The Cost-Effectiveness of Pre-Operative Imaging for Appendicitis after Indeterminate Ultrasound in the 2nd or 3rd Trimester of Pregnancy

Zachary J. Kastenberg, M.D.[1,2], **Michael P. Hurley, B.S.**[1], **Anna Luan, B.S.**[1], **Vidya Vasu-Devan, B.S.**[1], **David A. Spain, M.D.**[2], **Douglas K. Owens, M.D. M.S.**[3,1], and **Jeremy D. Goldhaber-Fiebert, Ph.D.**[1]

[1]Center for Health Policy and Center for Primary Care and Outcomes Research, Department of Medicine, Stanford University, Stanford, CA

[2]Department of Surgery, Stanford University, Stanford, CA

[3]Veterans Affairs Palo Alto Health Care System, Palo Alto, CA

Abstract

Objective—To assess the cost-effectiveness of diagnostic laparoscopy, computed tomography (CT), and magnetic resonance imaging (MRI) following indeterminate ultrasound in pregnant women with suspected appendicitis.

Methods—A decision-analytic model was developed to simulate appendicitis during pregnancy considering health outcomes for both the pregnant women and developing fetus. Strategies included diagnostic laparoscopy, CT, and MRI. Outcomes included positive appendectomy, negative appendectomy, maternal perioperative complications, preterm delivery, fetal loss, childhood cancer, lifetime costs, discounted life expectancy, and incremental cost-effectiveness ratios.

Results—Magnetic resonance imaging is the most cost-effective strategy, costing $6,767 per quality adjusted life year (QALY) gained relative to CT, well below the generally accepted $50,000 per QALY threshold. In a setting where MRI is unavailable, CT is cost-effective even when considering the increased risk of radiation-associated childhood cancer ($560 per QALY gained relative to diagnostic laparoscopy). Unless the negative appendectomy rate is less than 1%, imaging of any type is more cost-effective than proceeding directly to diagnostic laparoscopy.

Conclusions—Depending on imaging costs and resource availability, both CT and MRI are potentially cost-effective. The risk of radiation-associated childhood cancer from CT has little impact on population-level outcomes or cost-effectiveness, but is a concern for individual patients. For pregnant women with suspected appendicitis, an extremely high level of clinical diagnostic certainty must be reached prior to proceeding to operation without pre-operative imaging.

CORRESPONDING AUTHOR: Zachary Kastenberg M.D., Center for Health Policy and Center for Primary Care and Outcomes Research, 117 Encina Commons, Rm 114, Stanford, CA 94305-6019, Phone: (650) 736-0815/Fax: (650) 723-1919/ zjk1@stanford.edu.

INTRODUCTION

Acute appendicitis occurs in approximately 1 per 1000 pregnancies making it the most common indication for non-obstetric surgery in pregnant women (1, 2). The American College of Obstetricians and Gynecologists (ACOG) has supported the use of radiographic imaging in pregnant women to facilitate expeditious diagnosis (3). The ACOG recommendations, however, note the uncertainty surrounding the long-term effects of fetal radiation and do not comment on the potential economic burden of increased use of MRI. Further investigation is required to fully understand the long-term public health impact and cost-effectiveness of diagnostic imaging during pregnancy.

The unique diagnostic challenge of abdominal pain during pregnancy requires the expeditious, yet judicious use of adjunctive diagnostic studies. The practitioner must consider the characteristics of each test as well as the associated risks to the pregnant woman and the developing fetus. If the clinical concern for appendicitis remains high following an indeterminate ultrasound the clinician must decide between three existing strategies: diagnostic laparoscopy, computed tomography (CT), or magnetic resonance imaging (MRI). Diagnostic laparoscopy is available in any hospital staffed by a surgeon with general laparoscopic training, but is associated with negative appendectomy rates of up to 40% in pregnant women (4, 5). Computed tomography is relatively inexpensive and widely available, but involves exposure of the fetus to ionizing radiation. Magnetic resonance imaging does not involve radiation, but is expensive and not as readily available as CT.

