7-1-2015

Variation in the Diagnosis and Management of Appendicitis at Canadian Pediatric Hospitals

Graham C. Thompson
University of Calgary

Suzanne Schuh
Hospital for Sick Children University of Toronto

Jocelyn Gravel
CHU Sainte-Justine - Le Centre Hospitalier Universitaire Mère-Enfant

Sarah Reid
Children's Hospital of Eastern Ontario, Ottawa

Eleanor Fitzpatrick
Dalhousie University

See next page for additional authors

Authors

Graham C. Thompson, Suzanne Schuh, Jocelyn Gravel, Sarah Reid, Eleanor Fitzpatrick, Troy Turner, Maala Bhatt, and Darcy Beer

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL CONTRIBUTION

Variation in the Diagnosis and Management of Appendicitis at Canadian Pediatric Hospitals

Graham C. Thompson, MD, Suzanne Schuh, MD, Jocelyn Gravel, MD, Sarah Reid, MD, Eleanor Fitzpatrick, RN, MN, Troy Turner, MD, Maala Bhatt, MD, Darcy Beer, MD, Geoffrey Blair, MD, Robin Eccles, MD, Sarah Jones, MD, Jennifer Kilgar, MD, Natalia Liston, MD, John Martin, MD, Brent Hagel, PhD, and Alberto Nettel-Aguirre, PhD, on behalf of Pediatric Emergency Research Canada

Abstract

Objectives: The objective was to characterize the variations in practice in the diagnosis and management of children admitted to hospitals from Canadian pediatric emergency departments (EDs) with suspected appendicitis, specifically the timing of surgical intervention, ED investigations, and management strategies.

Methods: Twelve sites participated in this retrospective health record review. Children aged 3 to 17 years admitted to the hospital with suspected appendicitis were eligible. Site-specific demographics, investigations, and interventions performed were recorded and compared. Factors associated with after-hours surgery were determined using generalized estimating equations logistic regression.

Results: Of the 619 children meeting eligibility criteria, surgical intervention was performed in 547 (88%). After-hours surgery occurred in 76 of the 547 children, with significant variation across sites (13.9%, 95% confidence interval = 7.1% to 21.6%, $p < 0.001$). The overall perforation rate was 17.4% (95 of 547), and the negative appendectomy rate was 6.8% (37 of 547), varying across sites ($p = 0.004$ and $p = 0.036$, respectively). Use of inflammatory markers ($p < 0.001$), blood cultures ($p < 0.001$), ultrasound ($p = 0.001$), and computed tomography ($p = 0.001$) also varied by site. ED administration of narcotic analgesia and antibiotics varied across sites ($p < 0.001$ and $p = 0.001$, respectively), as did the type of surgical approach ($p < 0.001$). After-hours triage had a significant inverse association with after-hours surgery ($p = 0.014$).

Conclusions: Across Canadian pediatric EDs, there exists significant variation in the diagnosis and management of children with suspected appendicitis. These results indicate that the best diagnostic and management strategies remain unclear and support the need for future prospective, multicenter studies to identify strategies associated with optimal patient outcomes.

ACADEMIC EMERGENCY MEDICINE 2015;22:811–822 © 2015 by the Society for Academic Emergency Medicine

Appendicitis is the most common nontraumatic surgical emergency in children,[1,2] yet it continues to present diagnostic and management uncertainty.[3] Current strategies for diagnosing appendicitis include the use of clinical scoring systems,[4–7] laboratory markers of infection and inflammation,[8–10] and

From the Alberta Children's Hospital Research Institute and Department of Pediatrics, University of Calgary (GCT, RE, NL, BH, AN), Calgary AB; the Hospital for Sick Children, University of Toronto (SS, MB), Toronto, ON; the Centre Hospitalier Universitaire Ste-Justine, Universite de Montreal (JG), Montreal, QC; the Children's Hospital of Eastern Ontario, University of Ottawa (SR), Ottawa, ON; IWK Health Centre, Dalhousie University (EF), Halifax, NS; the Stollery Children's Hospital, University of Alberta (TT), Edmonton, AB; the Winnipeg Children's Hospital, University of Manitoba (DB), Winnipeg, MB; the British Columbia Children's Hospital, University of British Columbia (GB), Vancouver, BC; the Children's Hospital London Health Sciences Centre, Western University (SJ, JK), London, ON; the Janeway Children's Health and Rehabilitation Centre, Memorial University (JM), St. John's, NL; and the Department of Community Health Sciences, University of Calgary (BH, AN), Calgary, AB.

Received September 30, 2014; revisions received December 12, 2014, and January 12, 2015; accepted January 12, 2015.
Presented at the American Academy of Pediatrics National Conference and Exhibition, New Orleans, LA, October 2013.
All phases of this study were supported by an internal University Research Grants Committee (URGC) Seed Grant, University of Calgary, Calgary, AB. B. Hagel holds the Alberta Children's Hospital Foundation Professorship in Children Health and Wellness, funded through the support of an anonymous donor and the Canadian National Railway Company, as well as the Alberta Heritage Foundation for Medical Research (now Alberta Innovates-Health Solutions) Population Health Investigator Award.
The authors have no potential conflicts to disclose.
Supervising Editor: Elizabeth Alpern, MD.

Address for correspondence and reprints: Graham Thompson; e-mail: graham.thompson@albertahealthservices.ca.

doi: 10.1111/acem.12709
ISSN 1069-6563
PII ISSN 1069-6563583

diagnostic imaging studies such as ultrasound (US) or computed tomography (CT).[11–14] These tests are limited by suboptimal accuracy, limited availability, or potential for adverse effects[15] in the pediatric population, compelling health care providers to seek better diagnostic strategies for children presenting to the emergency department (ED) with suspected appendicitis. Recent evidence demonstrates that combining these strategies into clinical pathways may be an effective way to improve diagnostic accuracy;[16–19] however, the extent to which this knowledge has been translated into practice in EDs is not known.

Similarly, the optimal approach for managing children with appendicitis has not been conclusively identified. Traditionally, appendicitis has been considered a surgical emergency in an attempt to mitigate adverse patient outcomes (perforation, abscess formation, sepsis). Recent literature, however, demonstrates that delaying appendectomy until daytime hours may be safe practice and has fueled the debate between emergent and urgent appendectomy,[20–26] nonsurgical management of uncomplicated appendicitis,[27–29] and the potential effect these approaches may have on patient outcomes such as perforation. Antibiotic monotherapy in uncomplicated appendicitis has been proposed as an alternative to traditional triple therapy to simplify ED processes, reduce error, and decrease antibiotic resistance.[30] In addition, the use of analgesia has been shown to be highly variable in multiple painful conditions presenting to the ED,[31–35] and appendicitis is likely no exception.

Given the lack of conclusive national standards for the diagnosis and management of pediatric appendicitis in Canada, and the documented practice variation for other common pediatric emergency presentations,[36–42] the objective of this study was to characterize the variations in practice for the diagnosis and management of children with suspected appendicitis who were admitted to Canadian academic hospitals. The study aims were focused on 1) after-hours surgical intervention (primary aim, due to perceived implications for patient safety, and responsible resource utilization), 2) ED investigations including laboratory and imaging studies, and 3) ED interventions such as the administration of analgesia and antibiotics. This information will inform future outcome-focused research and knowledge translation platforms to optimize care of this population.

