (6/5084) was derived from what were considered the four highest quality sources, reporting mean estimates of 0.0008,[19] 0.0007,[22] 0.0009,[4] and 0.0023.[23] The range for sensitivity analysis included those with sample size greater than 1,000: 0.0007[22] to 0.0049.[17]

Leiomyosarcoma mortality estimates were derived from Surveillance, Epidemiology, and End Results reports.[26] First, we assumed women with metastatic disease would generally be identified pre-operatively and not candidates for our hypothetical cohort. In rare cases when it was not, surgical approach, with or without morcellation, would not change their stage (IV) and nor impact overall survival, which would be driven by the distant metastases. Therefore, occult leiomyosarcoma detected at the time of hysterectomy would be represented in the model by an International Federation of Obstetrics and Gynecology stage I or stage II (confined to the pelvis) diagnosis, with a 5-year mortality of 0.59. Second, we assumed morcellation could lend the same prognosis as spontaneous cancer spread, and thus the laparoscopic group was assigned a stage III (extra-pelvic disease) prognosis, with a 5-year mortality of 0.72 (i.e. all laparoscopic patients given a worse prognosis than abdominal patients).

In the model, morcellation indicated 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 which demonstrate survival differences in leiomyosarcoma patients who underwent surgery with and without morcellation include a heterogeneous set of extraction modalities.[7,8]

Health state utilities capture health-related quality of life and are measured on a scale of 0 to 1, where 0 represents death and 1 represents 1 year of life in perfect health. Each year of life spent at that health state can then be quantified in quality-adjusted life years. Using published literature, we derived utility estimates for each health state represented in the model as well as the average duration of each health state (Table 3).

To account for the possibility of experiencing multiple clinical events, each with varying duration and morbidity, we divided the 5-year (60-month) period into 1-month increments and used a selective weighted average to calculate 1-month utilities for each distinct pathway in the tree. We then summed across 5-years to obtain 5-year quality-adjusted life years for the laparoscopic and abdominal branches. To more accurately reflect real-world clinical scenarios, the model was built to reflect the fact that women could experience multiple clinical adverse events simultaneously (e.g., require a transfusion and have a wound infection). If events overlapped in time, the worse utility estimate was assigned for that period. We further assumed that death due to hysterectomy occurred immediately post-operatively—i.e., at the beginning of our study window. Accordingly, these persons contributed a utility weight of 0 to the model. For leiomyosarcoma-related deaths, these persons experience the quality-adjusted life-years associated with first- and second-line chemotherapy, as well as subsequent palliative care, and are assumed to die in year 5 of the model, using 5-year survival estimates.

Deterministic (one-way univariate) sensitivity analyses were performed to assess the robustness of the assumptions in the decision model,[27] including surgical complications, the probability of leiomyosarcoma, and probability of death from hysterectomy. The range of clinical outcomes (e.g. transfusion, wound infection, etc.) was evaluated by varying the input for each clinical event to its minimum and maximum. Given the limited reports on utilities for the health states in our model, we performed a sensitivity analysis by varying the utility by 20% higher and lower than each base-case estimate.

Results

The decision analysis predicted fewer overall deaths with laparoscopic hysterectomy compared to abdominal hysterectomy (98 vs. 103 per 100,000) (Table 4). While there were more deaths from leiomyosarcoma following laparoscopic hysterectomy (86 vs. 71 per 100,000), there were more hysterectomy-related deaths with abdominal hysterectomy (32 vs. 12 per 100,000). For surgical complications, the laparoscopic group had lower rates of transfusion (2,400 vs. 4,700 per 100,000), wound infection (1,500 vs. 6,300 per 100,000), venous thromboembolism (690 vs. 840 per 100,000) and incisional hernia (710 vs. 8,800 per 100,000), but a higher rate of vaginal cuff dehiscence (640 vs. 290 per 100,000), compared to the abdominal group.

In terms of quality of life, the laparoscopic group resulted in 499,171 quality-adjusted life years, compared to 490,711 in the abdominal group (incremental difference: 8,460 additional quality-adjusted life years gained among women undergoing laparoscopic hysterectomy). Stated another way, on average, women undergoing laparoscopic hysterectomy experience an additional 0.85 quality-adjusted life years over 5 years (1.02 months), compared to women undergoing abdominal hysterectomy.