Given the complexity of this issue, including the need to consider relatively rare, radiation-associated childhood cancers that may develop over time horizons of 10 years or longer, no single clinical trial will be capable of considering all the lifetime risks, benefits and costs associated with the strategies described above. Using a decision-analytic modeling approach, we performed a comprehensive cost-effectiveness analysis of the diagnostic strategies for appendicitis during pregnancy as a means to inform future policy and guideline development.

METHODS

The computer-based model simulates the natural history of appendicitis during pregnancy as well as the major dependent health outcomes for the pregnant woman and fetus including preterm delivery, fetal loss, and childhood cancer. A cohort of 25-year-old primigravid women in the second or third trimester of pregnancy enters the model with a valid clinical concern for appendicitis following an indeterminate ultrasound. Given that early pregnancy is typically considered a contraindication to MRI – due to the theoretical risks of miscarriage and developmental damage to the fetus – we excluded first trimester pregnancies from analysis (6).

The model compares three diagnostic strategies intended to identify women with appendicitis in need of an operation, reflecting the natural history for treated (true positive) and untreated (false negative) acute appendicitis as well as women without appendicitis who undergo negative appendectomies (false positives; Supplemental Figure 1). Markov models

capture long-term outcomes including the potential development of and treatment for childhood acute lymphoblastic leukemia (ALL), as leukemia is the most common childhood cancer linked to radiation exposure and ALL is the most common childhood leukemia (Supplemental Figure 2) (7–9).

Strategies are defined by the chosen diagnostic modality 1) diagnostic laparoscopy; 2) CT; or 3) MRI (Supplemental Figure 1). Diagnostic laparoscopy results in either a positive appendectomy or negative appendectomy. Computed tomography and MRI result in either a positive or negative scan, which then leads to either an operation or no operation, respectively. The women then undergo either expedited operation resulting in non-perforated appendicitis (true positive), a negative appendectomy (false positive), a delayed operation with perforated appendicitis (false negative), or no operation (true negative). The pregnant women's surgical outcomes include no complication, complication (simplified to surgical site infection, the most common complication following appendectomy), or death (10). As a simplification, we assumed that maternal death results in fetal death despite the clinical possibility that for a proportion of cases fetuses may be salvaged even when the mother dies. Given overall rarity of maternal death with fetal salvage, this scenario has a very small effect and does not change the overall study conclusions.

For surviving mothers, the subsequent fetal outcomes include full-term delivery, pre-term delivery, or fetal death. Surviving children enter a Markov simulation model to capture the risk of developing radiation-associated childhood ALL and associated health outcomes and costs (Supplemental Figure 2). In the model, all children are initially healthy but face risks of developing childhood ALL. Childhood ALL is modeled in terms of an initial three years of treatment followed by a period of remission for those children surviving to the end of treatment. While in remission, the child either continues in remission or relapses. Following the tenth year of disease-free remission the child is considered cured. The additional probability of radiation-associated childhood ALL for those in the CT cohort is decremented during the first 15 years of the child's life after which the risk of cancer returns to the baseline risk for the general population. The child faces age-specific risks of death from other causes at all times, as well as the additional risk of cancer death while being treated for ALL.

The base case assumes the societal perspective, but we also considered costs from the payer perspective in sensitivity analyses. The study was conducted according to the International Society for Pharmacoeconomics and Outcomes Research – Society for Medical Decision Making recommendations for Modeling Good Research Practices (11). We express costs in 2012 U.S. dollars with cost estimates from other years inflation adjusted using a gross domestic product deflator (12). Outcomes are summed across the lifetime of the mother and child. Future costs and life years are discounted at an annual rate of 3%. The value of the alternative diagnostic strategies is measured by calculating the incremental cost-effectiveness ratio, which is defined as the incremental cost divided by the incremental benefit in quality adjusted life years (QALYs) for each strategy relative to the next best alternative strategy. Incremental cost-effectiveness ratios were compared to $50,000 and $100,000 per QALY gained thresholds, which are typically used as benchmarks indicating

reasonable value for money where the incremental cost-effectiveness ratios of commonly accepted medical interventions typically fall below these thresholds.