METHODS

Study Design

This was a multicenter retrospective health record analysis. Protocol approval and waiver of consent from the research ethics board at each of the institutions was granted.

Study Setting and Population

Twelve health care institutions from across Canada participated in the study (Janeway Children's Health and Rehabilitation Centre, St. John's, NL; IWK Health Centre, Halifax, NS; Centre Hospitalier Universitaire Ste-Justine, Montreal, QC; Montreal Children's Hospital, Montreal, QC; Children's Hospital of Eastern Ontario, Ottawa, ON; Kingston General Hospital, Kingston, ON; Hospital for Sick Children, Toronto ON; Children's Hospital London Health Sciences Centre, London, ON; Winnipeg Children's Hospital, Winnipeg, MB; Alberta Children's Hospital, Calgary, AB; Stollery Children's Hospital, Edmonton, AB; British Columbia Children's Hospital, Vancouver, BC). All sites are tertiary-care hospitals with 24-hour ED coverage and are members of both Pediatric Emergency Research Canada (PERC) and Canadian Association of Pediatric Surgeons (CAPS). Eleven sites have dedicated pediatric EDs, and one has a general ED. The participating sites represent seven Canadian provinces and have between 23,000 and 81,800 pediatric ED visits annually.

Children aged 3 to 17 years with suspected appendicitis who were admitted to hospital from Canadian academic EDs were analyzed. Children admitted to the pediatric intensive care unit were excluded as they were more likely to be managed according to institutional sepsis pathways rather than receive routine appendicitis care. We excluded those children in whom the primary workup was performed outside of the managing hospital. Those under 3 years old were not included as these children have limitations in verbal skills and the presentation of appendicitis is often atypical.[43]

Study Protocol

Each of the participating institutions reviewed the health records of children consecutively admitted to hospital with suspected appendicitis during two study periods (starting February 1, 2010, and October 1, 2010) until at least 25 eligible subjects were reviewed for each time period, for a total of 50 children per site enrolled. The two distinct study periods were chosen to account for seasonal variability in ED presentations and practice patterns.

A standardized data extraction form was used to obtain relevant information from electronic and paper health records at each site. At each participating hospital, the department of medical records identified consecutive records of children admitted to hospital within the study time period using the International Classification of Disease-version 10-Canada (ICD-10-CA) discharge diagnosis codes for appendicitis, suspected appendicitis, or rule-out appendicitis (K35-37). Trained research assistants blinded to the primary research question reviewed all identified health records and entered relevant data from eligible records into REDCap,[44] a secure Web-based application designed to support data capture for research studies (hosted and supported by the Women and Children's Health Research Institute's Clinical Research Informatics Core at the University of Alberta). Data were included only from the ED visit that lead to admission. Extracted data included elements related to demographics, presenting signs and symptoms, investigations and interventions performed in the ED, hospital admission data, surgical interventions, and hospital discharge metrics.

Definitions. The outcome of appendicitis was defined as either 1) a pathology report documenting appendicitis or acute inflammation of the appendix or 2) an abdominal abscess related to perforated appendix requiring intravenous (IV) antibiotics and/or percutaneous drainage with interval appendectomy. Perforation was defined as either 1) pathology report indicating any positive documentation of perforation, rupture, or any disruption of the integrity of the appendix or 2) abdominal abscess related to perforated appendix requiring IV antibiotics and/or percutaneous drainage with interval appendectomy. After-hours surgery was defined as operative intervention occurring between midnight and 08:00 (daytime = 08:01 to 17:00, evening = 17:01 to midnight). Surgical intervention included delayed appendectomy following initial management with a drain and antibiotics.

Outcomes

The primary outcome was the performance of appendectomy after hours among children undergoing surgical intervention. Secondary outcomes included the negative appendectomy rate and perforation rate; the rate of laboratory and imaging studies, analgesics, and antibiotics performed in the ED; and the rate of laparoscopic and open surgical approaches. We also evaluated patient disposition and hospital flow metrics such as time from triage to admission, to surgery, and to discharge.

Data Analysis

As the after-hours time frame represents one-third of the day, the proportion of after-hours surgery was estimated at 0.33. To obtain a margin of error of less than 10% (0.09) for 95% confidence intervals (CIs), 105 appendectomies would be required prior to adjusting for the design effect of cluster sampling.[45] Enrolling 50 children from individual sites, with an estimated intraclass correlation (ICC) of 0.1 (conservative estimate to account for potential variation within clusters), the design effect was estimated at 5.9. Therefore, a total sample size of approximately 600 children would be required, with 12 sites enrolling 50 children each to provide sufficient numbers.

Data were analyzed using Stata version 12.1. Descriptive statistics are reported for patient characteristics and for the proportions of ED and surgical interventions. Continuous numerical variables were reported as means with standard deviation (SD) for normally and symmetrically distributed data or as medians with interquartile range (IQR) for nonnormal or nonsymmetrical distributions. Categorical variables were reported as proportions with 95% CI. Differences in baseline characteristics and between-site practices were tested using the chi-square or Fisher's exact tests for proportions and analysis of variance (ANOVA) for continuous variables. For ANOVA analyses in which the assumption of equality of variance was violated (Levene's t-test for equality of variance) or normality was violated, the Kruskal-Wallis test was performed.

Figure 1. Study eligibility. Dx = diagnosed; PICU = pediatric intensive care unit.

To test for predictors of after-hours surgery across sites, generalized estimating equations (GEE) logistic regression (binomial logit) with exchangeable correlation matrix was used. GEE modeling included the predetermined candidate variables of age, sex, after-hours triage, pediatric Canadian Triage and Acuity Scale (CTAS),[46] duration of abdominal pain, performance of at least one imaging study in the ED, performance of at least one US, performance of at least one CT, negative appendectomy, and perforation. Variables were selected based on biological and scientific plausibility related to patient characteristics, potential severity of illness, timing of presentation, and resource availability. Relaxation of the routine 10 cases per variable (i.e., rule of thumb for sample size) was used according to Vittinghoff and McCulloch,[47] as our event per variable rate was 7.6 and prevalence of outcome was 14%. Candidate variables were entered in the model, which was not weighted or reduced via elimination to ensure a more parsimonious model. The significance alpha level was set at 5% for statistical testing and 95% CIs are reported where appropriate. 95% CIs were reported using exponentiated coefficients. Inter-rater reliability was performed on a random sample of 2% of subjects enrolled using the primary outcome variable, and GEE modeling variables are reported as an overall kappa value as well as per variable (Data Supplement S1, available as supporting information in the online version of this paper).

RESULTS

Of the 937 records screened, 619 met eligibility criteria (Figure 1); 352 (56.9%) eligible children were males, and the mean (±SD) age was 11.4 (±3.5) years. The majority of children (325, 52.5%) presented to the ED during daytime hours and two-thirds were triaged for urgent assessment (CTAS 3).[46] Patient demographic data are shown in Table 1, and site-specific demographics are summarized in Data Supplement S2 (available as supporting information in the online version of this paper). A total of 547 of 619 children (88%) underwent surgical intervention (Table 2). The remaining 12% were discharged home following a period of observation. None of the children in this cohort were managed with nonoperative treatment of acute appendicitis.

Primary Outcome: After-hours surgery

After-hours surgery was performed in 76 of 547 children (13.9%, 95% CI = 7.1% to 21.6%) with significant variation across sites (Table 3). The calculated ICC and design effect from clustering were 0.10 and 5.41, respectively.

