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Research Paper

Interhospital variation in the non-operative management of uncomplicated appendicitis in adults

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ABSTRACT

Background: Recent randomized trials have suggested non-operative management to be a safe alternative to appendectomy for acute uncomplicated appendicitis. Yet, there remains significant variability in treatment approach. This study sought to characterize center-level variation in non-operative management within a national cohort of adults presenting with appendicitis.

Methods: The 2016–2020 Nationwide Readmissions Database was queried to identify all adult (≥18 years) hospitalizations for acute uncomplicated appendicitis. Hierarchical, mixed-effects models were developed to ascertain factors linked with non-operative management. Bayesian methodology was applied to predict random effects, which were then used to rank centers by increasing hospital-attributed rate of non-operative management. Institutions with high center-specific rates of non-operative management (>90th percentile) were considered low-operating hospitals (LOH).

Results: Of an estimated 447,500 patients, 52,523 (11.7 %) were managed non-operatively. Compared to those undergoing appendectomy, the non-operative cohort was older, more commonly male, and of a higher comorbidity burden. Approximately 30 % in the variability of non-operative management was attributable to hospital effects, with absolute, risk-adjusted rates ranging from 0.5 to 22.5 %. Centers with non-operative management rates ≥90th percentile were considered LOH.

Following risk adjustment, among patients undergoing appendectomy, care at LOH was linked with greater odds of postoperative infection, resource utilization, and non-elective readmission.

Conclusions: We identified significant interhospital variation in the utilization of non-operative management for acute uncomplicated appendicitis. Further, we found LOH to be associated with inferior outcomes following surgical management. Future work is needed to assess the care pathways that contribute to increased utilization of non-operative strategies, and disseminate best practices across institutions.

Introduction

With nearly 250,000 attributable hospitalizations each year in the U. S., appendicitis represents the most common intraabdominal emergency and accounts for an estimated $3 billion in total healthcare expenditures [1–3]. For the ~80 % of cases deemed uncomplicated, prompt appendectomy has traditionally served as the definitive treatment [4–6]. Despite being considered a low-risk procedure, however, appendectomy has been linked with postoperative complications rates ranging from 2 to 20 %, as well as longer-term risk of incisional hernias and other

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sequelae [6–9]. With the potential to avoid surgery and experience hastened recovery, non-operative management of acute appendicitis with antibiotics has garnered much attention [10–12]. Several randomized trials have compared appendectomy with non-operative therapy, demonstrating its safety and efficacy in select patients [13–16].

The decision to pursue non-operative management is undoubtedly influenced by patient factors such as age, comorbidity burden and physiologic severity of illness. Patient characteristics aside, there is growing awareness that differences in treatment strategy may stem from hospital-level factors. A body of literature has reported on the inter-hospital variation in postoperative ventilation time [17], incidence of complications [18,19], and costs [20] across a myriad of surgical procedures. While Rice-Townsend et al. [21] noted significant variation in the treatment of appendicitis at selected children's hospitals, hospital variability has yet to be quantified among adult patients at the national level. With professional society guidelines endorsing either operative and non-operative treatment as safe for uncomplicated appendicitis [22], the identification of interhospital variation could prove significant in both identifying opportunities for quality improvement as well as informing shared decision-making.

In the present study, we examined the presence of center-level variation in utilization of non-operative management for uncomplicated appendicitis in adults. We secondly aimed to characterize hospitals with high utilization of non-operative treatment (low-operative hospitals) and associated patient-level outcomes. We hypothesized the presence of significant hospital-level variation in use of non-operative management and that low-operative hospitals would demonstrate inferior clinical and financial outcomes following admission for appendicitis.

Methods

The 2016–2020 National Readmissions Database (NRD) was queried to identify all non-elective adult (≥18 years) hospitalizations entailing a principle diagnosis of acute appendicitis. As the largest national database detailing readmissions, the NRD uses validated survey-weighting methods to provide accurate estimates for ~60 % of all U.S. hospitalizations. Readmissions are tracked across hospitals within each calendar year using unique patient linkage numbers [23].

Records were stratified by receipt of operative or non-operative management. Patients presenting with abscess or perforation were not considered for analysis (17.8 %). Those missing key data regarding age, sex, or costs were similarly excluded (<1 %, Fig. 1).