Table 1 summarizes data used in the analysis. The references from which model inputs were extracted are listed in the Appendix. The baseline values represent the best available estimates derived from the existing literature. The ranges noted in Table 1 likewise reflect uncertainty in these estimates and were used to explore whether outcomes and conclusions of the analysis changed if different values within the ranges were used in both one-way sensitivity analyses and probabilistic sensitivity analysis. Review of the existing literature revealed three reports describing the use of CT (Appendix: 5, 13–15) and four reports describing the use of MRI (Appendix: 13, 16–19) during pregnancy. All studies were retrospective and included only those women who had previously had a negative or indeterminate ultrasound. The sensitivity and specificity of CT and MRI were drawn from a meta-analysis in which scan characteristics were pooled across these available studies (Appendix: 13). We applied Bayes' theorem to calculate the positive and negative predictive values of CT and MRI. Mean values for sensitivity and specificity were used in the base case analysis. The ranges for both CT and MRI represent 95% confidence intervals from meta-analyses, which were relatively wide given small sample sizes and the often-cited inter-center variability in the quality of MRI and CT interpretation.

Perioperative mortality was 0.1% in the base case analysis and ranged from 0–1% in sensitivity analysis. Many recent studies of appendectomy report maternal mortality rates of 0% (Appendix: 2, 20, 21). Surgical site infection is the most common complication following appendectomy occurring in 2–10% of patients. Cases of perforated appendicitis have higher rates of surgical site infection compared to non-perforated cases. Our base case assumed a surgical site infection rate of 2.5% for patients with non-perforated appendicitis and 10% for patients with perforated appendicitis. Perforated appendicitis was assumed to occur in all patients with a false negative imaging study (Appendix: 10, 22).

The probability of pre-term birth was 12% based on the National Vital Statistics Report on Births: Final Data for 2009 (Appendix: 23). The probability of fetal loss was 1% based on an estimate of second and third trimester pregnancy losses, excluding first-trimester miscarriages(Appendix: 24). We explored a wide uncertainty range around this variable, reflecting differences across trimesters and the exclusion of miscarriages. The increased probabilities of pre-term birth and fetal loss following surgery were estimated from multiple studies of appendectomy during pregnancy (Appendix: 25–39). In the decision-analytic model every pregnancy had the baseline risk of prematurity (12%) with those undergoing laparoscopy incurring additional risk of prematurity (12%–25%) based on estimates from the existing literature. If premature, the child's utility was estimated at 0.70. We examined how more extreme or less extreme assumptions about loss of health related quality of life due to prematurity impacted our results (changing the utility weight over a range from 0.25 to 1.00 – from debilitating to normal development). The costs associated with prematurity were derived from a comprehensive review on the societal cost of prematurity (mean $62,127). In sensitivity analysis we then used 2x the upper limit estimate for a <28-week delivery as the upper limit ($510,000).

The probability of developing radiation-associated childhood ALL integrated the incidence of childhood cancer in the general population (lower limit = incidence of childhood ALL, 5.0/100,000; base case = combined incidence of all childhood blood borne cancers, 8.9/100,000; upper limit = combined incidence of all childhood cancers, 23.2/100,000) with the relative risk of 1.4 for childhood cancer following fetal irradiation based on the BEIR VII report put forth by the National Research Council of the National Academies (Appendix: 40). Sensitivity analyses were conducted over a wide range – up to a relative risk of 100 – to conservatively reflect the uncertainty in estimating cancer risk.

For both mother and child, we derived age-specific mortality rates from U.S. life tables. For the child, these were used as the rates of non-cancer death (Appendix: 41). Additionally, for children developing ALL, they faced excess mortality rates for childhood ALL, which were estimated using mortality data for childhood leukemia reported by the National Cancer Institute and the Centers for Disease Control and Prevention (Appendix: 42).

We estimated the adjustments for quality of life from existing studies relevant to our population and subsequently conducted sensitivity analyses over a wide range for each condition. In the cited studies these values were calculated either by standard time trade-off methodology or by previously published expert opinion (Appendix: 43–48). Age-specific utility decrements were taken from a large study of self-reported quality-of-life weights for individuals aged 18 and older (Appendix: 49). The model assumed that the child's health did not influence the mother's quality of life.