At six of the 12 participating sites, after-hours surgery occurred in fewer than 10% of cases. Site ($p < 0.001$), after-hour triage ($p < 0.001$), and duration of abdominal pain ($p < 0.020$) were associated with after-hours surgery. Given 76 after-hours appendectomies and 10 variables (event per variable = 7.6), GEE logistic regression modeling indicated that after-hours triage (coefficient = –1.523; adjusted odds ratio = 0.217, 95% CI = 0.063 to 0.744) was inversely associated with after-hours surgery (Table 3). Minimal collinearity between predictor variables was seen (all square root of variance inflation factors < 2); moreover, there was no evidence of violation of linearity for continuous predictors. The model remained robust following exclusion of outliers and sequential exclusion of sites (to account for clustering).

Secondary Outcomes: Perforation and Negative Appendectomy

The overall performance rate was 17.4% (95 of 547), while the negative appendectomy rate was 6.8% (37 of 547). Perforation was associated with reported duration of abdominal pain ($p = 0.049$, unadjusted). Significant variation in both perforation and negative appendectomy rates existed across sites ($p = 0.004$ and $p = 0.036$, respectively). After-hours surgery was not an independent predictor of either perforation or of negative appendectomy (unadjusted p-value = 0.746 and p = 0.805, respectively).

Other Outcomes of Interest: Investigations

Figure 2 describes the use of laboratory investigations and the variation across sites. A white blood cell (WBC) count was the most commonly and consistently performed test (96.6%). Inflammatory markers (erythrocyte sedimentation rate, C-reactive protein) and blood

Table 1
Characteristics of Children Admitted to Hospital for Suspected Appendicitis (*N* = 619)

Characteristic	Overall Population*	Range Across Sites	p-value†
Number enrolled	619	50–55	
Age (yr), mean (±SD)	11.4 (±3.5)	10.0–12.9	<0.001
Male, *n* (%)	352 (57)	22–35 (40–70)	0.106
Triage time category (%)			0.602
Day (08:01–17:00)	325 (52)	22–33 (40–66)	
Evening (17:01–00:00)	203 (33)	13–23 (26–42)	
Night (00:01–08:00)	91 (15)	4–12 (8–24)	
Canadian Triage and Acuity Scale (%)			<0.001
1	11 (2)	0–11 (0–22)	
2	72 (12)	1–21 (2–42)	
3	412 (66)	24–42 (47–82)	
4	112 (18)	1–26 (2–47)	
5	2 (0)	0–1 (0–2)	
Prior ED visit for same illness (%)	56 (9)	1–10 (2–20)	0.026
Duration of abdominal pain in hours, median (±SD)	24 (±49)		<0.001

*Site-specific data available in Data Supplement S1.
†Comparison of data across sites based on individual-level data. Tested by chi-square, Fisher's exact, or ANOVA as appropriate.

Table 2
Management Strategies and Outcomes in Pediatric Appendicitis by Site (N = 619)

	Overall	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site 7	Site 8	Site 9	Site 10	Site 11	Site 12	p-value*
ED management	619	51	55	50	50	52	55	50	50	50	51	50	55	
Analgesia administered														
Any	381 (62)	31 (61)	20 (36)	34 (68)	41 (82)	31 (60)	30 (57)	32 (64)	35 (70)	31 (62)	36 (71)	26 (52)	34 (63)	0.001
Narcotic	265 (43)	21 (41)	9 (16)	24 (48)	37 (74)	19 (27)	25 (45)	19 (38)	17 (34)	30 (60)	23 (45)	23 (46)	17 (31)	0.001
Antibiotics administered														
Any antibiotic	411 (66)	28 (55)	22 (40)	36 (72)	42 (84)	34 (65)	40 (72)	31 (62)	31 (62)	31 (62)	45 (88)	21 (42)	50 (92)	<0.001
Single therapy	170 (27)	14 (27)	17 (31)	17 (34)	27 (54)	8 (15)	8 (15)	16 (32)	14 (28)	1 (2)	37 (73)	1 (2)	10 (18)	
Double therapy	177 (29)	13 (26)	4 (7)	1 (2)	3 (6)	23 (44)	32 (58)	2 (4)	14 (28)	24 (48)	7 (16)	19 (38)	35 (64)	
Triple therapy	60 (10)	1 (2)	1 (2)	16 (32)	11 (22)	3 (6)	0 (0)	13 (26)	3 (6)	6 (12)	0 (0)	1 (2)	5 (9)	
Other (% antibiotics)	4 (1)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	
Bolus IV fluids administered	570 (93)	41 (80)	54 (98)	49 (98)	50 (100)	37 (71)	46 (85)	48 (96)	47 (94)	50 (100)	48 (94)	49 (98)	51 (94)	<0.001
Disposition from ED														
Direct to OR	316 (51)	26 (51)	12 (22)	18 (36)	22 (44)	17 (33)	28 (51)	41 (82)	13 (26)	33 (66)	30 (59)	49 (98)	27 (50)	<0.001
Admit to ward	303 (49)	25 (49)	43 (78)	32 (64)	28 (56)	35 (67)	27 (49)	9 (18)	37 (74)	17 (34)	21 (41)	1 (2)	27 (49)	<0.001
Surgical intervention	547 (88)	50 (98)	24 (44)	47 (94)	48 (96)	49 (94)	54 (98)	44 (88)	41 (82)	45 (90)	49 (96)	50 (100)	46 (84)	<0.001
Approach														<0.001
Laparoscopic	446 (82)	44 (88)	7 (29)	44 (93)	26 (54)	43 (88)	30 (56)	44 (100)	38 (93)	44 (98)	44 (90)	42 (84)	40 (87)	
Laparoscopic to open	4 (1)	1 (2)	0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Open	90 (16)	5 (10)	17 (70)	1 (2)	22 (46)	6 (12)	22 (40)	0 (0)	0 (0)	1 (2)	4 (8)	8 (16)	4 (9)	
Percutaneous drain	7 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	3 (7)	0 (0)	1 (2)	0 (0)	2 (4)	
Surgical time category														
Day, 08:01–17:00	205 (37)	11 (22)	14 (58)	15 (32)	18 (38)	25 (51)	34 (63)	17 (39)	23 (56)	21 (47)	13 (27)	5 (10)	9 (20)	<0.001
Evening, 17:01–00:00	266 (49)	22 (44)	9 (38)	27 (57)	27 (56)	24 (49)	18 (33)	20 (45)	17 (41)	21 (47)	29 (59)	29 (58)	23 (50)	
Night, 00:01–08:00	76 (14)	17 (34)	1 (4)	5 (11)	3 (6)	0 (0)	2 (4)	7 (16)	1 (2)	3 (7)	7 (14)	16 (32)	14 (30)	
Pathologic diagnoses														
Perforation	95 (17.4)	4 (8.0)	5 (20.8)	11 (23.4)	15 (31.2)	4 (8.2)	14 (25.9)	10 (22.7)	6 (14.6)	5 (11.1)	9 (18.4)	11 (22.0)	1 (2.2)	0.004
Negative appendectomy	37 (6.8)	2 (4.0)	1 (4.2)	1 (2.1)	1 (2.1)	2 (4.1)	6 (11.1)	1 (2.3)	9 (22.0)	3 (6.7)	4 (8.2)	2 (4.0)	5 (10.9)	0.010

Data reported as n (%).
IV = intravenous; OR = operating room.
*Comparison across sites.