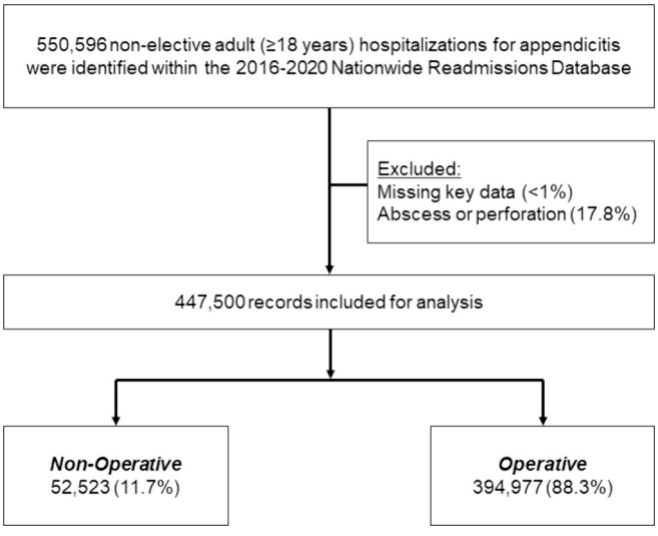

Fig. 1. Study consort diagram of survey-weighted estimates.
Of 550,596 non-elective hospitalizations, 447,500 were considered for analysis. Of these, 52,523 (11.7 %) entailed non-operative management.

Patient and hospital characteristics, including age, sex, insurance coverage, and hospital teaching status, were tabulated in accordance with the NRD Data Dictionary [24]. The burden of chronic disease was numerically captured using the van Walraven modification of the Elixhauser Comorbidity Index [25]. Comorbidities and perioperative complications were identified using relevant *International Classification of Diseases, Tenth Revision* (ICD-10) codes [26]. Complications were subsequently categorized as cardiac, gastrointestinal, infectious, renal, respiratory, and thrombotic. Major adverse events (MAE) were defined to comprise in-hospital mortality or the incidence of any perioperative complication. Center-specific cost-to-charge ratios were applied to compute episodic hospitalization expenditures, which were inflation-adjusted using the 2020 Personal Healthcare Price Index [27].

Continuous variables are reported as medians and interquartile range (IQR), while categorical data are detailed as proportion (%). The Mann-Whitney *U* test and Pearson χ^2 tests were applied for bivariate comparisons. Standardized mean differences (SMD) were additionally computed to ascertain effect size. The significance of temporal trends was evaluated using Cuzick's non-parametric test (nptrend) [28]. Mixed regression models were developed to assess the independent association of patient and hospital factors with likelihood of non-operative management. Model covariate selection was guided by elastic net regularization, a penalized least-squares methodology to minimize collinearity and overfitting [29]. Regression outputs are detailed as adjusted odds ratio (AOR) or β-coefficient (β), as appropriate, both with 95 % Confidence Intervals (CI).

Subsequently, a two-level, mixed-effects logistic regression model was developed to model the likelihood of non-operative management. Patient factors representing fixed effects comprised the first level, while unique hospital identifiers were considered the second level. We then calculated the intraclass correlation coefficient (ICC), representing the degree of variation in non-operative management attributable to center-level differences. Bayesian postestimation was applied to generate absolute rates of non-operative management for each institution. Hospitals in the ≥90th percentile of risk-adjusted rates of non-operative management were classified as Low Operative Hospitals (LOH) and compared with other centers (non-LOH).

The primary study endpoint was receipt of non-operative management. We subsequently considered factors linked with non-operative treatment. We evaluated rates of readmission at LOH, compared to other centers. Lastly, we assessed operative outcomes at LOH, including the incidence of perioperative complications, duration of hospitalization (LOS), hospitalization costs, non-home discharge and non-elective 30-day readmissions.

All statistical analyses were performed using Stata 16.1 (StataCorp, LLC, College Station, TX). Due to the deidentified nature of the NRD, this study was deemed exempt from full review by the Institutional Review Board at the University of California, Los Angeles.

