Interval Appendectomy: Finding the Breaking Point for Cost-Effectiveness

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BACKGROUND: Patients with phlegmonous appendicitis can be managed nonoperatively, yet debate continues about the need for interval appendectomy (IA), given the low risk of recurrence or neoplasm. We sought to determine for which patient age interval appendectomy is cost-effective.

METHODS: Using TreeAge software, a cost-effectiveness model was developed. Two strategies were compared, IA and no interval appendectomy (NIA). Interval appendectomy patients were modeled with probability of benign pathology, cancer or inflammatory bowel disease, and possible operative complications. Patients with NIA were modeled with the probability of recurrence. The probability of malignancy or inflammatory bowel disease developing, or death occurring during a lifetime, was modeled. Base case scenarios at 18, 35, and 50 years old were completed using a Monte Carlo microsimulation. Probabilistic sensitivity analysis was completed using 2-dimensional sample as a Monte Carlo microsimulation to account for variability for patients 18 to 60 years old. Probabilities of complications developing, pathologic diagnosis requiring additional management, and state utility were extracted from published data. Costs were collected from the Centers for Medicare and Medicaid Services and utility was quality-adjusted life years (QALY).

RESULTS: For an 18-year-old patient, IA costs $9,417.22 with a gain of 16.59 QALYs compared with NIA, which costs $11,613.57 with a gain of 16.52 QALYs. For a 35-year-old, IA costs $8,989.16 with 9.1 QALYs gained. No interval appendectomy costs $6,614.61 and 9.09 QALYs gained. For the 35-year-old patient, the interval cost-effectiveness ratio comparing NIA with IA is $237,455/QALY. As patient age increases, the interval cost-effectiveness ratio increases. Using a willingness-to-pay threshold of $50,000/QALY, IA remains cost-effective until the patient is 33 years old.

CONCLUSIONS: Interval appendectomy should be considered in patients younger than 34 years of age. (J Am Coll Surg 2016;223:632–643. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Patients with acute, uncomplicated appendicitis typically undergo appendectomy with low complication rates, early postoperative discharge, and low cost.[1,2] Patients with complicated appendicitis who have a phlegmon or abscess and receive immediate surgery might require larger colonic resection and have higher complication risk and longer hospital stay.[3] Therefore, these patients can be treated with antibiotics with image-guided drainage, as needed, without surgery in the acute setting.[1,4-19] This initial nonoperative management is safe; however, it is unclear if these patients need interval appendectomy (IA) after recovery from the acute illness.[6,7,10]

Proponents for IA cite the importance of eliminating the risk of recurrent appendicitis, as well as excluding other diagnoses, such as cancer, inflammatory bowel disease, or other rare pathology of the appendix, which would alter their subsequent treatment.[20-27]

Interval appendectomy is not, however, without risks, including deep and superficial surgical site infection, perioperative MI, pneumonia, ileus, and stroke. These risks vary with age and comorbidities and must be balanced with the modest risk of recurrent appendicitis and low

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Abbreviations and Acronyms

CMS = Centers for Medicare and Medicaid Services
IA = interval appendectomy
IBD = inflammatory bowel disease
ICER = incremental cost-effectiveness ratio
NIA = no interval appendectomy
PSA = probabilistic sensitivity analysis
QALY = quality-adjusted life years
WTP = willingness to pay

risk of cancer and inflammatory bowel disease, which also vary with age.[5,6,8,10,15,28-32] No interval appendectomy (NIA) eliminates the cost of appendectomy and any complications associated with the procedure.

Currently, there is no cost-benefit analysis to inform providers in the decision to proceed with IA after resolution of the acute episode. In addition, no patient-centered analysis exists to dictate the decision of IA or NIA. To assume that NIA would be more cost-effective than IA due to the absence of surgical costs would be an oversimplification because of the risk of recurrent appendicitis and missed diagnoses that could potentially present in a more-advanced stage, requiring more costly treatment and yield poorer patient outcomes and, therefore, decreased utility. We performed a cost-utility analysis to evaluate the lifetime cost and utility accumulated for each possible pathologic diagnosis related to phlegmonous appendicitis and stratified by patient age.

METHODS

Model

A decision tree was generated to determine the cost and the utility of treatment in patients after resolution of phlegmonous appendicitis IA or NIA. After the decision node, patients have their subsequent outcomes modeled by probabilities derived from previously published data.

For example, the hypothetical patient treated with IA has their probability of benign pathology and probability of identifying other pathology modeled. Thereafter, the risk of perioperative major and minor complications is modeled (Fig. 1).

The 3 outcomes after diagnosis of benign pathology are no complication, major complication, or minor complication. At this stage in the model, patients enter into a Markov model with initial state of alive, which is then modeled, with probability of death vs living over the patients' lifetime (Table 1).