Table 3
Predictors of After-hours Surgery as Determined by Generalized Estimating Equation (GEE) With Logistic Regression Modeling

Variable	After-hours Surgery (n = 76)	Regular Hours Surgery (n = 471)	Unadjusted p-value	GEE modeling	
				AOR	95%CI
Age (yr), mean (±SD)	11.5 (±3.3)	11.4 (±3.5)	0.225	1.009	0.936–1.088
Male, n (%)	48 (63.2)	274 (58.2)	0.452	0.802	0.474–1.357
After-hours triage (%)	2 (2.6)	89 (18.9)	0.001	0.217	0.063–0.744
CTAS, mean (±SD)	3 (0.7)	3 (0.6)	0.301	1.053	0.696–1.593
Reported duration of abdominal pain, hr, mean (±SD)	39.5 (±53.3)	38.4 (±49.7)	0.020	1.000	0.995–1.005
Any diagnostic imaging performed in the ED (%)	53 (69.7)	356 (75.6)	0.249	0.358	0.117–1.102
Any US performed in the ED (%)	49 (64.5)	309 (65.6)	0.885	1.467	0.500–4.305
Any CT performed in the ED (%)	4 (5.3)	18 (3.8)	0.528	1.337	0.301–5.935
Negative appendectomy*	4 (5.3)	33 (7.0)	0.805	1.420	0.409–4.935
Perforation†	12 (15.8)	83 (17.6)	0.746	1.044	0.548–1.987

AOR = adjusted odds ratio; CTAS = Canadian Triage and Acuity Scale; GEE = general estimating equation.
*As per pathology report
†As per pathology report or percutaneous drainage for appendiceal abscess.

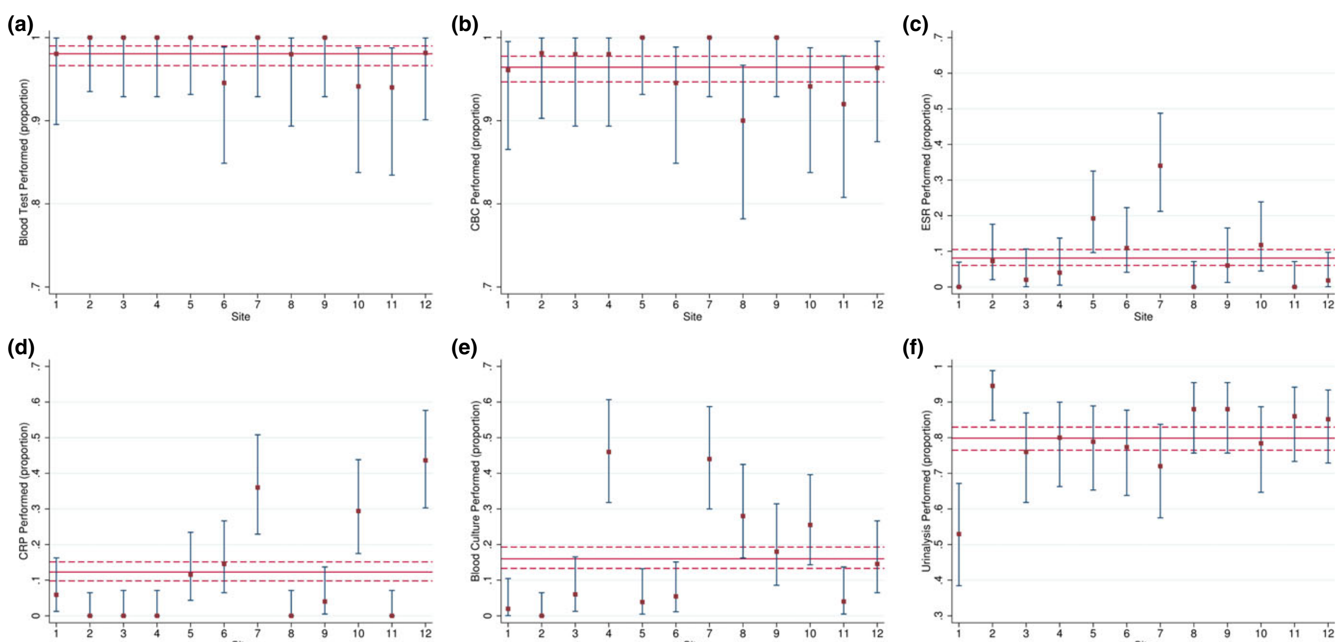

Figure 2. Variations in investigations performed in the ED by site. (a) Any blood tests performed in the ED; (b) CBC performed in the ED; (c) ESR performed in the ED; (d) CRP performed in the ED; (e) blood cultures performed in the ED; (f) urinalysis performed in the ED. Error bars represent 95% CIs. Horizontal solid and dotted lines represent the proportion in the overall population with 95% CIs. CBC = complete blood count; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

cultures were completed in a minority of patients, with significant variation across sites ($p < 0.001$ in each of the three variables). Urinalysis was performed in 80% of subjects and was more commonly performed in females than males (85.6% vs. 75.6%, p = 0.002).

Diagnostic imaging utilization varied significantly across sites (Figure 3). At least one imaging study was done in 477 of 619 children (77.5%), with significant variation between sites (p = 0.001). Abdominal plain films were performed in 131 (21.2%) children, with significant variation between sites (p = 0.001); one-third of all abdominal plain films were performed at a single site. US was completed in 415 (67.0%) children with significant variation between sites (p = 0.001). While one site performed US in all enrolled patients, US was used in less than 50% of children at three other sites. US utilization was significantly higher in females compared with males (198 of 267 = 74.2% vs. 217 of 352 = 61.6%; p = 0.001). The negative appendectomy rates for children with and without US were similar at 8.1 and 4.2% (p = 0.11). Twenty-two of 619 (3.6%) children had CT performed, with a significant variation between sites (p = 0.0035). Of the 22 children who underwent CT, initial US was performed in 13 (59.1%). The US was incon-