In the sensitivity analysis, our results were relatively robust to varying risks of postoperative complications, leiomyosarcoma, and hysterectomy-associated deaths across predefined ranges in the published literature (Table 4). Using the lowest estimate of leiomyosarcoma (0.007), the incremental difference in the number of deaths per 100,000 ranged from 11 to 19 more with abdominal hysterectomy, varying the rate of procedure-related death. With the high estimate (0.0049), the number ranged from 36 to 44 more deaths with laparoscopic hysterectomy. The incremental difference in death associated with laparoscopic hysterectomy was most conservative with the base-case estimates of procedure-related death (Figure 2). A hypothetical leiomyosarcoma incidence of 0.0015 would provide equivalent mortality between laparoscopic and abdominal groups, assuming base-case estimate for procedure-related death.

Quality-adjusted life year differences were robust across a +/− 20% utility range for sensitivity analysis. For example, if the hysterectomy utility estimate was, in fact, 0.72 rather than 0.9, the difference in total quality-adjusted life years over 5 years would be 16,438, with laparoscopic hysterectomy patients experiencing an additional 0.16 quality-adjusted life years over 5 years (1.97 months). Even without a decrement for hysterectomy, there remained a difference of 4,312 quality-adjusted life years (0.52 months). There was no scenario where a 20% adjustment in base-case utility resulted in more quality-adjusted life years for abdominal hysterectomy.

Comment

Using base-case estimates, our decision analysis predicted lower overall mortality from laparoscopic hysterectomy with morcellation than abdominal hysterectomy for treating the presumed fibroid uterus in premenopausal women. Abdominal hysterectomy was associated with more postoperative complications and lower quality of life.

A strength of the study includes its design as a decision analysis, a strategy particularly helpful when a comparative prospective study is challenging. In this case, it would not be feasible to conduct a randomized trial comparing laparoscopic hysterectomy with morcellation to abdominal hysterectomy because leiomyosarcoma is so rare. Further, the analysis incorporated mortality due to the procedure itself, not simply mortality associated with morcellation of leiomyosarcoma. Insight was also provided for multiple clinical outcomes, offering more information to guide surgeons in counseling women on approach for hysterectomy for fibroids. Lastly, outcomes were assessed by comprehensive literature review, and sensitivity analyses supported the model's conclusions, adding confidence to the applicability of these findings to a clinical setting.

Any discussion of risk associated with morcellation of presumed leiomyomata is limited by the paucity of data regarding the incidence of occult leiomyosarcoma in this setting. Currently available reports include very small numerators and denominators when considering the high number of uterine surgeries for fibroids that occurred during the respective time periods.[4, 17-25] The studies span several decades, with varying pathologic criteria to define leiomyosarcoma, and include data from five different countries. Some women in the reports were identified preoperatively and some included older, postmenopausal women. The population, therefore, does not necessarily reflect those at risk, as morcellation would not have been performed in the first place. Thus, limitations in the literature suggest our estimate was conservative, and updated estimates of leiomyosarcoma risk in this population are unlikely to alter the direction of our conclusions. Although the high end of leiomyosarcoma incidence in sensitivity analysis changed the direction of favorable mortality to abdominal hysterectomy, consideration of all the available literature suggests it is fair to at least grant near-equivalent mortality, with outcomes other than mortality still clearly favoring laparoscopy. Further, our estimates of mortality from the procedure itself were the most conservative of the candidates available in sensitivity analysis.

Data are limited regarding the specific impact of morcellation of occult leiomyosarcoma. The model assumed the behavior of a morcellated leiomyosarcoma would mimic that of spontaneous disease spread. A better understanding of the impact of leiomyosarcoma morcellation could alter the conclusions of our model, either positively or negatively.