Direct medical costs assumed the perspective of a third-party payer. The costs of laparoscopy, CT, and MRI used in the analysis came from the national averages reported by the Centers for Medicare and Medicaid Services (CMS) (Appendix: 50, 51). Given that the Medicare population is quite different from the pregnant population, with the latter more likely to be privately insured, we assessed the cost parameters over a wide range in both one-way deterministic and probabilistic sensitivity analyses. Lifetime medical costs were based on a large study of trends in medical spending in the United States (Appendix: 52). A mean additional lifetime cost of prematurity was obtained from a comprehensive review of preterm birth (Appendix: 53). We varied the cost of prematurity widely in a sensitivity analysis due to the limited literature addressing the outcomes of prematurity resulting from maternal surgical intervention. Stage-dependent costs of ALL therapy were estimated by combining expert opinion with a study of Surveillance Epidemiology and End Results – Medicare linked data analyzing the cost of treating leukemia (Appendix: 54).

We evaluated the uncertainty surrounding each model parameter in one-way deterministic sensitivity analyses. The uncertainty surrounding all parameters was then evaluated in a probabilistic sensitivity analysis using beta distributions for input probabilities and quality of life weights, normal distributions for defined procedural costs, and gamma distributions for lifetime costs. All distributions were calculated using the parameter ranges obtained from the literature (Table 1). This computer simulation modeling study was deemed exempt from human subject review because it uses only publicly available, de-identified and aggregate data sources.

RESULTS

For pregnant women with suspected appendicitis, MRI was the most effective strategy with a negative appendectomy rate of 2.8%; a delayed diagnosis rate of 8%; and a cumulative 49.78 discounted QALYs for the mother and child (Table 2). The CT strategy was the second most effective strategy with a negative appendectomy rate of 7.5%, a delayed diagnosis rate of 5.8%, and a cumulative 49.72 QALYs. Diagnostic laparoscopy was the least effective strategy with a cumulative 47.35 QALYs for the mother and child. The CT strategy led to one additional childhood cancer death per 13,699 CT scans performed during pregnancy (Table 3).

MRI was the most costly strategy with a discounted lifetime medical cost for the mother and child of $323,431, followed by CT at $323,025, and diagnostic laparoscopy at $321,693 (Table 2). Given the low overall cancer rate (8.9/100,000 in base case, relative risk 1.4 for those undergoing CT) the excess cost of childhood cancer in the CT cohort was proportionally small. The MRI strategy's larger benefits and costs yielded a cost per QALY gained of $6,767 relative to the CT strategy. The CT strategy was the next most costly and next most effective strategy, costing $560 per QALY gained relative to diagnostic laparoscopy (Supplemental Figure 3).

These findings remained robust even if MRI costs were substantially higher than those used in the base case analysis. In many regions/hospitals the cost for a single MRI scan may exceed the $1,274 (1.0x Centers for Medicare & Medicaid Services cost) used in the base case and may be differentially higher than other imaging tests like CT. In univariate sensitivity analysis an MRI scan cost of $3,980 (~3.1x Centers for Medicare & Medicaid Services cost with other test costs conservatively held at 1.0x) led to a cost per QALY gained of approximately $50,000 while an MRI scan cost of $7,068 (~5.6x Centers for Medicare & Medicaid Services cost with other test costs conservatively held at 1.0x) led to a cost per QALY gained of approximately $100,000 (Table 4).

Neither the sensitivity of MRI nor the sensitivity of CT impacted the overall conclusions. However, when the specificity of MRI was lower than 96.9% or the specificity of CT was above 99.1%, the cost per QALY gained for the MRI strategy exceeded $50,000 (Table 4). Furthermore, when the specificity of MRI was lower than 96.7% or the specificity of CT was above 99.3%, the cost per QALY gained for the MRI strategy exceeded $100,000. As the relative specificity of MRI decreases, the relative rate of false positive scans increases leading to more unnecessary operations. Importantly, in the existing reports of MRI during pregnancy the specificity of MRI was never below the threshold of 96.9% (Appendix: 13, 16–19).