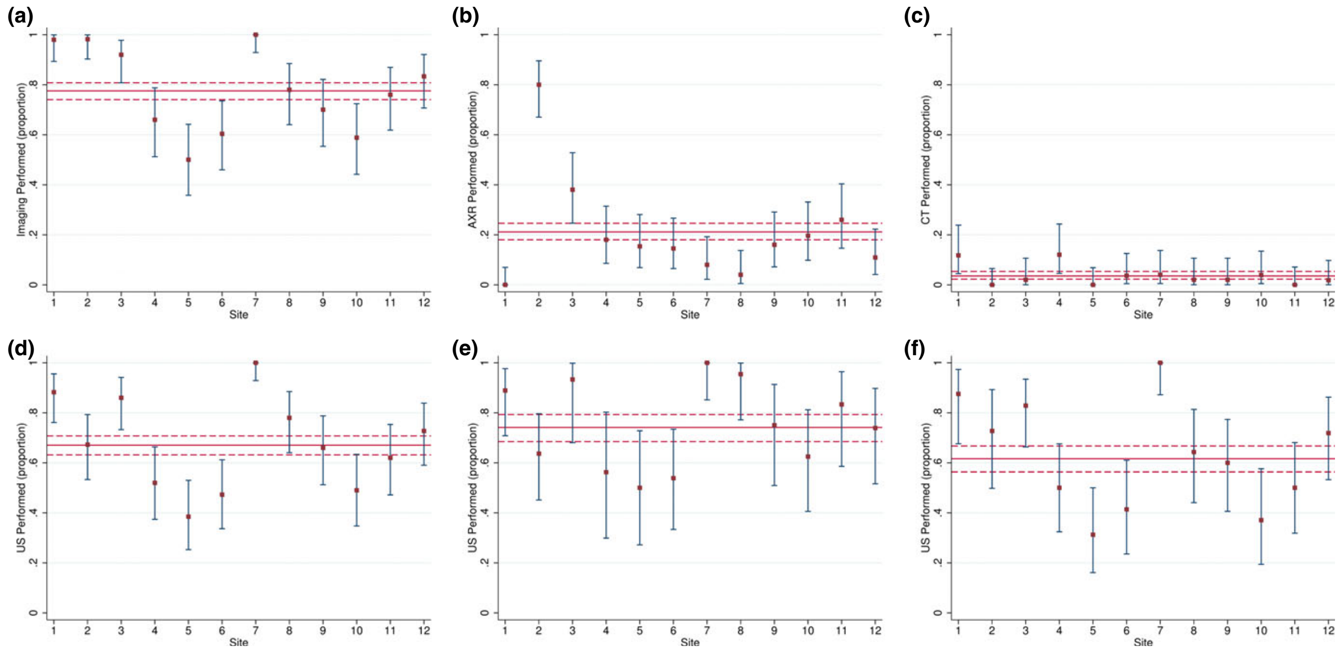

Figure 3. Variations in diagnostic imaging performed in the ED by site. Error bars represent 95% CIs. (a) Any diagnostic imaging performed in the ED; (b) abdominal X-ray performed in the ED; (c) computed tomography performed in the ED; (d) ultrasonography performed in the ED; (e) ultrasonography performed in the ED, females; (f) ultrasonography performed in the ED, males. Horizontal solid and dotted lines represent the proportion in the overall population with 95% CIs. AXR = abdominal X-ray; CT = computed tomography; US = ultrasound.

clusive in nine of these children; the remaining four had associated abscesses that were further delineated with the CT scans. In 181 of 547 children (33.1%) who underwent appendectomy, neither US nor CT was performed preoperatively. Data Supplement S3 (available as supporting information in the online version of this paper) describes the relationship between imaging results and diagnosis of appendicitis.

Other Outcomes of Interest: Management Strategies

Other ED and surgical management strategies are summarized in Table 2. Less than half of all children (265 of 619) received narcotic analgesia during their ED stays, while two-thirds (411 of 619) received antibiotics. A laparoscopic approach (laparoscopy or laparoscopy to open) was used in 450 of 547 (82.3%) cases, with significant variation between sites ($p < 0.001$). Hospital flow metrics for the entire sample are presented in Table 4. Figure 4 illustrates variations in flow metrics by site using median time and IQRs.

DISCUSSION

To the best of our knowledge, we have conducted the first nationwide clinical study describing the variation in diagnostic and management strategies used in children admitted to Canadian academic hospitals with suspected appendicitis. A similar study evaluating trends in imaging studies has been conducted in the United States by Bachur and Hennelly.[48] Our results demonstrate significant site-specific variations in after-hours surgical intervention, perforation rates, and negative appendectomy rates, as well as in the majority of investigations and interventions performed.

Although acute appendicitis has historically been considered a surgical emergency requiring prompt inter-

Table 4
Flow Metrics (Median Time From Triage to Intervention) in Children Presenting to the ED With Suspected Appendicitis*

Metric	Mean (±SD)	Median	IQR	p-value†
Triage to laboratory investigations sent (min)	147 (±117)	116	73–185	<0.001
Triage to analgesia administered (min)	252 (±221)	196	102–308	<0.001
Triage to US performed (min)	378 (±304)	275.3	176–469	<0.001
Triage to antibiotics administered (min)	402 (±256)	331.0	233–474	<0.001
ED LOS (min)	464 (±294)	395	278–544	<0.001
Triage to appendectomy performed (min)	717 (±435)	608	394–950	0.003
Hospital LOS (days)	3.2 (±3.1)	1.98	1.24–3.93	<0.001

IQR = interquartile range.
*For those children exposed to the intervention.
†Comparison across sites using Kruskal-Wallis testing.

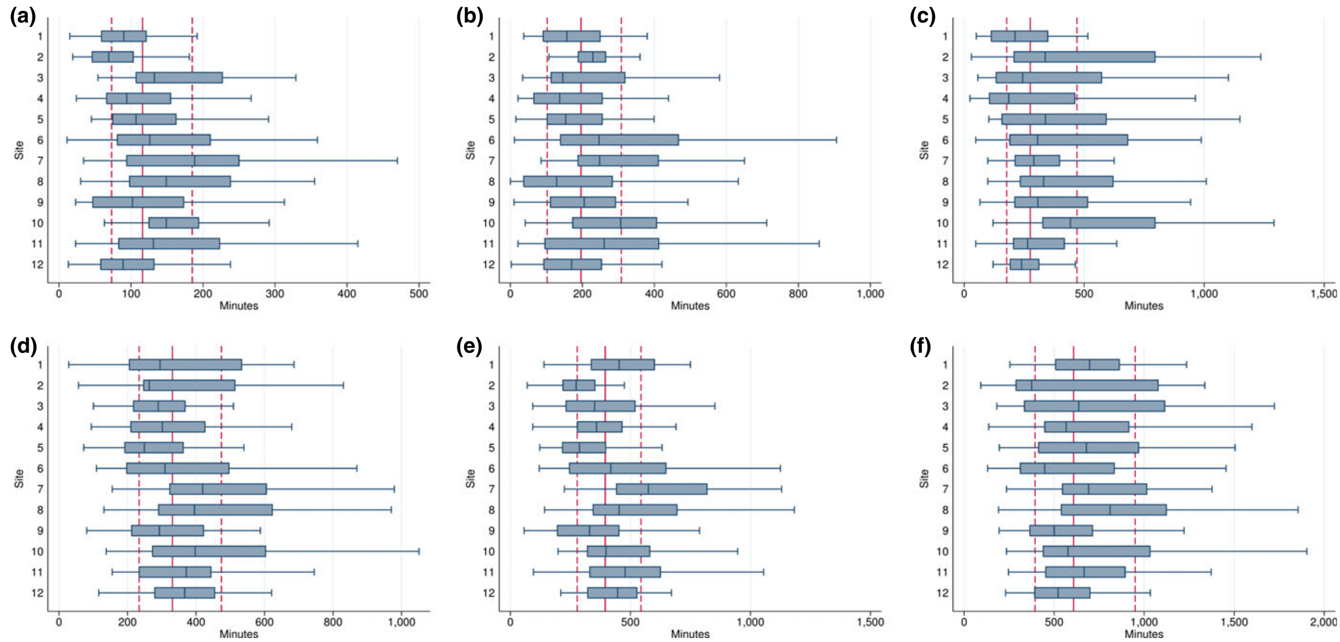

Figure 4. Boxplots demonstrating the variations in flow metrics of children presenting to the ED with suspected appendicitis, by site. (a) Time from triage to blood test; (b) time from triage to analgesia; (c) time from triage to ultrasound; (d) time from triage to antibiotics; (e) emergency department length of stay; (f) time from triage to appendectomy. Vertical solid and dotted lines represents the median and interquartile range values for the population as a whole.

vention to reduce risk of morbidity (perforation, wound infection, abscess formation, and sepsis), renewed debate regarding optimal timing of surgical intervention reveals contradictory data.[20–25,49–53] The results of our study demonstrate that appendectomy is infrequently performed after hours in Canadian tertiary hospitals, although variation across sites does exist. This practice variation could be explained by site-specific surgical policies or established management pathways, resource availability, or the use of ED observation units. Our data support previous studies that have demonstrated that low rates of after-hours surgery did not appear to be associated with perforation, although further prospective studies in the pediatric population should be performed to confirm these results. One would expect that after-hours appendectomy has implications in health care utilization and costs relating to maintaining operating rooms during times when fee codes are higher and staffing allocation is lower. Therefore, efforts to minimize the proportion of after-hours surgeries may represent responsible stewardship of resources in the nationally governed and provincially administered Canadian public health system.