The results are subject to uncertainty in the estimates of rare events such mortality. In particular, in the absence of randomization, unmeasured factors could influence the relationship between type of surgery and death. Further, randomized trials involving the specific target population were not always available, so we attempted to account for this uncertainty by conducting sensitivity analyses, varying point estimates of these events with ranges reported in existing literature.

Data were also limited in assigning utilities to various complications associated with hysterectomy, but our findings were robust to a 20% manipulation of the estimates. In all scenarios, laparoscopic hysterectomy was favored in terms of quality of life.

Finally, this analysis was conducted specifically on clinical outcomes. Assessing cost associated with surgery is notoriously difficult, but monetary estimates for the procedure and associated post-operative events could add depth to the consideration of approach for hysterectomy to treat leiomyomata. Not all clinical outcomes were assessed, but more recent literature suggests the rate of visceral injury is not different between laparoscopic and abdominal hysterectomy.[10] The outcomes included in our study are not as likely to change based on improvement in technique (e.g. venous thromboembolism), and, if anything, would favor a laparoscopic approach (e.g. blood loss).

Morcellation is currently one the most debated issues in gynecologic surgery, both in the media and in the medical arena, prompted by a recent Food and Drug Administration safety notification[5] and the response of several large Obstetrics and Gynecology organizations regarding its use.[28, 29] The Food and Drug Administration report emphasizes risk associated with morcellation, nearly to the exclusion of the benefits of minimally invasive surgery for leiomyomata.[9, 15] The benefits could be further improved by reducing risk associated with morcellation (e.g. specimen containment) rather than abandoning minimally invasive treatment for fibroids. Better understanding of risk factors for leiomyosarcoma, new diagnostics to preoperatively distinguish benign from malignant myomata, and enhanced methods of tissue extraction represent potential avenues for improvement in the safety and care of women with uterine disease.

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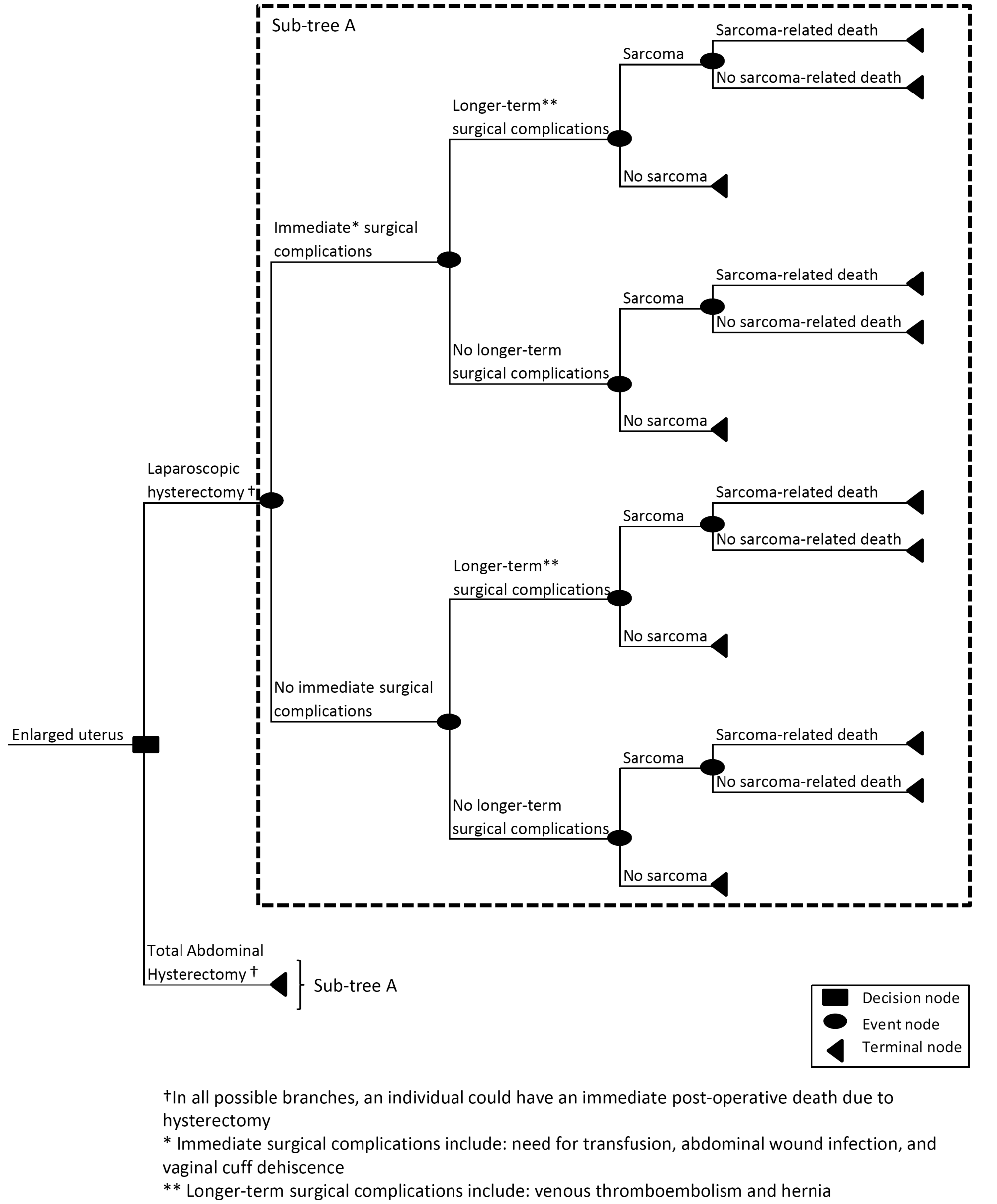