Results

Baseline characteristics of the study cohort

An estimated 447,500 patients met inclusion criteria, of whom 52,523 (11.7 %) were managed non-operatively (Fig. 1). Of note, the proportion of patients managed non-operatively decreased over the study period, from 11.8 % in 2016 to 9.6 % in 2020 (Fig. 2).

Compared to the operative cohort, patients treated non-operatively were older (52 [35–66] vs 43 years [29–58], $P < 0.001$), less commonly female (47.2 vs 48.5 %, $P < 0.001$), and more often insured by Medicare (28.8 vs 17.6 %, $P < 0.001$). The non-operative group more frequently presented with congestive heart failure (6.0 vs 2.3 %, $P < 0.001$), cardiac arrhythmias (10.6 vs 6.0 %, $P < 0.001$), and chronic pulmonary disease (10.9 vs 9.3 %, $P < 0.001$). Relative to operatively managed patients, the non-operative cohort was more often treated at

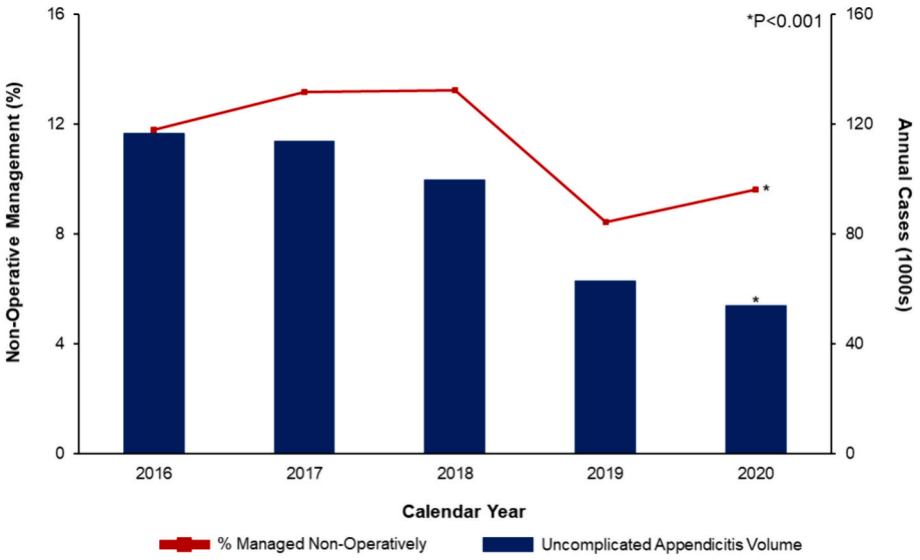

Fig. 2. Trends in non-operative management.
Over the study period, utilization of non-operative management decreased from 11.8 % in 2016 to 8.4 % in 2019 and 9.6 % in 2020.

metropolitan teaching hospitals (73.3 vs 63.5 %, P < 0.001) (Supplemental Table S1).

Factors linked with non-operative management across centers

After risk adjustment, increasing age (AOR 1.02 per year, CI 1.01–1.02) and Elixhauser comorbidity index (AOR 1.09 per point, CI 1.07–1.10) were linked with greater odds of non-operative management. Relative to private insurance, Medicare (AOR 1.08, CI 1.03–1.13) and Medicaid coverage (AOR 1.11, CI 1.07–1.16) also remained associated with increased likelihood of non-operative care (Fig. 4).

Hierarchical modeling

Following the development of a two-level, multivariable regression model, postestimation of random effects demonstrated 30 % in the variability of non-operative management that is not otherwise explained by patient factors (Intraclass correlation coefficient = 0.30; C-statistic: 0.72). The absolute, risk-adjusted rate of non-operative treatment for appendicitis ranged from 0.5 to 22.5 %, with centers exhibiting a risk adjusted rate of non-operative management >10.2 % (>90th percentile) designated as LOH (Fig. 3).

Compared to non-LOH, LOH had lower annual volume of both appendicitis admissions (37 [13–66] vs 41 cases [18–79], P = 0.008) and appendectomy (24 [8–49] vs 36 cases [16–70], P < 0.001). LOH were more often private, not-profit hospitals (72 vs 68 %, P = 0.001) and metropolitan teaching centers (52 vs 46 %, P < 0.001), compared to Non-LOH.

