

## SAMPLE TITLE PAGE

**Title:** Your Title Here

**Authors:** List of Authors' First and Last Names

**List of Institutions Represented:** Institution List

**Corresponding Author Name:** Name

**Corresponding author address:** address

**Corresponding author Tel.:** 555-555-5555

**Corresponding author email:** email

**Study conception and design:** Relevant author names here

**Acquisition of data:** Relevant author names here

**Analysis and interpretation of data:** Relevant author names here

**Drafting of manuscript:** Relevant author names here

**Critical revision of manuscript:** Relevant author names here

**Annotations of changes:** Identifying information that should be included in the final manuscript

**Level of evidence:** example – Level II

**Type of study:** example – Diagnostic Study

# SAMPLE MANUSCRIPT

**Title:**

**Level of Evidence:**

**Type of Study:**

**Abstract:**

**Background/Purpose:** Surgical site infection (SSI) rate in pediatric appendicitis is a commonly used hospital quality metric. We hypothesized that surveillance of organ-space SSI (OSI) using cultures alone would fail to capture many, clinically-important events.

**Methods:** A prospective, multidisciplinary surveillance program recorded 30-day SSI and hospital length of stay (LOS) for patients <18 years undergoing appendectomy for perforated appendicitis from 2012-2015. Standardized treatment pathways were utilized and OSI were identified by imaging and/or bacterial cultures.

**Results:** 410 appendectomies for perforated appendicitis were performed, and a total of 84 OSI (20.5%) were diagnosed with imaging. Positive cultures were obtained for 39 (46%) OSI, whereas 45 (54%) had imaging only. Compared to the mean LOS for patients without OSI ( $5.2 \pm 2.9$  days), LOS for patients with OSI and positive cultures ( $13.7 \pm 5.4$  days) or with OSI without cultures ( $10.4 \pm 3.7$  days) was significantly longer (both  $p < 0.001$ ). The OSI rate identified by positive cultures alone was 9.5%, whereas the clinically-relevant OSI rate was 20.5%.

**Conclusions:** Using positive cultures alone to capture OSI would have identified less than half of clinically-important infections. Utilizing clinically-relevant SSI is an appropriate metric for comparing hospital quality but requires agreed upon standards for diagnosis and reporting.

**Key words:** appendicitis, surgical site infection, surveillance, organ space infection, quality metric

The surgical site infection (SSI) rate is a commonly used quality metric for inter-hospital comparisons [1]. Since 2012, hospital-specific SSI rates have been publically reported by the Centers for Medicare and Medicaid Services on the Hospital Compare website [2]. However, ongoing concerns exist about this type of reporting given the unknown reliability of capturing and reporting patient-related outcomes [1,3]. Unreliable quality metrics, in turn, may lead to misclassification of hospitals and poorer public perception and reimbursements [1].

Currently, the lack of a universal standard for diagnosing SSI has led to significant variability in SSI reporting. The SSI rates reported on the Hospital Compare website are based on the Center for Disease Control and Prevention's National Healthcare Safety Network (NHSN) definitions [4], which differ substantially from those used by other reporting agencies including the American College of Surgeons National Surgical Quality Improvement Project (NSQIP) [5]. For example, to diagnose an organ/space SSI (OSI) after an appendectomy, the NHSN requires positive bacterial cultures be isolated from an OSI whereas NSQIP requires radiographic evidence alone.

Given the disparities in SSI reporting requirements, we hypothesized that a multidisciplinary SSI surveillance program would lead to an enhanced capture rate of OSI and that surveillance of positive cultures alone would fail to identify many, clinically-important OSI.

## **1. Methods**

### *1.1 Setting*

This was an Institutional Review Board approved (HSC-MS-12-0018), prospective cohort study conducted (ENTER INSTITUTION IN FINAL SUBMISSION) from January 2012 – July 2015. (INSTITUTION) is a tertiary children's hospital (ENTER SYSTEM IN FINAL SUBMISSION). The Pediatric Surgery Department at (INSTITUTION)H is comprised of 9 board certified pediatric surgeons, and the Infection Control Department consists of one pediatric infectious disease physician and a surveillance officer.