Figure 1. Decision Tree

Premenopausal 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).

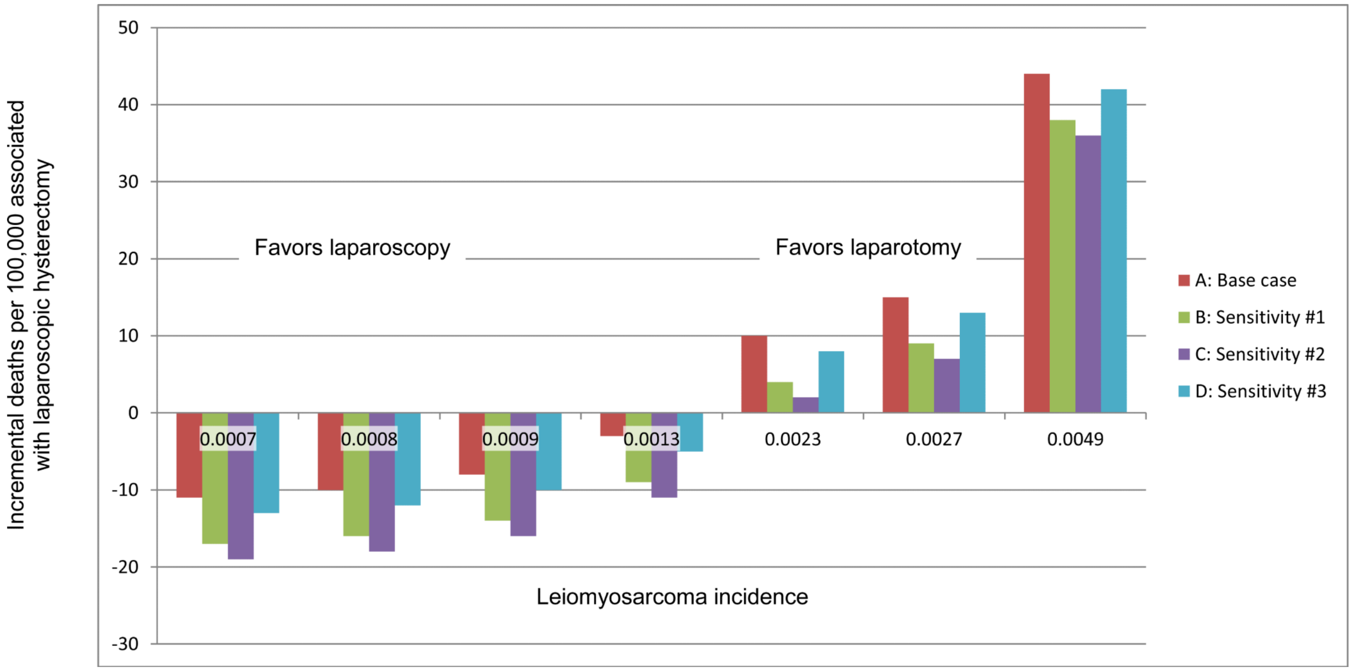

Figure 2.