Using the prevalence of disease as a surrogate for pre-test probability we performed a univariate sensitivity analysis on prevalence of appendicitis over a range of 0–100%. At a prevalence of appendicitis above 99.5%, both MRI and CT have a cost per QALY gained of greater than $50,000 relative to diagnostic laparoscopy (Figure 1). This cost does not exceed $100,000 per QALY gained until prevalence reaches 100%.

The relative risk of radiation-associated childhood cancer did not significantly influence the results of the analysis when tested across reasonable estimates (the BEIR VII report estimates the risk of radiation-associated childhood cancer at 1.4-fold the baseline risk) (Appendix: 40). A risk of 77-fold the baseline risk of childhood cancer increased the cost per QALY gained for the CT strategy to $50,000 relative to diagnostic laparoscopy. This cost per QALY gained did not increase to $100,000 until reaching 98-fold excess of the baseline risk. The main conclusions of the analysis did not change when all other variables were varied in univariate sensitivity analyses across their uncertainty ranges (Table 1).

The effect on the policy conclusions of the uncertainties surrounding all model inputs was assessed using a probabilistic sensitivity analysis. The probability of MRI being the most cost-effective strategy was approximately 70%, of CT being the most cost-effective strategy was 30%, and for diagnostic laparoscopy was nearly 0% at a willingness to pay of $50,000 per QALY gained (Supplemental Figure 4). These probabilities changed to approximately 73% and 27% for MRI and CT, respectively, at a willingness to pay of $100,000 per QALY.

DISCUSSION

Appendicitis during pregnancy presents a complex diagnostic dilemma with direct implications for both the pregnant woman and developing fetus. To date, no study has assessed both the costs and health outcomes associated with this clinical scenario. To comprehensively address this issue from a public health perspective, the current analysis considered the costs, the short- and long-term risks of the intervention, and various quality of life measures across the lifetime of both the pregnant women and developing fetus. Obtaining an MRI prior to operation was the most cost-effective strategy with a cost of $6,767 per QALY gained relative to CT. Given that MRI is not always an option due to resource constraints, an important secondary finding was the cost of $560 per QALY gained for CT relative to diagnostic laparoscopy. The vast majority of U.S. hospitals have MRI scanners, likely >95% for hospitals with over 200 beds. However, for hospitals that do not have MRI scanners or do not have 24-hour scanner availability, the question of using a CT scan in place of an MRI is clinically relevant.

These findings are directly relevant to the pregnant patient with suspected appendicitis after indeterminate ultrasound, outlining a hierarchical approach to assessing both the effectiveness and the cost-effectiveness of diagnostic imaging. Magnetic resonance imaging should be obtained if both the technology and skilled interpretation of the results are available. If MRI is not an option, CT should be undertaken prior to proceeding to laparoscopy. Diagnostic laparoscopy should be reserved for extreme situations in which either the other diagnostic technology is unavailable or the clinical situation dictates emergent operation. Given the extremely high pre-test probability required to proceed directly to the operating room these findings hold for most clinical situations encountered, however, the physician must always interpret these recommendations in the context of each individual patient.

Importantly, despite MRI being the most cost-effective strategy in the base case, the cost per QALY gained rose from $6,767 to $50,000 when the cost of an MRI scan was $3,980

(~3.1x Centers for Medicare and Medicaid Services cost). The cost per QALY gained increased to $100,000 when the cost of the MRI was $7,068 (~5.6x Centers for Medicare and Medicaid Services cost). Depending on the willingness to pay threshold, CT may become the most cost-effective strategy. This finding highlights the importance of considering the cost of the interventions in systems where these decisions will be made and of increasing cost and charge transparency at the institutional and system levels.

Despite exploring increases in childhood cancer risk due to CT across an extreme range, CT did not reach a cost per QALY gained of greater than $100,000 until the risk increased to 98-fold the baseline risk. These results indicate that radiation-associated childhood cancers have little impact on the cost-effectiveness of CT relative to diagnostic laparoscopy (when MRI is unavailable). Instead, the outcomes are driven primarily by the rates of prematurity and fetal loss associated with the operation itself, thus making the scan characteristics, not radiation exposure, the most important factors. It is most important, therefore, to make an accurate diagnosis and to limit the number of negative appendectomies performed – a finding that is consistent with the ACOG guidelines on the use of radiographic imaging during pregnancy (3).