### *1.2 Subjects*

Patients less than 18 years undergoing an appendectomy for acute appendicitis were included in the study. The severity of appendicitis was described by the operating surgeon as simple, gangrenous, or perforated. Appendiceal perforation was defined as a gross hole in the appendix or the presence of intra-abdominal stool at the time of operation [6].

### *1.3 Treatment protocol*

Figure 1

Since 2011, all patients in our institution with suspected appendicitis have been initiated on a standardized preoperative protocol which entails *nil per os* status, intravenous fluids, and parenteral piperacillin/tazobactam or ciprofloxacin and metronidazole if penicillin allergic (Figure 1). Upon being diagnosed intraoperatively with perforated appendicitis, patients are placed on the appropriate postoperative protocol comprised of early ambulation, gradual advancement of the diet, and scheduled parenteral antibiotics until all discharge criteria are met. The discharge criteria include: reassuring abdominal exam, temperature less than 38.5° C (101.4° F) for >24 hours, tolerating a regular diet, pain controlled with oral analgesics, and ambulation with minimal assistance, as age appropriate.

Patients who fail to meet these discharge criteria by the seventh postoperative day undergo a computed tomography (CT) of the abdomen and pelvis. If a fluid collection consistent with an OSI is identified by the pediatric radiologist, the interventional radiology (IR) service is consulted for CT-guided aspiration and/or drain placement. Based on OSI size and location, the IR physician elects whether or not to attempt drainage. When IR is able to access the fluid collection, bacterial cultures are routinely sent and antibiotics are adjusted accordingly. Once patients meet discharge criteria, the drains are removed. Home antibiotics were not routinely prescribed during the study period. Routine follow-up in the outpatient clinic was scheduled within two weeks after discharge.

#### *1.4 Multidisciplinary Surveillance*

In January 2012, the Pediatric Surgery and Pediatric Infection Control Departments implemented a multidisciplinary surveillance program aimed at identifying 30-day postoperative SSI. The impetus for the joint surveillance program was improving the reliability of SSI reporting in order to develop targeted quality improvement initiatives.

The Pediatric Surgery Department recorded SSI based on imaging results during the initial hospital stay, patient encounters during follow up appointments, and 30-day chart review. Specifically, an OSI was documented when CT evidence of an intra-abdominal rim-enhancing or suspicious fluid collection was present and confirmed by a pediatric radiologist [7,8]. A standardized appendectomy form is filled out during the follow up appointment which documents any postoperative complications such as wound

problems, emergency room visits, or hospital readmissions. Patients were called at least 30-days after appendectomy, and the same form was filled out via a phone interview. A research coordinator inputs data from the chart review and clinic forms into a quality improvement database on a weekly basis.

The Pediatric Infection Control Department recorded SSI based on monthly reviews of bacterial culture data according to the NHSN guidelines [4]. Since it is possible that patients treated at CMHH present to emergency rooms and are readmitted to other Memorial Hermann hospitals, and vice versa, all Memorial Hermann records and cultures were reviewed to increase the scope of surveillance. After implementation of the multidisciplinary program, both departments met on a monthly basis to review all documented SSI.

### *1.5 Hospital length of stay*

To evaluate whether or not OSIs were clinically relevant, we examined hospital length of stay (LOS) for patients diagnosed with and without OSI. Since patients may develop OSI after discharge, we determined and report on thirty-day LOS, which represents the aggregate of days spent in the hospital during the initial hospitalization and any additional appendicitis-related readmissions within 30-days of surgery.

### *1.6 Statistical analysis*

Data are reported as frequencies, means  $\pm$  standard deviations, or medians (interquartile range) based on their distribution. Statistical testing was performed with  $\chi^2$ , Student's t-tests, or Mann Whitney-U tests. P-values  $\leq 0.05$  were considered statistically significant. Stata 13.1 (College Station, Texas) was utilized for all statistical analyses.