Characteristics of patients at LOH and Non-LOH

Of the total study cohort, 61,718 (13.8 %) were treated at LOH. On average, LOH patients were older (45 [31–60] vs 44 years [30–59], P < 0.001), less often female (47.1 vs 48.5 %, P < 0.001), but had a similar Elixhauser comorbidity index (1 [0–2] vs 1 [0–2], P = 0.67). In addition, the LOH group was more commonly privately insured (52.1 vs 48.9 %, P < 0.001) and of highest income quartile (31.1 vs 21.6 %, P < 0.001), relative to others. Compared to those at Non-LOH, Patients at LOH were more frequently non-operatively managed (33.0 vs 8.3 %, P < 0.001) and more commonly received a drain (4.6 vs 1.9 %, P < 0.001). Further, the LOH cohort more often underwent delayed appendectomy >2 days following admission (1.2 vs 1.0 %, P = 0.04) (Table 1).

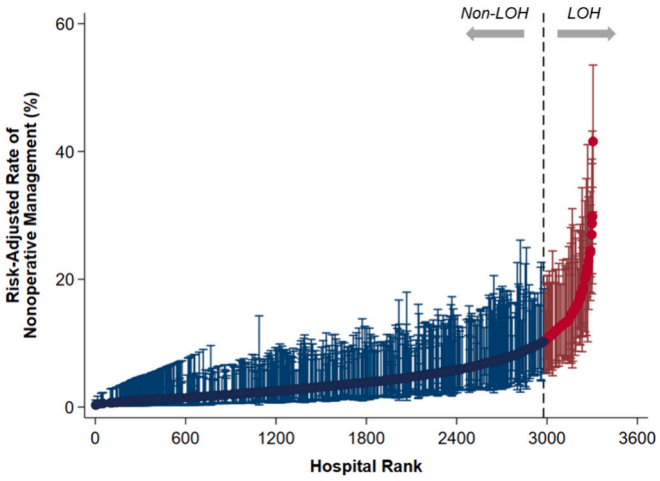

Fig. 3. Interhospital variation in non-operative management of uncomplicated appendicitis.
Hospitals were ranked by hospital-attributable, risk-adjusted rates of non-operative management. Centers in the ≥90th percentile of non-operative management rates were considered low-operating hospitals (LOH). Error bars represent 95 % confidence intervals. For visual clarity, only centers captured in the 2019 Nationwide Readmissions Database are displayed.

Outcomes following operative management at LOH

Considering only those undergoing appendectomy, patients at LOH faced similar rates of MAE, but greater frequency of infection, thromboembolism, and need for blood transfusion. Further, the LOH cohort more often required readmission within 30 days of index discharge (Table 2).

Following risk adjustment, and with Non-LOH as reference, LOH remained associated with similar odds of MAE (AOR 1.03, CI 0.96–1.12), but greater likelihood of infectious sequelae (AOR 1.27, CI 1.11–1.46), gastrointestinal complications (AOR 1.19, CI 1.01–1.39), and need for blood transfusion (AOR 1.50, CI 1.16–1.93). Additionally, LOH faced an incremental increase in per-patient expenditures (β + $950, CI + $540–1370) and significantly increased odds of non-elective readmission within 30-days of discharge (AOR 1.21, CI 1.12–1.30) (Fig. 5).

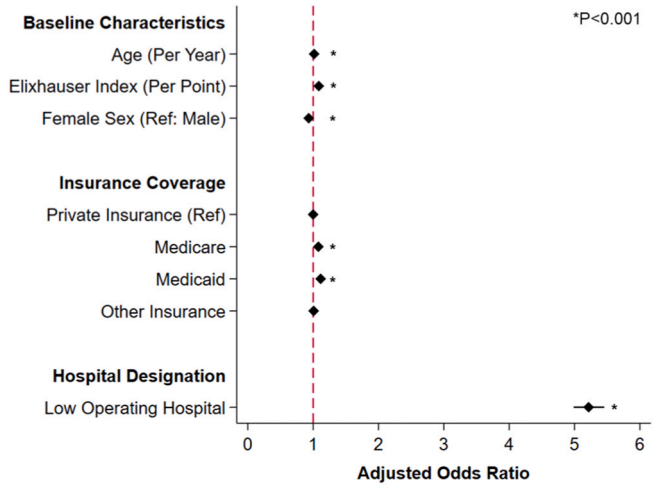

Fig. 4. Coefficient plot demonstrating factors associated with non-operative management.
Following risk adjustment, care at low-operating hospital remained linked with a significant increase in odds of non-operative management for uncomplicated appendicitis. Increasing age, higher Elixhauser comorbidity index, and Medicare and Medicaid coverage (relative to private insurance) were similarly associated with non-operative treatment.