In patients without benign pathology after IA, the probability of other diagnoses is modeled (patients younger than 50 years, 0.15% or patients 50 years and older, 1.1%).[8,38] Those diagnosed with inflammatory bowel disease (IBD) have risk of no complication, major complication, and minor complication modeled, as well as Markov modeling for risk of death during the patient's lifetime (Table 2). The probability of appendiceal cancer and carcinoid are modeled along with the likelihood of

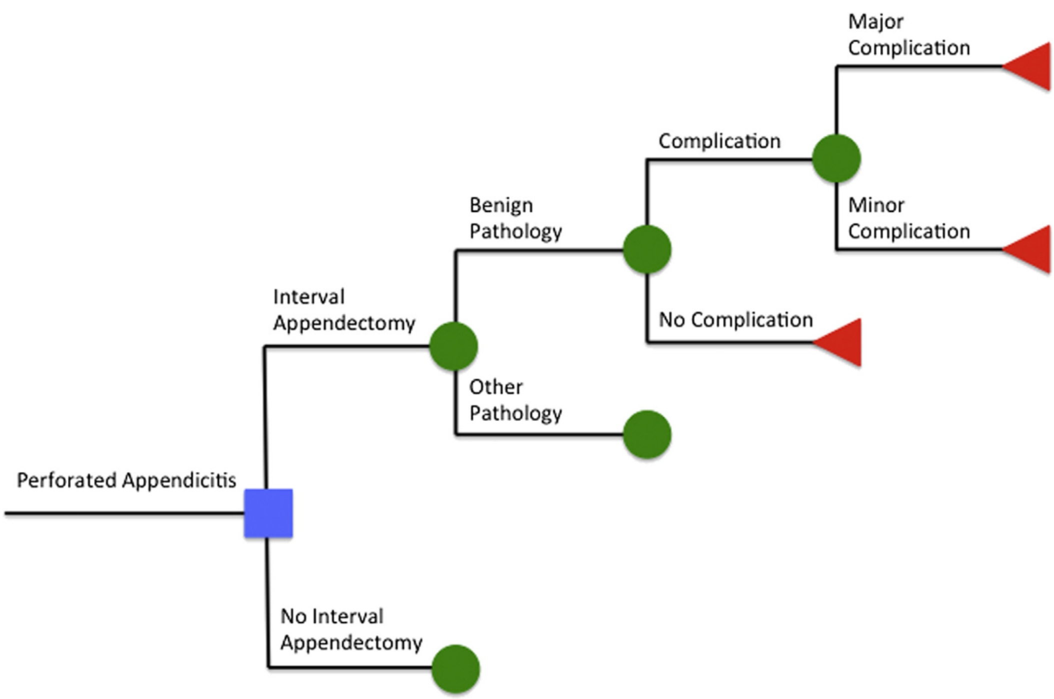

Figure 1. Initial decision node schema in patients with interval appendectomy.

Table 1. Input Variables: Probabilities

Variable	Base case probability	Low probability	High probability	SD	References
Other diagnosis at appendectomy					
<50	0.0015	0.0000	0.0050	0.0013	3
≥50	0.0110	0.0001	0.0270	0.0067	3
IBD at early appendectomy					
<50	0.0070	0.0000	0.0040	0.0010	3,11
≥50	0.0150	0.0010	0.0290	0.0070	3,11
Any cancer at early appendectomy					
<50	0.0020	0.0000	0.0050	0.0013	3,11,19,27,33,34
≥50	0.0140	0.0010	0.0027	0.0004	3,11,19,27,33,34
Any complication elective appendectomy	0.0670	0.0413	0.0990	0.0144	12,17,32,35
Complication being major after elective appendectomy	0.0080	0.0060	0.0100	0.0010	10,27
Complication being minor after elective appendectomy	0.1460	0.0030	0.2450	0.0605	3,7,9,14,31,36
Carcinoid vs other cancer at early appendectomy	0.2018	0.1430	0.2840	0.0353	20,33,34,37
Other cancer vs carcinoid at early appendectomy	0.8040	0.7550	0.8570	0.0255	20,33,34
Local carcinoid vs advanced at early appendectomy	0.6500	0.6000	0.7000	0.0250	20,24
Local other cancer vs advanced at early appendectomy	0.1915	0.1100	0.2730	0.0408	20
Failure of nonoperative management at 1 year	0.1169	0.0300	0.2550	0.0563	3,5,6,8,10,14,28-31,36
Any complication emergent appendectomy	0.1488	0.0900	0.1900	0.0250	10,30,38
Complication being major after emergent appendectomy	0.0188	0.0040	0.0503	0.0116	4,12,16,32,35
Complication being minor after emergent appendectomy	0.1427	0.0180	0.3600	0.0855	1,2,13,14,16,31
Late inflammatory bowel disease diagnosis	0.0043	0.0002	0.0126	0.0031	39-41
Late any cancer diagnosis	0.0022	0.0001	0.0017	0.0004	21,22,42,43
Late carcinoid vs late other cancer diagnosis	0.3444	0.1700	0.5700	0.1000	21,22,24,26,44,45
Local carcinoid vs advanced at late diagnosis	0.5300	0.4400	0.6000	0.0400	24,44,46
Local other cancer vs advanced at late diagnosis	0.3420	0.1000	0.6400	0.1350	24,25,44
Local cancer to advanced	0.3500	0.1700	0.3800	0.0525	25
Advanced cancer to death	0.2969	0.2812	0.3128	0.0079	44