## **2. Results**

### *2.1 Patient and operative characteristics*

A total of 1,301 appendectomies were performed for acute appendicitis. Simple (or suppurative) appendicitis was diagnosed most often (n=811, 62.3%) whereas 80 (6.2%) patients were diagnosed with gangrenous appendicitis and 410 (31.5%) were diagnosed with perforated appendicitis. Patients who

were diagnosed with perforated appendicitis and who developed an OSI were younger and underwent a longer operation than patients who did not develop an OSI (Table 1).

Table 1

## 2.2 SSI Surveillance

The overall SSI rate was 1.6%, 5.0%, and 21.0% for patients with simple, gangrenous, and perforated appendicitis, respectively. Superficial and deep incisional wounds were diagnosed more often in simple (n=12, 1.5%) and gangrenous (n=2, 2.5%) appendicitis patients compared to patients with perforated appendicitis (n=3, 0.7%).

Among patients with perforated appendicitis, a total of 84 OSI (20.5%) were diagnosed, of which 39 (46.4%) positive cultures were obtained postoperatively. The majority of positive culture (n=35, 89.7%) were obtained by IR through aspiration or drain placement. The remaining (n=4, 10.3%) were obtained at reoperation or through an existing drain. The OSI rate based on positive cultures alone was 39/410 or 9.5%.

Among the 84 patients with OSI, 45 (53.6%) had negative cultures or no cultures at all. IR obtained negative cultures in 12 (26.7%) patients, and IR was unable to obtain cultures for 33 (73.3%) patients due to OSI size or location. All patients with OSI and negative or no cultures were treated with intravenous antibiotics until the time of discharge. One patient (2.2%) required reoperation during which no cultures were obtained. The OSI rate based on imaging alone without positive cultures was 45/410 or 11.0% (Figure 2).

Figure 2

Of the 51 cultures (61%) that were obtained, 39 (76%) were positive and 12 (24%) were negative. OSI cultures were both monomicrobial (n=17, 44%) and polymicrobial (n=22, 56%). The most commonly isolated bacteria was escherichia coli (n=32, 82%). Other bacteria isolates from OSI included: streptococcus, pseudomonas, enterococcus, klebsiella, and staphylococcus.

The median (interquartile range) postoperative day of OSI diagnosis was 7 (6-8), and 59 (71%) OSI were diagnosed during the initial hospital stay.

Prior to the institution of the multidisciplinary surveillance program, documented 30-day follow up was 27%. Since 2012, documented 30-day follow up has improved annually from 65% to 91% ( $p < 0.001$ ). The primary reason for ongoing failure to document follow up is the inability to reach the patient by phone call after 30 days due to an incorrect phone number or lack of returned call. Surveillance of facilities outside of (INSTITUTION) found one patient (1.1%) with perforated appendicitis to have an OSI.

### 2.3 Length of stay

The mean 30-day LOS for all perforated appendicitis patients during the study period was  $6.5 \pm 4.2$  days. Compared to patients without OSI, the LOS for patients with OSI with or without positive cultures was significantly longer (Figure 3). Patients with OSI and positive cultures had significantly longer LOS than patients with OSI with negative or no cultures ( $13.7 \pm 5.4$  days vs  $10.4 \pm 3.7$  days,  $p = 0.001$ ).

Figure 3

### 3. Discussion

The diagnosis of SSIs can vary between institutions and reporting agencies. A multidisciplinary approach improved the reliability of capturing OSI by combining clinical encounter data with institution-wide surveillance of bacterial culture results. By using positive cultures alone to identify OSI, only half of clinically-important infections would have been captured and reported.

According to both NHSN and NSQIP guidelines, SSIs are classified as superficial incisional, deep incisional, and OSI [4,5]. However, upon examining the definitions for each of these three SSI categories, substantial variation exists. For example, the NHSN requires a positive bacterial culture for documenting an OSI whereas NSQIP requires either radiographic evidence, drainage of purulence from a fluid collection, or the documentation of an OSI in the medical chart by a surgeon or attending physician. Both the NHSN and NSQIP definitions of OSI require that multiple criteria be met, and the NHSN even includes multiple levels of evidence laid out on separate pages of their guidelines. This lengthy process may be hard for both clinicians and data abstractors to apply [4]. In fact, a recent systematic review found that of 42 clinical trials focused on treating appendicitis, only 4 (<10%) attempted to utilize standardized OSI definitions [9].