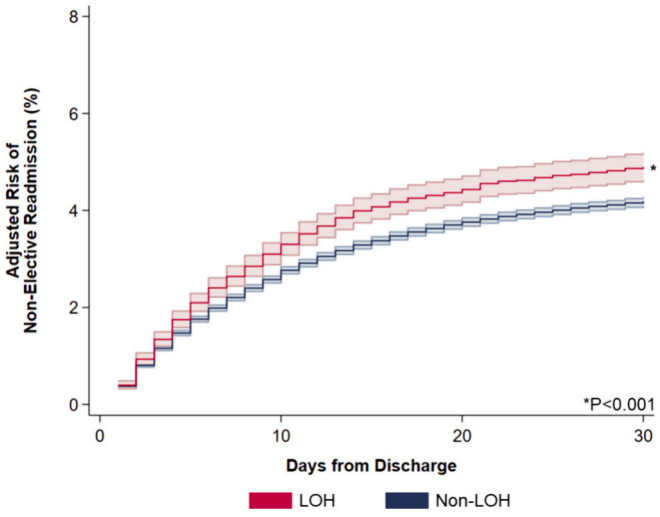

Fig. 5. Cumulative risk of readmission within 30 days of discharge.
Notably, undergoing appendectomy at a low-operating hospital (LOH) was associated with a ~20 % increase in relative risk of non-elective readmission within 30 days of discharge, relative to treatment at other centers. Log-rank P < 0.001.

Readmission following non-operative management

Of the ~25,628 patients across the entire study sample readmitted within 90 days of discharge, 6348 (25.8 %) were initially non-operatively managed.

Evaluating patients who were non-operatively managed, those initially treated at LOH more frequently re-presented with appendicitis (54.7 vs 49.0 %, P = 0.003) and perforated appendix (1.5 vs 0.7 %, P = 0.03), but similarly often with appendiceal abscess (4.3 vs 3.5 %, P = 0.30), compared to Non-LOH. Further, the LOH cohort more commonly received percutaneous drainage upon readmission (12.8 vs 9.9 %, P = 0.01) but faced similar rates of appendectomy at re-hospitalization compared to those initially treated at non-LOH (20.6 vs 23.1 %, P = 0.12).

Table 1
Demographic, clinical, and hospital characteristics, stratified by care at LOH. Reported as proportions unless otherwise noted. Statistical significance was set at α = 0.05. Statistical significance is detailed using P-values and standardized mean differences (SMD).
LOH, Low Operating Hospital; IQR, inter-quartile range; SMD, Standardized Mean Difference.

	LOH (n = 61,718)	Non-LOH (n = 385,782)	P-value	SMD
Age (years [IQR])	45 [31–60]	44 [30–59]	<0.001	0.04
Female (%)	47.1	48.5	<0.001	0.02
Elixhauser Comorbidity Index (median [IQR])	1 [0–2]	1 [0–2]	0.67	0.02
Non-operative management (%)	33.0	8.3	<0.001	0.63
Delayed appendectomy (>day 2)	1.2	1.0	0.04	0.01
Income percentile (%)			<0.001	0.23
76th–100th	31.1	21.6		
51st–75th	25.3	25.4		
26th–50th	23.3	26.3		
0–25th	20.3	26.7		
Insurance coverage (%)			<0.001	0.09
Private	52.1	48.9		
Medicare	19.3	18.9		
Medicaid	17.2	19.0		
Other Payer	11.4	13.1		
Comorbidities (%)				
Cardiac arrhythmias	7.6	6.4	<0.001	0.04
Coagulopathy	1.8	1.5	0.002	0.02
Congestive heart failure	3.3	2.6	<0.001	0.04
Coronary artery disease	5.4	5.2	0.20	0.01
Cerebrovascular disorders	2.0	1.8	0.05	0.01
Chronic pulmonary disease	9.7	9.5	0.25	0.01
Diabetes	10.2	10.1	0.92	0.01
Hypertension	27.7	28.3	0.26	0.02
Late-stage kidney disease	0.9	0.6	<0.001	0.03
Liver disease	2.9	2.8	0.30	0.01
Obesity	14.3	14.6	0.52	0.01
Peripheral vascular disease	2.1	1.6	<0.001	0.04