presenting with localized or metastatic disease.[20,33,34,37] Major and minor complications, as well as the lifetime risk of death, are modeled. The final Markov model in patients with local cancer puts the patient in a well state after 2 years if they are still alive. For patients with advanced cancer, the initial Markov state is cancer, and after 5 years patients that remain alive enter the well state and have their probability of death modeled over their remaining lifetime.

The probability of recurrent appendicitis (11.6 ± 5.6) was determined from previous data extraction.[3,5,6,8-10,14,15,28-31,35,36,49] In these patients that fail nonoperative management (appendicitis within 1 year after NIA), the outcomes are modeled identically to IA, however, complication rates were different, as this was an emergency surgery.

The NIA patients without recurrent appendicitis enter into a Markov model (Fig. 2) in the well state and transition to death, IBD, local cancer, or advanced cancer based on probability of diagnosis (Table 3). Patients with IBD remain in that state and transition to either local or advanced cancer based on probabilities. Patients with local cancer who remain alive for 2 years return to the well state or can transition into advanced cancer. In patients with advanced cancer, those who remain alive for 5 years return to the well state. Death is the absorbing state, and probability of death is determined by patient diagnosis.[50]

Base cases

Base case analysis uses mean value of each parameter as determined in previous trials and databases. Means are

Table 2. Input Variables: Years after Diagnosis

Transition state, years after diagnosis	Probability of event	Reference
IBD to cancer		47
0	0.0000	
10	0.0100	
20	0.0150	
30	0.0270	
40	0.0510	
IBD to death		48
10	0.0017	
20	0.0011	
30	0.0025	
49	0.0095	
60	0.0130	
70	0.0290	
80	0.0734	
90	0.2200	
100	0.4998	
110	0.8722	
120	1.0000	
Local cancer to death		44
0	0.0000	
30	0.1294	
40	0.1661	
50	0.1849	
60	0.1994	
70	0.2379	
80	0.3091	

IBD, inflammatory bowel disease.

shown in Table 1. The base case scenarios for this model were completed using Monte Carlo patient level simulation of theoretical patients at 18 years old, 35 years old, and 50 years old. Microsimulation included 10,000 random walks for each base case analysis. Patients were all treated for phlegmonous appendicitis without surgical intervention before simulation. All analyses were completed using TreeAge software (TreeAge Pro, 2014). The time horizon for this model was patient lifetime. The perspective was a third-party payer in the United States.

Sensitivity analysis

Probabilistic sensitivity analysis (PSA) allows numerous parameters to be varied simultaneously to address uncertainty in the estimates of the values. Probabilistic sensitivity analysis was completed as a Monte Carlo microsimulation via a 2-dimensional sample to account for uncertainties of the model inputs and individual patient variability. The inner loop of the microsimulation included 10,000 random walks at the individual level. The outer loop involved 10,000 samples to simultaneously account for uncertainties in all input variables in the model. The mean quality-adjusted life years (QALY) and cost are the result after analysis at each age. Input values were randomly drawn from distributions of each variable. In PSA, utility values and probabilities were sampled from beta distributions and costs were log normal or gamma distributions. The variables for IBD treatment costs were sampled from a triangular distribution. The low value was zero and the likeliest was the mean total cost of IBD treatment. Probabilistic sensitivity analysis was completed for patients at each age from 18 years through 60 years by increments of 5 years. For patients 30 to 35 years old, PSA was run by 1-year patient increments.

Using the standard willingness to pay value (WTP) of $50,000, incremental cost against incremental effectiveness was plotted on the incremental cost-effectiveness plane. Cost-effectiveness acceptability curves were generated using the incremental cost-effectiveness plane.[52] A scatter plot of the bootstrapped probability of an intervention being cost-effective at each patient age was identified at a WTP value of $50,000.