Unfortunately, while standardizing the definition of OSI may help to improve its diagnostic reliability, ongoing auditing is essential as correct application of the definition is not guaranteed. In a recent NSQIP report of OSI rates for complicated appendicitis in which trained nurses used standardized definitions that did not include bacterial cultures, inter-hospital OSI rates ranged from 0-83%. While this enormous variation in OSI rates may actually represent discrepancies in quality of care, it seems rather unlikely. Other peer-reviewed publications of perforated appendicitis, which use institution-specific definitions similar to those of NSQIP, describe OSI rates ranging from 16-24% [7,8,10]. Clearly, the use of both standardized and non-standardized diagnostic criteria can result in significantly different rates of OSI, leading clinicians to question the reliability and validity of published results.

Based on results from recently performed clinical trials, a realistic rate of clinically significant OSI is approximately 20% among pediatric patients with perforated appendicitis [7,8]. This rate is consistent with the findings of our study, which applied a robust, multidisciplinary approach to SSI surveillance. Reporting clinically significant OSI rates instead of rates based on cultures alone is critical since the location or size of the OSI or the availability of IR for drainage oftentimes precludes the option to obtain cultures. Only 56% of OSI were accessible by IR in our institution, and even when cultures were acquired for our study cohort, we found that 24% of them were negative. In addition to avoiding reliance on culture results, performing consistent and thorough follow-up after discharge is crucial to avoid detection bias when reporting clinically-important OSIs. Importantly, 30% of OSI in our study were captured after discharge. Without any structured follow-up in place, our clinically-relevant OSI rate would have been significantly lower at 14%. Hence, employing a multidisciplinary approach to not only review cultures but to also improve surveillance after discharge is paramount in order to determine and report accurate and reliable OSI rates.

Not only is surveillance important for outcome reporting, but it is also an excellent avenue for improving patient care. The ability to reliably capture clinically significant outcomes over time allows institutions to enact and measure the effectiveness of local quality improvement efforts. Additionally, using a multidisciplinary approach allowed the pediatric surgery and infection control departments to collaborate on efforts to reduce SSI including standardization of pre- and postoperative protocols as well as improved adherence to Surgical Care Improvement Project measures [11]. Accountability between



the departments also likely played a role in the dramatically improved follow up rate after implementation of the joint program.

The results of this study should be interpreted in light of several limitations. As an academic, tertiary children's hospital, our results may be more generalizable to similar institutions that treat a higher percentage of children with more severe disease. Furthermore, the capabilities and availability of IR at each institution may be different, which could result in different bacterial culture rates. Without standardized definitions of OSI, treatment protocols, or discharge criteria, different centers may diagnose OSI differently and perform postoperative imaging more or less frequently. This in turn could lead to different OSI detection and culture rates. In centers such as ours that employ care pathways with established protocols, it may be that imaging is performed too early for some patients who may simply require another day or two of antibiotics and conservative care to resolve their underlying disease process.

In conclusion, diagnostic criteria for SSI vary between institutions and reporting agencies and may lead to misleading rates of reported SSI. Implementation of a multidisciplinary SSI surveillance program ensured that patients with OSI with or without positive cultures were captured, reviewed, and reported. By relying on clinical and radiographic findings instead of culture alone, our diagnostic criteria for OSI closely resemble those used by NSQIP. Using this approach, the clinically relevant OSI rate was two times the rate of culture positive OSI, which has important implications for reporting as well as future quality improvement efforts. Hence we would advocate that institutions adopt the NSQIP definition in order to capture and report OSI since institutions that rely solely on cultures to diagnose and report OSI are likely to grossly underestimate their OSI rate. Utilizing SSI as a quality metric for hospital comparisons should focus on clinically-relevant SSI rates using agreed upon definitions.