Discussion

Since the publication of McBurney's landmark study in 1891, appendectomy has been considered the definitive treatment for acute appendicitis [30]. Yet, a growing body of work has evaluated the use of non-operative management for uncomplicated cases, yielding mixed results [13,15,31–34]. In the present national analysis, we characterized the presence of interhospital variation in treatment approach. Notably, we identified 30 % of variability in non-operative management to be attributable to hospital-level factors. We subsequently noted low-operating hospitals to generally be metropolitan teaching institutions with lower annual appendicitis diagnosis volumes. Lastly, we report patients undergoing appendectomy at such low-operating centers to more frequently experience complications and non-elective readmissions, compared to others. With implications for policy and practice, several of these findings merit further discussion.

We report significant center-level variation in utilization of non-operative management strategies for acute uncomplicated appendicitis. Upon further analysis of center characteristics, we found low-operating centers to have lower annual appendicitis diagnosis volume, as well as appendectomy caseloads, compared to others. The volume-outcome relationship for acute appendicitis and appendectomy outcomes has been well described, such that lower volume centers yield inferior outcomes [35,36]. In agreement with prior reports [37,38], these hospitals were also more often private hospitals and teaching institutions. While hospital teaching status has been linked with similar outcomes as non-teaching centers [37], teaching institutions may be more likely to trial novel evidence-based techniques, such as non-operative management [38]. Even after adjustment for hospital diagnosis volume and teaching status, however, patients at LOH

Table 2
Unadjusted and adjusted outcomes following appendectomy at LOH and Non-LOH.
Outcomes reported as proportions or as Adjusted Odds Ratio (AOR) with 95 % confidence intervals (95 % CI). Reference: Non-LOH.
LOH, Low Operating Hospital; IQR, interquartile range; USD, United States dollar; SMD, Standardized Mean Difference.

	Unadjusted				Adjusted		
	LOH	Non-LOH	P	SMD	LOH	95 % CI	P
Clinical outcomes							
Major adverse events	5.9	6.1	0.45	0.01	1.03	0.96–1.12	0.41
Gastrointestinal complications	0.9	0.8	0.08	0.01	1.19	1.01–1.39	0.04
Cardiac complications	0.4	0.3	0.84	0.01	1.03	0.79–1.34	0.83
Infectious complications	1.5	1.2	0.002	0.02	1.27	1.11–1.46	0.002
Respiratory complications	1.1	1.3	0.10	0.01	1.01	0.87–1.17	0.90
Thrombotic complications	0.2	0.1	0.03	0.02	1.42	0.87–2.34	0.16
Need for blood transfusion	1.8	1.2	0.001	0.08	1.50	1.16–1.93	0.002
Acute kidney injury	2.9	3.3	0.01	0.01	0.92	0.82–1.04	0.17
Non-home discharge	1.3	1.4	0.71	0.03	1.11	0.96–1.29	0.15
Resource utilization							
Duration of stay (days) [IQR]	2 [1–3]	2 [1–3]	0.17	0.10	+0.14	+0.07–0.21	<0.001
Costs (USD $1000) [IQR]	10.7 [8.2–14.7]	10.2 [8.0–13.5]	<0.001	0.03	+0.95	+0.54–1.37	<0.001
Non-elective readmission within 30 days	4.9	4.2	<0.001	0.07	1.21	1.12–1.30	<0.001

demonstrated a five-fold increase in likelihood of being non-operatively treated. Altogether, our findings suggest systemic factors in the structure or quality of care at LOH may contribute to the use of non-operative management.