Assumptions

All patients were assumed to have 1 of 3 diagnoses after appendectomy cancer, IBD, or benign pathology. Before the final Markov model, simulated patients with acute surgical complications were assumed to return to baseline state of health. Treatment for patients after a diagnosis of IBD was based on previously completed CEA.[53] As patients with IBD do not have similar symptoms requiring the same treatment, this cost was assumed to vary from zero to the mean value of treatment costs.

Patients who had recurrent appendicitis in the NIA treatment arm were assumed to recur within 1 year of initial diagnosis. These patients were assumed to have the same probability of IBD or cancer as those patients treated with IA. In patients treated with IA, it was assumed these were elective procedures and complication rates were calculated as such. It was assumed that patients who recurred after nonoperative management had appendectomy completed in an emergent setting and the probability of complications was evaluated for emergent surgery.

The probability of complication was the same across all ages (18 to 60 years). The range incorporated was the mean with SD from previous data with varying patient ages.[12,17,32,33] This was true for both major and minor complication probability. After appendectomy, it was

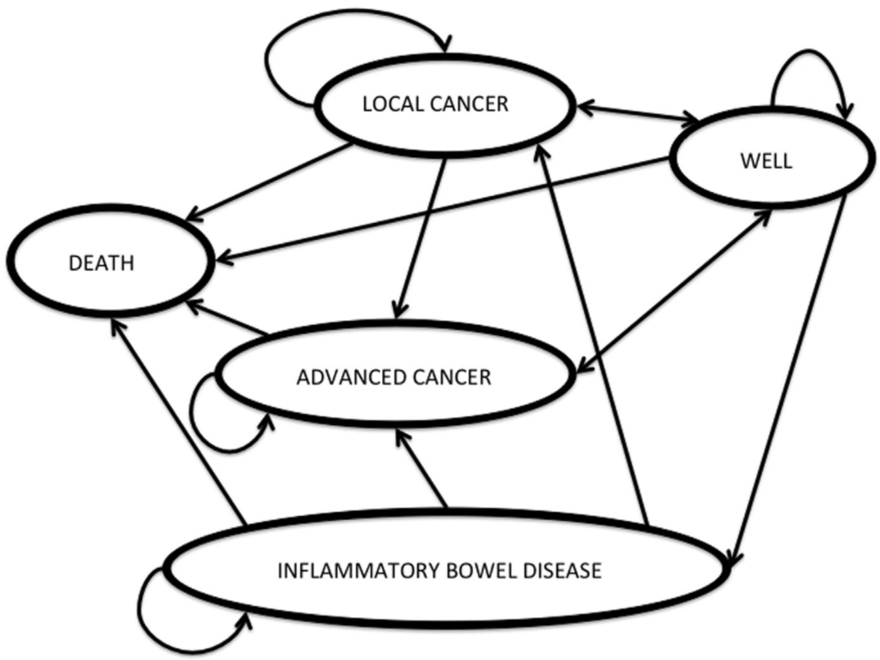

Figure 2. Markov model no interval appendectomy: patients that do not have interval appendectomy and without recurrent appendicitis.

assumed that patients could not develop additional appendix pathology or stump appendicitis.

Local carcinoid was defined as cancer that was ≤2 cm and not involving the base of the appendix.[24] After appendectomy, these patients were assumed to have the same yearly screening regardless of patient age. If patients with local cancer were not absorbed into the terminal state of death after 2 years, they returned to baseline state of well. Patients who were diagnosed with advanced carcinoid were assumed to have the same treatment regardless of age. If this patient was not absorbed into the terminal death state after 5 years, they returned to well state.

Patients diagnosed with other cancer were defined as local cancer or advanced. Advanced cancer was any positive nodal disease, cancer involving the muscularis propria, involving the surrounding fat, or adherent to surrounding organs. Surviving patients with local cancer returned to well state after 2 years and advanced disease after 5 years.

Model parameters

Cost

All cost data were derived from the Centers for Medicare and Medicaid Services (CMS) website (Table 4).[63] This model was a third-party payer perspective. The most recent cost was from 2012, therefore, any missing values from the CMS database were converted to 2012 dollars. Doctors' fees for both hemicolectomy (CPT code 44145: $1,715.23) and laparoscopic appendectomy (CPT code 44970: $617.65) were determined using CPT codes.[63] Mean costs with SE as reported in the database were used for the model. The costs of postoperative complications were also collected from the CMS database. For minor complications, the weighted mean ($8,217.00 ± $487.00) of urinary tract infection, cellulitis, deep vein thrombosis, and organ space infection was determined. The weighted mean was calculated by multiplying the cost of these complications by the probability of each occurring. For major complications ($16,387.00 ± $859.00) the weighted mean was determined from stroke, MI, and pulmonary embolus.