Importantly, an appendicitis prevalence of greater than 99.5% was required before either MRI or CT cost more than $50,000 per QALY gained relative to diagnostic laparoscopy. This sensitivity analysis implies that an acceptable rate of negative appendectomies in pregnant patients taken directly to operation without imaging should be < 1%. Therefore, the diagnostic certainty must be greater the 99% prior to diagnostic laparoscopy becoming the preferred option. In current clinical practice this level of accuracy has not been achievable (4, 5).

It is important to note that this analysis did not include an active observation strategy. This method is commonly employed in children and non-pregnant adults when the diagnosis of appendicitis is uncertain. It was not included here, however, given the high rates of complication for both mother and fetus associated with delayed diagnosis. Our analysis indicates that an active observation strategy would not be a cost-effective option here, however, as it is highly unlikely that any reasonable duration of observation would lead to >99.5% diagnostic certainty. Furthermore, in the current analysis we included only those women indeterminate ultrasounds. The high rate of indeterminate ultrasound examinations may call into question the cost-effectiveness of directed abdominal ultrasonography in the context of a 2nd or 3rd trimester pregnancy. Given the highly variable results reported in the literature this is an important and complex topic for future study.

Our analysis has several limitations. First, there is little prospective data regarding the risk of childhood radiation-associated cancer. However, in using conservative estimates of the cancer rates in both the base case and subsequent sensitivity analyses the overall results remained robust. Second, there is limited empirical data regarding the quality of life decrements used in this analysis, but again taking a conservative approach and performing sensitivity analyses across wide ranges the utility inputs had little impact on the overall results. Third, our base case analysis included many simplifications of reality. Such

assumptions, however, were modeled to bias in favor of diagnostic laparoscopy by both increasing the cost and decreasing the effectiveness of the MRI and CT strategies.