Importantly, patients undergoing appendectomy at LOH more frequently experienced infection and required blood transfusions during hospitalization. Of note, these findings persisted after adjustment for various patent demographic and clinical characteristics. While patients most commonly underwent appendectomy on the day of admission at both LOH and non-LOH, it is possible that delays of several hours could contribute to added infection risk [39]. Further, even after adjusting for complications experienced during hospitalization, we noted care at LOH to be linked with a ~ $950 increase in per-patient expenditures. This finding may be attributed to more inefficient care processes, repeated testing, or delays in discharge due to continued observation and medical management. Critically, while certain work has proposed non-operative management to be less resource intensive than appendectomy [14,40,41], others have suggested the total cost of care to be >5 % higher among patients managed non-operatively [12,42]. While the present work only considered expenditures linked with initial hospitalization, additional studies are needed to consider the comprehensive cost burden experienced by patients treated at LOH.

Considering all patients, we found those who received initial care at LOH experienced a ~ 10 % increase in relative risk of non-elective readmission within 90 days of discharge. Non-operatively managed patients at LOH more frequently re-presented with appendicitis and experienced perforation, compared to those originally treated at other centers. These sequelae may indicate inadequacies in selection criteria and should be used as metrics for quality improvement. Importantly, the risk of re-hospitalization – and associated costs - may extend far beyond the initial post discharge time period. Indeed, Findlay et al. [43] reported a 29 % risk of antibiotic failure and appendicitis recurrence at one year. Additional work is needed to more comprehensively ascertain the patient factors linked with greater risk of recurrent appendicitis, and identify those who would most benefit from appendectomy over non-operative treatment. Further, the risk of missed appendiceal malignancy must be addressed as part of patient counseling. Whether related to inherent severity or sequelae of management strategy, non-operatively treated patients have also been reported to experience reduced quality of life, relative to those who underwent appendectomy [33]. However, the integration of patient choice and shared decision-making has been associated with improved success of non-operative therapy [44]. Therefore, while continuing to rely on clinical experience and thorough risk assessment, care teams should seek out patients' perspectives and allow for informed conversations around treatment options, risks, and benefits as part of operative decision-making.

This study has several important limitations. The NRD offers a large, nationally-representative cohort for analysis, but relies on ICD coding, which can vary by clinician, hospital, or region. We could not capture granular radiologic, laboratory, or physiologic data during the hospitalization. We could not identify whether diagnosis of acute appendicitis was based on imaging, nor could we ascertain the specific imaging modalities, if any, used as part of a patient's workup. Further, operative decision-making was not reported. Data regarding antibiotic duration, route and coverage were not available. While we considered center-level volume, surgeon volume or experience was not detailed within the NRD. Additionally, we did not have the granularity to ascertain the underlying factors contributing to hospital-level operating rates. Future single- or multi-center studies should build on this work to evaluate the precise underlying mechanisms shaping LOH. Despite such limitations, however, we used a large national database and applied robust statistical methods to address known confounders and increase the generalizability of our findings.

In conclusion, we identified significant hospital-level variation in the non-operative management of uncomplicated appendicitis. Further, we defined and characterized low-operating centers, and found them to be associated with increased complications and readmissions. Our findings call for a reexamination of care pathways that may contribute to increased utilization of non-operative strategies at these institutions. Ultimately, more granular investigations are needed to identify best practices and disseminate such protocols across hospitals to improve quality of care and post-treatment outcomes.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sopen.2024.05.008.

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Ethics approval

This study was deemed exempt from full review by the Institutional Review Board at the University of California, Los Angeles, due to the deidentified nature of the NRD.

CRediT authorship contribution statement

Baran Khoraminejad: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Sara Sakowitz:** Conceptualization, Data curation,

Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing. **Giselle Porter:** Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **Nikhil Chervu:** Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – review & editing. **Konmal Ali:** Data curation, Formal analysis, Methodology, Visualization, Writing – review & editing. **Saad Mallick:** Validation, Visualization, Writing – review & editing. **Syed Shahyan Bakhtiyar:** Methodology, Project administration, Supervision, Validation, Writing – review & editing. **Peyman Benharash:** Conceptualization, Formal analysis, Methodology, Project administration, Resources, Software, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors have no related conflicts of interest or disclosures to declare.

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