Cost for patients with the diagnosis of IBD and the yearly treatment costs were based on a previous cost-effectiveness study.[53] The initial cost of appendectomy ($7,667.00 ± $67.00) with doctors fee was no different in patients with benign pathology, IBD, or cancer. In patients with IBD, the first year after diagnosis included one initial hospital admission for IBD ($4,017.00 ± $1,507.00), 1 year of acetylsalicylic acid ($7,324.00 ± $2,746.00) and azathioprine ($4,177.00 ± $1,566.00), 1 month of prednisone ($20.00 ± $7.50), a CT scan of the abdomen ($8,046.00 ± $258.00), and a colonoscopy ($910.00 ± $250.00). Costs after the first year included cost of acetylsalicylic acid and

Table 3. Input Variables: Years of Well State

Transition state, years of well state	Probability of event	Reference
Well to death		50
0	0.0000	
20	0.0011	
30	0.0014	
40	0.0021	
50	0.0052	
60	0.0109	
70	0.0241	
80	0.0612	
90	0.1692	
100	0.3570	
110	0.5815	
120	0.9020	
Well to cancer		
0	0.000000	21,22,42,43
30	0.000001	
40	0.000002	
50	0.000002	
60	0.000002	
70	0.000002	
80	0.000001	
Well to inflammatory bowel disease		39-41,51
0	0.00000	
5	0.00005	
10	0.00009	
15	0.00022	
20	0.00150	
30	0.00208	
40	0.00235	
50	0.00277	
60	0.00315	

azathioprine, as well as one colonoscopy, one CT of the abdomen and one admission for IBD ($6,482.00 ± $557.00) each year the patient remained in the alive state. The cost for treatment of IBD was varied to include zero yearly costs, as some patients would not require IBD treatment based on variability of IBD symptoms.

Costs for patients with localized carcinoid included an initial cost of appendectomy and the associated doctors fee, followed by colonoscopy and CT abdomen. Yearly they incurred a cost of one CT of the abdomen and one colonoscopy for screening which ended after 2 years. Patients with advanced carcinoid incurred the same initial costs with the addition of hemicolectomy ($12,607.00 ± $130.00) and the associated doctors fee. These patients also incurred a yearly CT abdomen and colonoscopy for 5 years.

Costs for patients with other appendix cancer included appendectomy and doctor's fee, subsequent hemicolectomy, and doctor's fee followed by CT scan and colonoscopy. Screening costs were for one CT scan and one colonoscopy yearly for 2 years if local disease, and 5 years if advanced.

In patients that failed nonoperative management, they were assumed to have emergent appendectomy, which warranted a higher procedural cost ($10,670.00 ± $125.00).

Utilities

In our evaluation, outcomes were adjusted for patient preference, or utility, which is measured in a 0 to 1 scale. One indicates perfect health and 0 is death. Utilities were derived from the Tufts Cost Effectiveness Registry (Table 4).[64] Utility weights that were published at this site were then confirmed through assessment of the original publication. Only utilities from studies of adults were included (older than 18 years).[54-57,59-62,65] All articles were published in English in developed countries. All hospitals were in the United States, with the exception of one from England.[58]

Probabilities

Probabilities for each occurrence started with a PubMed keyword search (Table 1). Keywords included *appendectomy, appendicitis, complications, inflammatory bowel disease, colon cancer, carcinoid,* and *interval appendectomy.* Trials that included probabilities were adult patients exclusively. All articles were in English and published from developed countries. High-quality data (met analyses or randomized control trials) was used when available, however, few randomized controlled trials exist for this population and most studies were retrospective cohort studies of large databases, such as the Nationwide Inpatient Sample or American College of Surgeons NSQIP.[39-48,51] Complication probabilities were the weighted mean of the complications.[66] Major complications were MI, pulmonary embolus, or stroke. Minor complications were urinary tract infection, deep vein thrombosis, cellulitis, or organ space infection.