While the test characteristics of commonly used laboratory investigations[3] may limit their utility in diagnosing appendicitis, almost all children in our study had at least one blood test performed in the ED. It is possible that the high rate of WBC measurement in our population is related to its presence in both the Pediatric Appendicitis Score[4] and Alvarado Score,[5] which some clinicians may have used during their decision-making processes. Other investigators have shown a decreasing trend in measurement of WBC in children with suspected appendicitis over time.[54] We have also shown that utilization of other blood tests varied significantly across sites, which may be related to test characteristics that make them inadequate for routine use. While there is promising preliminary evidence for several novel markers used to identify appendicitis,[10,55–57] these are currently unavailable for routine clinical practice.

Our study has demonstrated significant site-specific variation in the use of imaging studies for children with suspected appendicitis. At some sites, up to 50% of children had appendectomies performed on clinical assessment alone, while one site performed imaging studies on every child. Overall, US performed by diagnostic imaging staff represented the most common imaging study performed, while the use of CT was infrequent. Our very low rate of CT utilization in suspected appendicitis across Canadian sites is in contrast to recent studies in the United States demonstrating median rates of CT utilization of 34% to 40%.[48,58] Recent concerns regarding long-term effects of ionizing radiation[15] have led to attempts to limit exposure while maintaining low negative appendectomy rates by using clinical scoring systems or starting with US as the initial imaging modality.[59–61] Our study demonstrates that children admitted to hospital from Canadian pediatric EDs with suspected appendicitis have a very low rate of CT exposure and that overall almost one-third of appendectomies were performed without prior imaging studies.

The relatively low rate of analgesia administration found in our study is concerning and reflects previous studies evaluating the use of analgesics for children with painful conditions in the ED.[62] Historical reluctance toward early administration of narcotic medications in suspected appendicitis has since been refuted by evidence indicating that use of narcotics neither changes the accuracy of diagnosing appendicitis nor does it delay the decision for surgical intervention.[63–65] A clear limitation to reporting pain management administration retrospectively is that it does not identify children who were offered analgesia but declined. One previous review of analgesia administration in children presenting with suspected appendicitis emphasizes the need to appropriately manage patients in pain.[66] Several studies have demonstrated improved rates of analgesia administration following the implementation of departmental protocols and pathways.[67] Integration of pain management into clinical ED appendicitis pathways may improve rates of analgesic administration across the country.

While traditional antimicrobial therapy for appendicitis has been "triple therapy," with ampicillin, gentamicin, and metronidazole, recent Surgical Infection Society (SIS) guidelines recommend that children with uncomplicated appendicitis receive prophylaxis with either single or double therapy to provide Gram-negative and anaerobic coverage.[68] For those children in our study who received antibiotics in the ED, the majority were managed with single or double therapy, in keeping with the above SIS guidelines, although significant variability was shown; for example, some sites appeared to favor specific therapeutic agents, but most proved less specific in their approach to antimicrobial prophylaxis. Implementing SIS guidelines into departmental clinical pathways may be useful in standardizing the approach to antimicrobial administration in children with appendicitis.

The most common surgical approach in our study sites was laparoscopy. A review of Pediatric Health Information System data demonstrated an increasing rate of laparoscopic approach from 22% in 1999 to 91% in 2010. Lower rates of wound infection and intestinal obstruction were noted with laparoscopy compared with the open approach.[69] Laparoscopy in Australian children increased from <1% in 1999 to 70% in 2009.[70] Although the 2012 data from the National Survey of Research Commercialization in the United Kingdom demonstrated somewhat lower rates of laparoscopy for appendicitis (60%), this population included adults and nontertiary sites, and some centers did not offer laparoscopy after hours or on weekends.[71] A recent Cochrane review, and a pediatric-focused literature review, recommended that the laparoscopic approach be used unless there is a contraindication.[72,73] While some surgeons may prefer an open approach in children with perforated appendicitis, previous studies have suggested that complication rates in this population may be no different with the use of laparoscopy compared to the open technique.[74]

Despite variations in practice, the overall negative appendectomy rate in our study was low; the majority of sites had rates of less than 5%, although variation certainly exists. Our data are consistent with the recent Kids Inpatient Database analysis that showed a negative appendectomy rate of 7%.[75] Bachur and Hennelly[48] also demonstrated a rate less than 5% in their analysis of 40 pediatric EDs across America. Differences in negative appendectomy rates across sites in our study may be attributed to variations in the use of diagnostic strategies, although further prospective studies are required. The negative appendectomy rate should also be viewed in light of its balancing measure: the perforation rate. Several factors are thought to increase the rate of perforation, including young age,[43] obesity, duration of symptoms,[21,25] and air quality index.[76,77] Our overall perforation rate (17.4%) was lower than those recently reported by Aarabi et al.[76] and Bachur and Hennelly[48] (28 and 24%, respectively). This difference may be explained by our exclusion of children less than 3 years of age, who are known to have increased perforation rate.[43]

LIMITATIONS

Although our study may be limited by its retrospective nature, we standardized the methodology across all sites. In addition, we enrolled consecutive hospital diagnoses of appendicitis and suspected appendicitis over two different time periods to decrease the likelihood of seasonal effects on care provided in the ED. This study excluded children who required intensive care (and thus a portion of children with perforation), as we postulated that this population is more likely to receive initial management according to ED sepsis guidelines; our aim was to characterize the more common scenario of the stable child with suspected appendicitis.

Assessment of bias from missed cases was not performed; however, we used a standardized process across sites to identify consecutive health records. We did not examine the effect of weekday versus weekend presentations, but as mentioned, we standardized methodology across sites. Because our study was a retrospective review, we did not perform independent review of the pathology samples to confirm appendicitis or rupture; however, we applied a standardized approach to determining appendicitis and perforation using pathology reports. As our study was performed exclusively at academic centers across the country, the results may not be generalizable to general and community EDs and may underestimate the variation across the population as a whole. While the diagnosis and management of pediatric appendicitis is multidisciplinary in nature (emergency medicine, surgery, radiology), we were unable to ascertain how practice variations between these specialties affected management. However, our design gave us the unique opportunity to explore how our colleagues in Canadian pediatric hospitals manage children admitted for suspected appendicitis and the associated patient outcomes. Our study is limited to those children who were admitted to hospital; future studies should report the practice variations of those children who were evaluated for suspected appendicitis and subsequently discharged from the ED.

CONCLUSIONS

Across Canadian pediatric EDs, there exists significant variation in the diagnosis and management of children at high risk of appendicitis. After-hours appendectomies are performed infrequently in Canadian children while use of diagnostic tests, management strategies, and hospital flow metrics exhibit major variation across sites. Our results indicate that the best approach to diagnosing and managing pediatric appendicitis remains unclear, and we support the need for future prospective, multicenter studies to optimize patient and health care system outcomes.