Number of incremental deaths per 100,000 associated with laparoscopic hysterectomy by varying the candidates for leiomyosarcoma incidence used in the sensitivity analysis. At incidence of 0.007, 0.008, 0.009, and 0.0013, there were more deaths per 100,000 associated with abdominal hysterectomy. At incidence of 0.023, 0.027, and 0.049, there were more deaths per 100,000 associated with laparoscopic hysterectomy. (A) Base-case estimate: abdominal hysterectomy mortality 0.00032, laparoscopic hysterectomy mortality 0.00012. (B) Sensitivity analysis estimate #1: abdominal hysterectomy mortality 0.00038, laparoscopic hysterectomy mortality 0.00012. (C) Sensitivity analysis estimate #2: abdominal hysterectomy mortality 0.00038, laparoscopic hysterectomy mortality 0.000096. (D) Sensitivity analysis estimate #3 abdominal hysterectomy mortality 0.00032, laparoscopic hysterectomy mortality 0.000096.

Table 1

Parameter estimates, hysterectomy for presumed leiomyomata

Parameter	Laparoscopic Hysterectomy Estimate	Range	Abdominal Hysterectomy Estimate	Range	Sources	Level of Evidence [g]
Transfusion	0.024	[0.013, 0.035]	0.047	[0.043, 0.047]	Wiser, Nieboer, Wallenstein[15, 9, 14]	I
Wound infection	0.015	[0.00055, 0.015]	0.063	Not varied	Nieboer, Wallenstein[9,14]	I
Vaginal cuff dehiscence [a]	0.0064	[0.0002, 0.0089]	0.0029	[0.0015, 0.006]	Hur, Koo, Ucella[30-32]	II-2
Venous thromboembolism	0.0069	[0.003, 0.009]	0.0084	[0.0072, 0.0084]	Wiser, Nieboer, Ritch, Harrki-Siren, Wallenstein[15,9,33,34,14]	I
Hernia [b]	0.0071	[0.0014, 0.09]	0.0880	[0.045, 0.098]	Brown, Bickenbach, Le Huu Nho, Hussain, Swank[35-39]	I
Occult leiomyosarcoma incidence [c]	0.0012	[0.0007, 0.0049]	--	--	Parker, Leung, Kamikabeya, Seidman, Leibsohn[19,22,33,4,17]	II-3
Procedure-related death	0.00012	[0.000096, 0.00012]	0.00032	[0.00032, 0.00038]	Wiser, Wallenstein [e], McPherson [f] [13-15]	II-3
Death from leiomyosarcoma [d]	0.72	Not varied	0.59	Not varied	Kosary[26]	III

[a] A weighted average was used as the incidence was low and the difference varied between groups among candidate studies.

[b] It was assumed most candidate fibroid uteri large enough to need morcellation during laparoscopic hysterectomy would require a vertical midline incision if removed via laparotomy. The rate of incisional hernia after hysterectomy was not readily identified in the gynecologic literature and was thus extrapolated from general surgery reports. The incidence of hernia with a transverse incision reported in a Cochrane review was used for the lower estimate in sensitivity analysis.

[c] The same estimate and range was used for the incidence of occult leiomyosarcoma in laparoscopic and abdominal hysterectomy.

[d] The abdominal hysterectomy group was assigned the 5-year death rate for International Federation of Obstetrics and Gynecology stage I-II leiomyosarcoma and laparoscopic hysterectomy that for stage III leiomyosarcoma according to Surveillance, Epidemiology, and End Results reports.