Probability of IBD or cancer pathology was 0.0015 ± 0.0013 in patients younger than 50 years old and 0.011 ± 0.0067 for patients 50 years and older.[3]

Outcomes

Primary end point for this model was cost per QALY to determine the incremental cost-effectiveness ratio (ICER) at each patient age evaluated. Incremental

Table 4. Input Variables: Utilities at 1 Year and Cost

Variable	Base mean	Low	High	SD	Reference
Utilities at 1 year					
Appendectomy					
No complication	1.00	—	—	—	
Minor complication	1.00	—	—	—	
Major complication	0.85	0.84	0.86	0.01	49,54-56
Surgery with IBD diagnosis					
No complication	0.94	0.91	0.97	0.03	57,58
Minor complication	0.94	0.91	0.97	0.03	57,58
Major complication	0.79	0.76	0.82	0.03	49,54-56
Surgery with local cancer diagnosis					
No complication	0.77	0.75	0.79	0.02	57,59,60
Minor complication	0.77	0.75	0.79	0.02	57,59,60
Major complication	0.74	0.70	0.78	0.04	49,54-56,61
Surgery with invasive cancer diagnosis					
No complication	0.69	0.65	0.73	0.04	57,59,61
Minor complication	0.68	0.62	0.74	0.06	59,61
Major complication	0.59	0.54	0.64	0.05	60,61
No recurrence and no future diagnosis	1.00	—	—	—	
IBD flair without need for surgery	0.48	0.38	0.58	0.10	53
Well state	1.00	—	—	—	
Death	0.00	—	—	—	
Any advanced cancer diagnosis	0.66	0.61	0.71	0.05	61
Any localized cancer diagnosis	0.80	0.72	0.88	0.08	53,61,62
Chronic IBD without flair	0.90	0.84	0.96	0.06	53,58
Remission after cancer	0.87	0.85	0.89	0.02	61
Cost, $					
Elective appendectomy	7,667.00	7,600.00	7,734.00	67	63
Postoperative major complication	16,387.00	1,5528.00	17,246.00	859	63
Postoperative minor complication	8,217.00	7,730.00	8,704.00	487	63
Acetylsalicylic acid, 1 year	7,324.00	4,578.00	10,070.00	2,746	53
Azathioprine, 1 year	4,177.00	2,611.00	5,743.00	1,566	53
1 colonoscopy	910.00	660.00	1,160.00	250	53
1 CT scan of the abdomen	8,046.00	7,788.00	8,304.00	258	53
Prednisone, 1 month	20.00	12.50	27.50	7.5	53
Elective bowel resection	12,607.00	12,477.00	12,737.00	130	63
5-flourouricil	28,909.00	1,460.00	56,358.00	27,449	53
Emergency appendectomy	10,670.00	10,545.00	10,795.00	125	63
Initial IBD admission	4,017.00	2,510.00	5,524.00	1,507	63
IBD flair requiring admission	6,482.00	5,925.00	7,039.00	557	63
Doctors' fees					
Elective appendectomy	617.65	—	—	—	63
Elective hemicolectomy	1,715.23	—	—	—	63

IBD, inflammatory bowel disease.

cost-effectiveness ratio is defined as the ratio between the change in cost per the change in effect, comparing NIA with IA. If the strategy was determined to be both less costly and more effective, it was determined to be the dominant strategy. When a strategy dominates, there is no ICER for that patient age. If the strategy was more effective but also more costly, an ICER was calculated for the particular patient age. Using the standard WTP

Table 5. Base Case Analysis of 35-Year-Old Patients

Strategy	Cost, $	QALY	Change in cost, $	Change in QALY	ICER, $
Interval appendectomy	8,989.16	9.10			
No interval appendectomy	6,614.51	9.09	2,374.55	0.01	237,455.00

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years.

of $50,000/QALY, a treatment with an ICER higher than this would reject the treatment strategy.

RESULTS

Base case

In the 18-year-old patient who presents with phlegmonous appendicitis, the total cost for IA is $9,317.22 for 16.59 QALYs gained. If NIA is used, the cost is $11,613.57 for 16.52 QALYs gained. Therefore, IA is the dominant strategy.

In the 50-year-old patient, IA costs $9,568.11 with 5.09 QALYs gained. The NIA costs $4,277.55 with 5.10 QALYs gained. The dominant strategy for this patient is NIA, as it costs less and yields a greater increase in QALYs.

When a 35-year-old patient is modeled, the cost of IA is $8,989.16 with 9.10 QALYs gained (Table 5). The NIA costs $6,614.61 and 9.09 QALYs gained. For the 35-year-old patient, the ICER comparing NIA with IA is $237,455.

Sensitivity analysis

When the input variables for all utilities, probabilities, and costs were varied across ranges found in the literature, the most cost-effective strategy varied by patient age (Table 1). From age 18 to 25 years, IA is the most cost-effective strategy (Table 6). The NIA costs less and yields a greater increase in QALY in patients aged 50 to 60 years and is therefore the most cost-effective strategy in this age cohort (Table 6).