Using cost-effectiveness modeling with a broad public health perspective, this analysis highlights the importance of timely diagnosis and expeditious treatment when confronted with appendicitis during pregnancy. Certainly, scenarios will occur that require the clinician to act expeditiously without preoperative imaging. However, the results of this study indicate that in the vast majority of cases both individual patient outcomes and public health interests will benefit from the use of preoperative imaging – MRI if available, otherwise CT – in the pregnant patient with suspected appendicitis following an indeterminate ultrasound.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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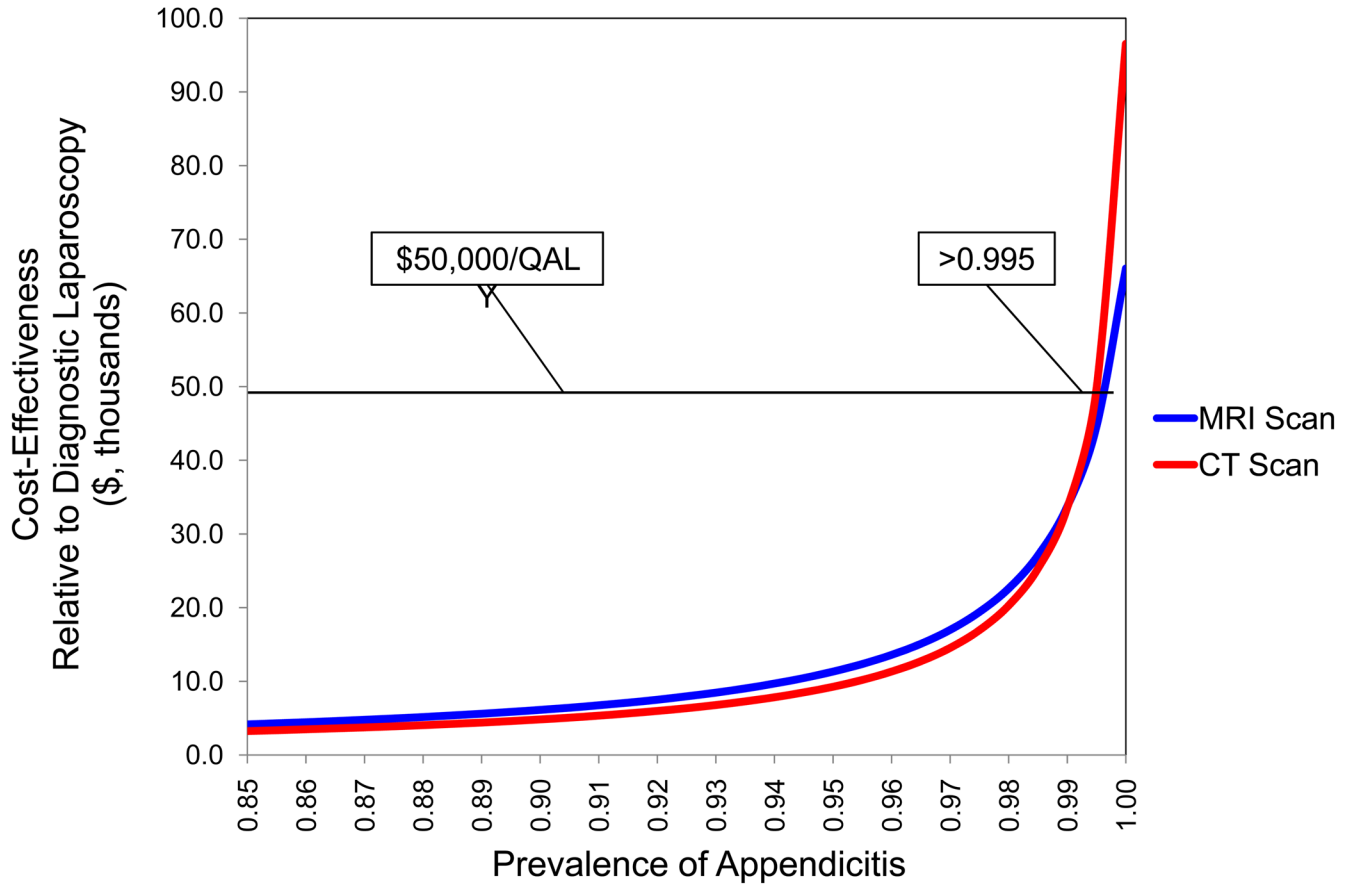
Figure 1. CE of Imaging versus the Prevalence of Appendicitis

The pre-test probability, a surrogate for diagnostic certainty, must be greater than 99.5% prior to diagnostic laparoscopy becoming the most effective strategy at a willingness to pay of $50,000 per QALY.

Table 1

Model Parameters (Probabilities, Utilities, Costs)

Parameter	Baseline Value	Range	References
Probabilities			
Prevalence of Appendicitis in Base Case	0.30	0.24–0.37	(5, 14–19)
MRI			
Sensitivity	0.80	0.44–0.97	(13, 16–19)
Specificity	0.99	0.94–1.00	(13, 16–19)
CT			
Sensitivity	0.86	0.64–0.97	(5, 13–15)
Specificity	0.97	0.86–1.00	(5, 13–15)
Maternal Outcomes			
SSI (non-perforated/perforated)	0.025/0.10	0.00–0.15	(10, 22)
Perioperative mortality	0.001	0.00–0.01	(2, 20, 21)
Fetal Outcomes			
Prematurity, baseline	0.12	N/A	(55)
Prematurity, following surgery	0.167	0.12–0.25	(25–39)
Fetal loss, baseline	0.01	0.003–0.05	(24)
Fetal loss, following surgery	0.11	0.06–0.19	(25–39)
Childhood Cancer			
Baseline (incidence/100,000)	8.9	5.0–23.2	(56)
After CT (relative risk)	1.4	1.4–100	(40)
Death During Induction Therapy	0.03	0–0.05	(57, 58)
Relapse (10 yr. incidence)	0.20	0.18–0.23	(57)
Death During Relapse	0.70	0.50–1.00	(59)
Lifetime Mortality	Life Table	Age Specific	(41)
Utilities[*]			
Mother			
Acute appendicitis	0.73	0.50–1.00	(43, 47, 48)
Well	Table	Age Adjusted	(49)
Child			
Premature	0.70	0.25–1.00	(44, 45)
Cancer (Leukemia)	0.80	0.10–0.90	(46, 48)
Premature/Cancer	0.56	0.18–0.92	
Well	Table	Age Adjusted	(49)
Costs (2010 $)			
Procedural			
Appendectomy, Non-perforated	$11,130	$7,932–$18,474	(50, 51)
Appendectomy, Perforated	$18,474	$11,130–$26,103	(50, 51)