[e] Wallenstien et al was used only for the laparoscopic hysterectomy estimate

[f]McPherson et al was used only for the abdominal hysterectomy estimate

[g]U.S. Preventative Services Task Force level of evidence for highest-quality source,

Table 2

Rate of leiomyosarcoma for women undergoing surgery for presumed fibroids

Study	Publication Year	Study Years	Country	Age (yrs)	Leiomyosarcoma cases	Total patients	Rate of leiomyosarcoma
Leibsohn [17]	1990	1983-1988	USA	36-62	7	1,429	0.0049
Reiter [18]	1992	1986-1989	USA	42 (mean)	0	104	0.0
Parker [*19]	1994	1988-1992	USA	22-86	1	1,332	0.0008
Takamizawa [20]	1999	1983-1997	Japan	26-75	1	923	0.0011
Sinha [*21]	2008	1998-2005	India	34 (mean)	2	505	0.0040
Kamikabeya [22]	2010	1987-2008	Brazil	Not reported	1	1,364	0.0007
Rowland [†24]	2011	2006-2011	USA	Not reported	3	1,115	0.0027
Leung [23]	2012	1999-2005	France	34-77	3	1,297	0.0023
Seidman [*‡4]	2012	1999-2010	USA	Not reported	1	1,091	0.0009
Theben [25]	2013	2005-2010	Germany	28-81	2	1,584	0.0013

[*] Included myomectomies

[†] Abstract only

[‡] Denominator included only morcellated cases

Table 3

Utilities

Parameter	Estimate	Range *	Duration (months)	Source
Hysterectomy for fibroids *a*	0.9	[0.72, 1.0]	6	O'Sullivan[40]
Transfusion	0.48	[0.38, 0.58]	1	Klarenbock[41]
Wound infection	0.607	[0.49, 0.73]	1	Chatterjee[42]
Vaginal cuff dehiscence	0.54	[0.43, 0.65]	1	Chatterjee[42]
Venous thromboembolism	0.8	[0.64, 0.96]	12	Spangler[43]
Hernia	0.77	[0.62, 0.92]	24	Hynes[44]
Leiomyosarcoma (1st 6 months chemotherapy) *b*	0.76	[0.61, 0.91]	6	Reichardt[45]
Leiomyosarcoma progression (additional 12-months chemotherapy) *c*	0.66	[0.53, 0.79]	12	Reichardt[45]
Leiomyosarcoma progression (palliative care) *d*	0.71	[0.57, 0.85]	36	Health Quality Ontario[46]
Alive	1.0	Not varied	Varies	

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

*a*Decrement applied only to abdominal hysterectomy

*b*For women with leiomyosarcoma diagnosed at time of surgery, we presumed all would receive a minimum 6 months of chemotherapy (approximately 6 cycles). Responders would get no more treatment and return to normal health.

*c*Non-responders after 6 months would get additional chemotherapy (up to 12 months).

*d*Non-responders after 12 months of chemotherapy would go on to palliative care and ultimately die of their disease

Table 4

Clinical outcomes: per 100,000 women undergoing hysterectomy for presumed fibroids

Outcome	Laparoscopic hysterectomy: Base-case [range] *	Abdominal hysterectomy: Base-case [range] *	Incremental Difference (Laparoscopic–abdominal)
Leiomyosarcoma cases	120	120	n/a
Leiomyosarcoma deaths	86 [50-353]	71 [41-289]	15
Hysterectomy-related deaths	12 [10-12]	32 [28-32]	−20
Total deaths	98 [60-365]	103 [69-321]	−5
Transfusion	2,400 [1,300-3,500]	4,700 [4,300-4,700]	−2,300
Venous thromboembolism	690 [30-900]	840 [720-840]	−150
Vaginal cuff dehiscence	640 [200-890]	290 [150-600]	350
Abdominal wound infection	1,500 [55-1,500]	6,300 [6,300]	−4,800
Hernia	710 [140-900]	4,500 [4,500-9,800]	−8,090
Quality-adjusted life years	499,171 [499,062-499,280]	490,711 [482,733-486,270]	8,460

* Sensitivity analyses were conducted using the ranges outlined in Tables 1 and 3, i.e. the one-way sensitivity analysis for each input