Table 6. Summary of Cost and Utility

Age, y	Interval appendectomy, cost, $ (QALY)	No interval appendectomy, cost, $ (QALY)
18	9,250.56 (16.58)*	11,607.41 (16.52)
20	9,227.99 (15.49)*	11,109.28 (15.43)
25	9,171.11 (13.03)*	9,606.68 (12.98)
50	9,578.35 (5.09)	4,346.99 (5.11)†
55	9.481. 73 (4.17)	3,652.33 (4.19)†
60	9,402.41 (3.41)	3,017.79 (3.42)†

*Interval appendectomy dominant at each age, so no ICER is calculated.
†No interval appendectomy is dominant at each age, so no ICER is calculated.
QALY, quality-adjusted life years.

When the sensitivity analysis is completed varying all input variables across distributions in 30- to 35-year-olds, the cost of IA is more, but the QALYs gained are also more relative to NIA (Table 7). As patient age varies, the ICER increases. In the 33-year-old patient, the ICER is $39,046.5 and in the 34-year-old patient the ICER is $60,514.67 (Fig. 3). Using the standard WTP value of $50,000, cost-effectiveness acceptability curve shows the probability of IA being cost-effective (Fig. 4). The probability of IA being cost-effective remains >50% until the patient age of 34 years. At patient age 33 years, the probability of NIA being cost-effective is 52%.

DISCUSSION

Determining the best strategy for treating patients after medical management of phlegmonous appendicitis is complex, as patients present with different baseline health at the time of initial appendicitis. After this, patients also have variable courses after medical management, as some have no additional symptoms, and others might be plagued with ongoing pain and fevers. By performing IA on all patients, some patients will have a definitive diagnosis that can lead to earlier treatment of cancer or IBD. However the majority of patients will have inflammatory changes, no pathology, or recurrent appendicitis, thereby questioning the need for IA. Add to this the risk of surgical intervention, and the result is an ongoing debate about whether IA should or should not be performed; however, our data indicate that this should not be an absolute decision across the entire patient population, but should change as the risks for recurrent appendicitis and cancer change with age.

We found that the most cost-effective strategy varies with patient age. Interval appendectomy is the most cost-effective strategy for those aged 18 to 25 years. In the patient 50 years and older, the dominant strategy is NIA. In patients 30 to 45 years, the most cost-effective strategy is determined by the WTP. We chose the standard WTP of $50,000, which makes IA the chosen strategy until age 33 years. When the patient is 34 years old, NIA becomes the chosen strategy.

Table 7. Calculation of Incremental Cost-Effectiveness Ratio

Age, y, strategy*	Cost, $	QALY	Change in cost, $	Change in QALY	ICER, $
30					
IA	9,118.38	10.92			
NIA	8,296.08	10.88	822.30	0.04	20,557.50
31					
IA	9,114.43	10.53			
NIA	8,045.06	10.49	1,069.37	0.04	26,734.25
32					
IA	9,102.71	10.16			
NIA	7,740.21	10.12	1,362.50	0.04	34,062.50
33					
IA	9,098.28	9.80			
NIA	7,536.41	9.76	1,561.87	0.04	39,046.75
34					
IA	9,086.42	9.44			
NIA	7,270.98	9.41	1,815.44	0.03	60,514.67
35					
IA	9,071.47	9.11			
NIA	7,051.85	9.08	2,019.62	0.03	67,320.67
40					
IA	9,049.26	7.55			
NIA	6,033.44	7.53	3,015.82	0.02	150,791.00
45					
IA	9,017.46	6.23			
NIA	5,110.59	6.22	3,906.87	0.01	390,687.00

*No strategy is dominant in this age range.
IA, interval appendectomy; ICER, incremental cost-effectiveness ratio; NIA, no interval appendectomy; QALY, quality-adjusted life years.