Parameter	Baseline Value	Range	References
CT	$694	$480 – $941	(50, 51)
MRI	$1,274	$940 – $10,441	(50, 51)
Fetal Loss	$24,882	$0–$248,819	**
Surgical Site Infection	$3,132	$0 – $31,323	(60)
Lifetime	Table	Age Adjusted	(52)
Prematurity	$64,867	$0 – $532,491	(53)
Childhood Cancer			
First Year of Treatment	$74,287	$74,287 – $148,573	(54)**
Second Year of Treatment	$9,375	$9,375 – $18,750	(54)**
Third Year of Treatment	$9,375	$9,375 – $18,750	(54)**
Cancer Death	$177,317	$177,317 – $354,635	(54)**
Non-Cancer Death	$24,882	$24,882 – $49,764	(54)**

*
The utility decrement associated with appendicitis lasted one month; the utility decrement for prematurity was continued for the life of the child to simulate the potential for life-long disability; the utility decrement for childhood cancer was continued until either cancer-related death or cancer cure.

**
Expert opinion and/or unpublished data was used in determination of the base case parameterization. A cost for fetal loss was included to simulate a period of fetal distress, the need for removal of the products of conception, or the possibility of longer hospitalization.

***
References listed in Appendix

Table 2

Base Case Analysis[*]

	Negative Appendectomy, False Positive (%)	Delayed Diagnosis, False Negative (%)	Incremental Life Expectancy (Years)	Total Life Expectancy (Years)	Incremental Effectiveness (QALYs)	Total Effectiveness (QALYs)	Incremental Cost ($)	Total Cost ($)	Incremental Cost Effectiveness Ratio ($/ QALY)
Laparoscopy	70.00	0.00	N/A	54.23	N/A	47.35	N/A	321,693	N/A
CT	7.50	5.80	2.12	56.35	2.38	49.72	1,332	323,025	560
MRI	2.80	8.00	0.05	56.40	0.06	49.78	406	323,431	6,767

[*]The results depicted here represent the point estimate outcomes when inputting the baseline values from Table 1 into the model.

Table 3

Strategy-Specific Outcomes[*]

	Fetal Loss	Premature Births	Childhood Cancer Cases[**]	Childhood Cancer Deaths
Laparoscopy	11,000	16,700	8.9	18.1
CT	4,210	13,509	12.5	25.4[***]
MRI	4,070	13,443	8.9	18.1

[*] Outcomes listed as cases/100,000 patients

[**] Childhood cancer cases listed as cases/100,000 patients/year

[***] This number indicates 1 additional cancer-related death/13,699 CT scans

Table 4

Deterministic Sensitivity Analyses[*]

Parameter	Base Case (Range)	Threshold, CT Most Effective Strategy: Willingness To Pay $50,000	Threshold, CT Most Effective Strategy: Willingness To Pay $100,000
Probabilities			
Prevalence of Appendicitis	0.30 (0.24–0.37)	never	never
CT			
Sensitivity	0.86 (0.64–0.97)	never	never
Specificity	0.97 (0.86–1.00)	> 0.991	> 0.993
MRI			
Sensitivity	0.80 (0.44–0.97)	never	never
Specificity	0.99 (0.94–1.00)	< 0.969	< 0.967
Costs			
CT	$694 ($480–$941)	never	never
MRI	$1,274 ($940 – $10,441)	> $3,98[**]	> $7,068[***]

[*] Depicted here are the model parameters for which there existed threshold values within the uncertainty ranges noted in Table 1.

[**] 3.1x Centers for Medicare and Medicaid Services cost for MRI with other test costs conservatively held at 1.0x CMS

[***] 5.6x Centers for Medicare and Medicaid Services cost for MRI with other test costs conservatively held at 1.0x CMS