The authors thank Joanne Bleackley, Rachel Kim, and Daniel Rosenfield for their significant contribution to data collection/management.

References

1. Hennelly K, Bachur R. Appendicitis update. Curr Opin Pediatr 2011;23:281–5.
2. Guthery SL, Hutchings C, Dean JM, Hoff C. National estimates of hospital utilization by children with gastrointestinal disorders: analysis of the 1997 kids' inpatient database. J Pediatr 2004;144:589–94.
3. Bundy DG, Byerley JS, Liles EA, Perrin EM, Katznelson J, Rice HE. Does this child have appendicitis? JAMA 2007;298:438–51.
4. Samuel M. Pediatric appendicitis score. J Pediatr Surg 2002;37:877–81.
5. Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med 1986;15:557–64.
6. Kulik DM, Uleryk EM, Maguire JL. Does this child have appendicitis? A systematic review of clinical prediction rules for children with acute abdominal pain. J Clin Epidemiol 2013;66:95–104.
7. Schneider C, Kharbanda A, Bachur R. Evaluating appendicitis scoring systems using a prospective Pediatric cohort. Ann Emerg Med 2007;49:778–84.
8. Beltrán MA, Almonacid J, Vicencio A, Gutiérrez J, Cruces KS, Cumsille MA. Predictive value of white blood cell count and C-reactive protein in children with appendicitis. J Pediatr Surg 2007;42:1208–14.
9. Gavela T, Cabeza B, Serrano A, Casado-Flores J. C-reactive protein and procalcitonin are predictors of the severity of acute appendicitis in children. Pediatr Emerg Care 2012;28:416–9.
10. Kharbanda AB, Rai AJ, Cosme Y, Liu K, Dayan PS. Novel serum and urine markers for pediatric appendicitis. Acad Emerg Med 2012;19:56–62.
11. Puig S, Staudenherz A, Felder-Puig R, Paya K. Imaging of appendicitis in children and adolescents: useful or useless? A comparison of imaging techniques and a critical review of the current literature. Semin Roentgenol 2008;43:22–8.
12. Frush DP, Frush KS, Oldham KT. Imaging of acute appendicitis in children: EU versus U.S. ... or US versus CT? A North American perspective. Pediatr Radiol 2009;39:500–5.
13. Holscher HC, Heij HA. Imaging of acute appendicitis in children: EU versus U.S.. or US versus CT? A European perspective. Pediatr Radiol 2009;39: 497–9.
14. Doria AS, Moineddin R, Kellenberger CJ, et al. US or CT for diagnosis of appendicitis in children and adults? A Meta-Analysis 1. Radiology 2006;241:83–94.
15. Brenner DJ, Hall EJ. Computed tomography–an increasing source of radiation exposure. N Engl J Med 2007;357:2277–84.
16. Thompson G, DeForest E, Eccles R. Ensuring diagnostic accuracy in pediatric emergency medicine. Clin Pediatr Emerg Med 2011;12:121–32.
17. Saucier A, Huang EY, Emeremni CA, Pershad J. Prospective evaluation of a clinical pathway for suspected appendicitis. Pediatrics 2014;133:e88–95.
18. Russell WS, Schuh AM, Hill JG, et al. Clinical practice guidelines for pediatric appendicitis evaluation can decrease computed tomography utilization while maintaining diagnostic accuracy. Pediatr Emerg Care 2013;29:568–73.
19. Fleischman RJ, Devine MK, Yagapen MA, et al. Evaluation of a novel pediatric appendicitis pathway using high- and low-risk scoring systems. Pediatr Emerg Care 2013;29:1060–5.
20. Hall AB, Freeman T, Banks S. Is it safe? Appendectomies at night at a low-volume center. J Surg Educ 2011;68:199–201.
21. McCartan DP, Fleming FJ, Grace PA. The management of right iliac fossa pain - is timing everything? Surgeon 2010;8:211–7.
22. Giraudo G, Baracchi F, Pellegrino L. Dal Corso HM, Borghi F. Prompt or delayed appendectomy? Influence of timing of surgery for acute appendicitis. Surg Today 2012;43:392–6.
23. Taylor M, Emil S, Nguyen N, Ndiforchu F. Emergent vs urgent appendectomy in children: a study of outcomes. J Pediatr Surg 2005;40:1912–5.
24. Yardeni D, Hirschl RB, Drongowski RA, Teitelbaum DH, Geiger JD, Coran AG. Delayed versus immediate surgery in acute appendicitis: do we need to operate during the night? J Pediatr Surg 2004;39:464–9.
25. Bickell NA, Aufses AH Jr, Rojas M, Bodian C. How time affects the risk of rupture in appendicitis. J Am Coll Surg 2006;202:401–6.
26. Wu J, Counihan T, Eko F, Ryb G, Drager L, Goldwater E. Ideal timing of surgery for acute uncomplicated appendicitis. N Am J Med Sci 2013;5:22–7.
27. Varadhan KK, Neal KR, Lobo DN. Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials. BMJ 2012;344:e2156.
28. Mason RJ. Non-operative management of uncomplicated acute appendicitis: using antibiotics is effective and decreases morbidity. Evid Based Med 2013;18:67–8.
29. Mason R, Moazzez A. Meta-analysis of randomized trials comparing antibiotic therapy with appendectomy for acute uncomplicated (no abscess or phlegmon) appendicitis. Surg 2012;13:74–84.
30. Lee SL, Islam S, Cassidy LD, Abdullah F, Arca MJ. 2010 American Pediatric Surgical Association Outcomes and Clinical Trials Committee. Antibiotics and appendicitis in the pediatric population: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. J Pediatr Surg 2010;45:2181–5.
31. Ali S, Drendel AL, Kircher J, Beno S. Pain management of musculoskeletal injuries in children: current state and future directions. Pediatr Emerg Care 2010;26:518–24.