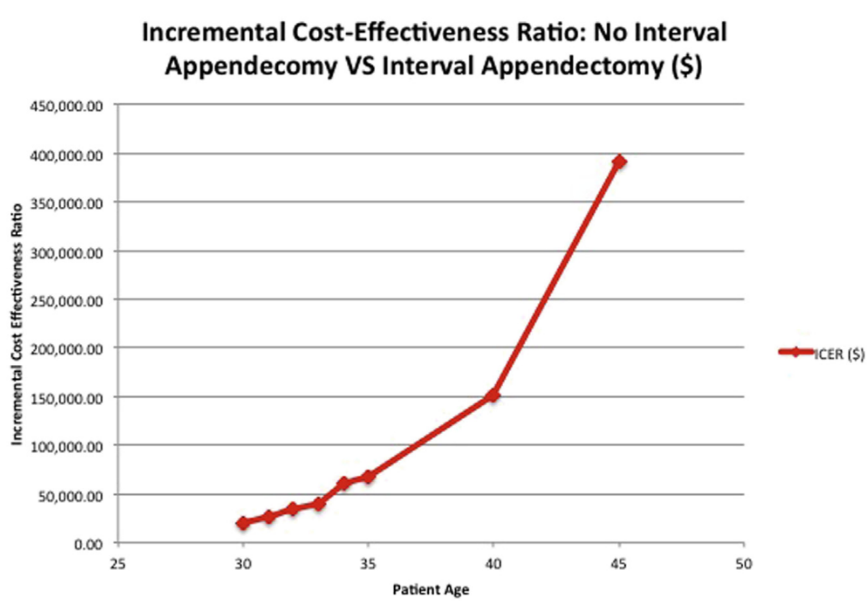

Figure 3. Interval cost-effectiveness ratio (ICER) by patient age from 30 years old to 45 years old. Note that ICER was not calculated for patients younger than 30 years old or older than 45 years old as there is a dominant treatment strategy in these age ranges.

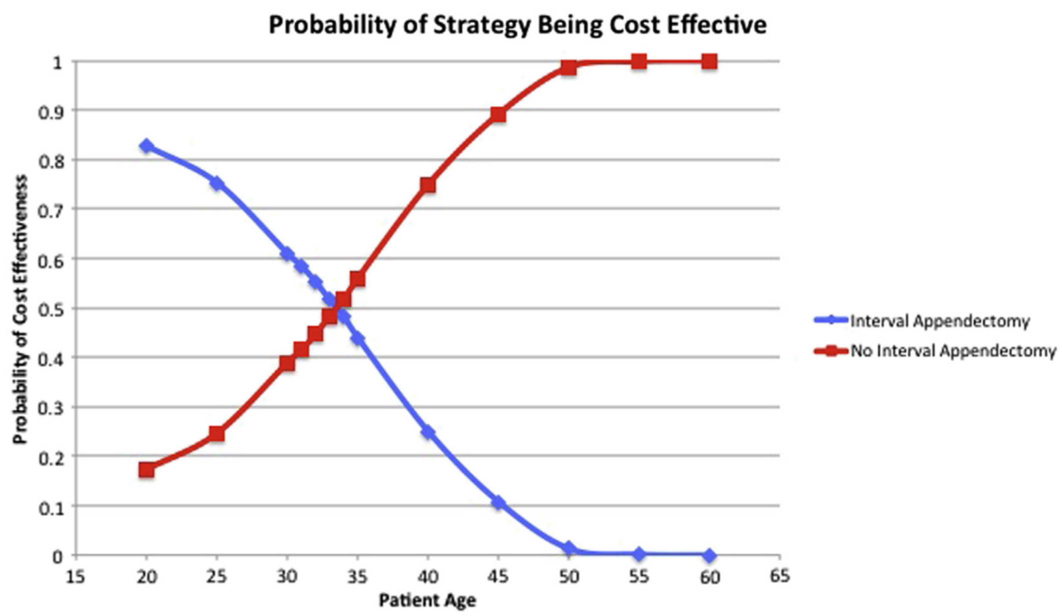

Figure 4. Cost-effectiveness acceptability curve: probability of treatment strategy being cost-effective at each age.

The findings here must be considered in the constraints of the limitations of this study. As with any decision analysis, the available data limit the validity of the results. By evaluating our results in sensitivity analysis, we maximized the validity of our results at all patient ages. As sensitivity analysis allows for variation of all input values, this takes into account variability of not only age, but also the range of probability of cancer, IBD, and costs (Table 1). Additionally, some of the assumptions made within this analysis might not be clinically accurate in all cases, but the assumptions made were based on current literature and should therefore be generalizable. Based on the probability of one strategy being dominant over another, it seems that for those who are young, IA should be practiced, and for those who are old, NIA should be practiced.

We would caution clinicians, however, in choosing NIA in patients based on age alone, as patients baseline health can dramatically change even between 2 patients of the same age. Some patients will present with signs or symptoms of IBD. Likewise, patients might have a strong family history of colon cancer and, therefore, their management should be more aggressive in terms of ruling out more sinister pathologies.

CONCLUSIONS

The most cost-effective treatment for patients after phlegmonous appendicitis is IA if the patient is 33 years old or younger. This recommendation maximizes patient utility and minimizes cost. Although nothing can replace clinical judgment, clinicians should use this as a guide to treat any patient after conservative treatment of complicated appendicitis. In the absence of atypical symptoms or family history of cancer, NIA should be considered for those to 34 years of age and older.

Author Contributions

Study conception and design: Nirula, Senekjian, Bellows, Nelson
Acquisition of data: Senekjian
Analysis and interpretation of data: Senekjian, Nirula, Bellows, Nelson
Drafting of manuscript: Senekjian
Critical revision: Senekjian, Nirula

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