32. Donald C, Duncan R, Blair L, Thakore S, Clark M. Paediatric analgesia in the emergency department, are we getting it right? Eur J Emerg Med 2007;14:157–9.
33. Dong L, Donaldson A, Metzger R, Keenan H. Analgesic administration in the emergency department for children requiring hospitalization for long-bone fracture. Pediatr Emerg Care 2012;28:109–14.
34. Goldman RD, Narula N, Klein-Kremer A, Finkelstein Y, Rogovik AL. Predictors for opioid analgesia administration in children with abdominal pain presenting to the emergency department. Clin J Pain 2008;24:11–5.
35. Goldman RD, Crum D, Bromberg R, Rogovik A, Langer JC. Analgesia administration for acute abdominal pain in the pediatric emergency department. Pediatr Emerg Care 2006;22:18–21.
36. Freedman SB, Gouin S, Bhatt M, et al. Prospective assessment of practice pattern variations in the treatment of pediatric gastroenteritis. Pediatrics 2011;127:e287–95.
37. Richer LP, Laycock K, Millar K, et al. Treatment of children with migraine in emergency departments: national practice variation study. Pediatrics 2010;126:e150–5.
38. Goldman RD, Scolnik D, Chauvin-Kimoff L, et al. Practice variations in the treatment of febrile infants among pediatric emergency physicians. Pediatrics 2009;124:439–45.
39. Hampers LC, Faries SG. Practice variation in the emergency management of croup. Pediatrics 2002;109:505–8.
40. Plint AC, Johnson DW, Wiebe N, et al. Practice variation among pediatric emergency departments in the treatment of bronchiolitis. Acad Emerg Med 2004;11:353–60.
41. Jain S, Elon LK, Johnson BA, Frank G, Deguzman M. Physician practice variation in the pediatric emergency department and its impact on resource use and quality of care. Pediatr Emerg Care 2010;26:902–8.
42. Jain S, Cheng J, Alpern ER, et al. Management of febrile neonates in US pediatric emergency departments. Pediatrics 2014;133:187–95.
43. Bansal S, Banever GT, Karrer FM, Partrick DA. Appendicitis in children less than 5 years old: influence of age on presentation and outcome. Am J Surg 2012;204:1031–5.
44. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
45. Lenth R. Java Applets for Power and Sample Size. Available at: http://homepage.stat.uiowa.edu/~rlenth/Power/. Accessed April 7, 2015.
46. Warren DW, Jarvis A, LeBlanc L, et al. Revisions to the Canadian Triage and Acuity Scale paediatric guidelines (PaedCTAS). CJEM 2008;10:224–43.
47. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol 2007;165:710–8.
48. Bachur R, Hennelly K. Advanced radiologic imaging for pediatric appendicitis, 2005-2009: trends and outcomes. J Pediatr 2012;160:1034–8.
49. Cappendijk VC. The impact of diagnostic delay on the course of acute appendicitis. Arch Dis Child 2000;83:64–6.
50. Papandria D, Goldstein S, Rhee D. Risk of perforation increases with delay in recognition and surgery for acute appendicitis. J Surg 2013;184:723–9.
51. Teixeira PG, Sivrikoz E, Inaba K, Talving P, Lam L, Demetriades D. Appendectomy timing. Ann Surg 2012;256:538–43.
52. Clyde C, Bax T, Merg A, et al. Timing of intervention does not affect outcome in acute appendicitis in a large community practice. Am J Surg 2008;195:590–3.
53. Dunlop JC, Meltzer JA, Silver EJ, Crain EF. Is nonperforated pediatric appendicitis still considered a surgical emergency? A survey of pediatric surgeons. Acad Pediatr 2012;12:567–71.
54. Tsze DS, Asnis LM, Merchant RC, Amanullah S, Linakis JG. Increasing computed tomography use for patients with appendicitis and discrepancies in pain management between adults and children: an analysis of the NHAMCS. Ann Emerg Med 2012;59:395–403.
55. Jangjoo A, Varasteh AR, Mehrabi Bahar M, et al. Is urinary 5-hydroxyindoleacetic acid helpful for early diagnosis of acute appendicitis? Am J Emerg Med 2012;30:540–4.
56. Bealer JF, Colgin M. S100A8/A9: a potential new diagnostic aid for acute appendicitis. Acad Emerg Med 2010;17:333–6.
57. Kentsis A, Ahmed S, Kurek K, et al. Detection and diagnostic value of urine leucine-rich α-2-glycoprotein in children with suspected acute appendicitis. Ann Emerg Med 2012;60:78–83.
58. Hryhorczuk AL, Mannix RC, Taylor GA. Pediatric abdominal pain: use of imaging in the emergency department in the United States from 1999 to 2007. Radiology 2012;263:778–85.
59. Rezak A, Abbas HM, Ajemian MS, Dudrick SJ, Kwasnik EM. Decreased use of computed tomography with a modified clinical scoring system in diagnosis of pediatric acute appendicitis. Arch Surg 2011;146:64–7.
60. Santillanes G, Simms S, Gausche-Hill M, et al. Prospective evaluation of a clinical practice guideline for diagnosis of appendicitis in children. Acad Emerg Med 2012;19:886–93.
61. Saucier A, Huang EY, Emeremni CA, Pershad J. Prospective evaluation of a clinical pathway for suspected appendicitis. Pediatrics 2014;133:e88–95.
62. MacLean S, Obispo J, Young KD. The gap between pediatric emergency department procedural pain management treatments available and actual practice. Pediatr Emerg Care 2007;23:87–93.
63. Bailey B, Bergeron S, Gravel J. Efficacy and impact of intravenous morphine before surgical consultation in children with right lower quadrant pain suggestive of appendicitis: a randomized controlled. Ann Emerg Med 2007;50:371–8.

64. Green R, Bulloch B, Kabani A, Hancock BJ, Tenenbein M. Early analgesia for children with acute abdominal pain. Pediatrics 2005;116:978–83.
65. Frei SP, Bond WF, Bazuro RK, Richardson DM, Sierzega GM, Wasser TE. Is early analgesia associated with delayed treatment of appendicitis? Am J Emerg Med 2008;26:176–80.
66. Bromberg R, Goldman RD. Does analgesia mask diagnosis of appendicitis among children? Can Fam Physician 2007;53:39–41.
67. Corwin DJ, Kessler DO, Auerbach M, Liang A, Kristinsson G. An intervention to improve pain management in the pediatric emergency department. Pediatr Emerg Care 2012;28:524–8.
68. Nadler EP, Gaines BA. The Surgical Infection Society guidelines on antimicrobial therapy for children with appendicitis. Surg Infect (Larchmt) 2008;9:75–83.
69. Gasior AC. St Peter SD, Knott EM, Hall M, Ostlie DJ, Snyder CL. National trends in approach and outcomes with appendicitis in children. J Pediatr Surg 2012;47:2264–7.
70. Wilson BE, Cheney L, Patel B, Holland AJ. Appendicectomy at a children's hospital: what has changed over a decade? ANZ J Surg 2012;82:639–43.
71. Surgical N. Multicentre observational study of performance variation in provision and outcome of emergency appendicectomy. Br J Surg 2013;100: 1240–52.
72. Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database Syst Rev 2010;(10):CD001546.
73. Esposito C, Calvo AI, Castagnetti M, et al. Open versus laparoscopic appendectomy in the pediatric population: a literature review and analysis of complications. J Laparoendosc Adv Surg Tech A 2012;22:834–9.
74. Vahdad MR, Troebs RB, Nissen M, Burkhardt LB, Hardwig S, Cernaianu G. Laparoscopic appendectomy for perforated appendicitis in children has complication rates comparable with those of open appendectomy. J Pediatr Surg 2013;48:555–61.
75. Oyetunji TA. Ong'uti SK, Bolorunduro OB, Cornwell EE, Nwomeh BC. Pediatric negative appendectomy rate: trend, predictors, and differentials. J Surg Res 2012;173:16–20.
76. Aarabi S, Sidhwa F, Riehle KJ, Chen Q, Mooney DP. Pediatric appendicitis in New England: epidemiology and outcomes. J Pediatr Surg 2011;46:1106–14.
77. Kaplan GG, Tanyingoh D, Dixon E, et al. Ambient ozone concentrations and the risk of perforated and nonperforated appendicitis: a multicity case-crossover study. Environ Health Perspect 2013;121:939–43.

Supporting Information

The following supporting information is available in the online version of this paper:

Data Supplement S1. Inter-rater agreement in data for primary outcome and generalized estimating equation variables.

Data Supplement S2. Characteristics of children admitted to hospital for suspected appendicitis per site (n = 619).

Data Supplement S3. Results of advanced diagnostic imaging and concordance of diagnosis to appendicitis.