## References

- [1] Kao LS, Ghaferi AA, Ko CY, Dimick JB. Reliability of superficial surgical site infections as a hospital quality measure. *J Am Coll Surg* 2011;213:231–5.
- [2] Medicare.gov and Hospital Compare. Available at: <https://www.medicare.gov/hospitalcompare/search.html> Accessed December 10, 2014.
- [3] Lawson EH, Louie R, Zingmond DS, Brook RH, Hall BL, Han L, et al. A comparison of clinical registry versus administrative claims data for reporting of 30-day surgical complications. *Ann Surg* 2012;256:973–81.
- [4] Centers for Disease Control and Prevention's National Healthcare Safety Network . Procedure-associated Module, SSI. Available at: [www.cdc.gov/nhsn/PDFs/pscManual/9pscSSIcurrent.pdf](http://www.cdc.gov/nhsn/PDFs/pscManual/9pscSSIcurrent.pdf) Accessed February 10, 2012.
- [5] American College of Surgeons National Surgical Quality Improvement Program. User Guide for the Participant Use Data File. Available at <https://www.facs.org/quality-programs/pediatric/program-specifics/quality-support-tools/puf> Accessed October 18, 2015.
- [6] St Peter SD, Sharp SW, Holcomb GW, Ostlie DJ. An evidence-based definition for perforated appendicitis derived from a prospective randomized trial. *J Pediatr Surg* 2008;43:2242–5.
- [7] Blakely ML, Williams R, Dassinger MS, Eubanks JW, Fischer P, Huang EY, et al. Early vs interval appendectomy for children with perforated appendicitis. *JAMA Surg* 2011;146:660–5.
- [8] St. Peter SD, Tsao K, Spilde TL, Holcomb GW, Sharp SW, Murphy JP, et al. Single daily dosing ceftriaxone and metronidazole vs standard triple antibiotic regimen for perforated appendicitis in children: a prospective randomized trial. *J Pediatr Surg* 2008;43:981–5.
- [9] Hall NJ, Kapadia MZ, Eaton S, Chan WWY, Nickel C, Pierro A, et al. Outcome reporting in randomised controlled trials and meta-analyses of appendicitis treatments in children: a systematic review. *Trials* 2015;16:275.

- [10] Fallon SC, Hassan SF, Larimer EL, Rodriguez JR, Brandt ML, Wesson DE, et al. Modification of an evidence-based protocol for advanced appendicitis in children. *J Surg Res* 2013;185:273–7.
- [11] Putnam LR, Chang CM, Rogers NB, Podolnick JM, Sakhuja S, Matuszczak M, et al. Adherence to surgical antibiotic prophylaxis remains a challenge despite multifaceted interventions. *Surgery* 2015;158:413–9.

**Figure 1** Standardized Care Pathway and Multidisciplinary SSI Surveillance Program

**Figure 2** Flow diagram of study cohort and OSI culture status

**Figure 3** Variation in 30-day length of stay based on OSI and culture status

**Table 1 Patient and Operative characteristics**

	All patients, n = 410	Patients without OSI, n = 327	Patients with OSI, n = 83	p-value*
Female gender, n (%)	159 (39)	128 (39)	31 (37)	0.764
Age (y), mean $\pm$ SD	9.4 $\pm$ 4.0	9.1 $\pm$ 4.0	10 $\pm$ 3.7	0.029
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	20 $\pm$ 6.1	20 $\pm$ 6.3	21 $\pm$ 5.4	0.551
Race/ethnicity, n (%)				0.527
Asian	8 (2)	8 (3)	0 (0)	
Black	30 (7)	23 (7)	7 (8)	
Non-white Hispanic	256 (63)	204 (62)	52 (63)	
White	116 (28)	92 (28)	24 (29)	
Operative technique, n (%)				
Laparoscopic	384 (94)	306 (94)	78 (94)	0.894
Open	26 (6)	21 (6)	5 (6)	
<u>Case duration (min), mean <math>\pm</math> SD</u>	<u>56 <math>\pm</math> 20</u>	<u>55 <math>\pm</math> 18</u>	<u>62 <math>\pm</math> 25</u>	<u>0.005</u>

\*chi-squared comparing the groups of patients diagnosed with and without OSI



**Fig 1**

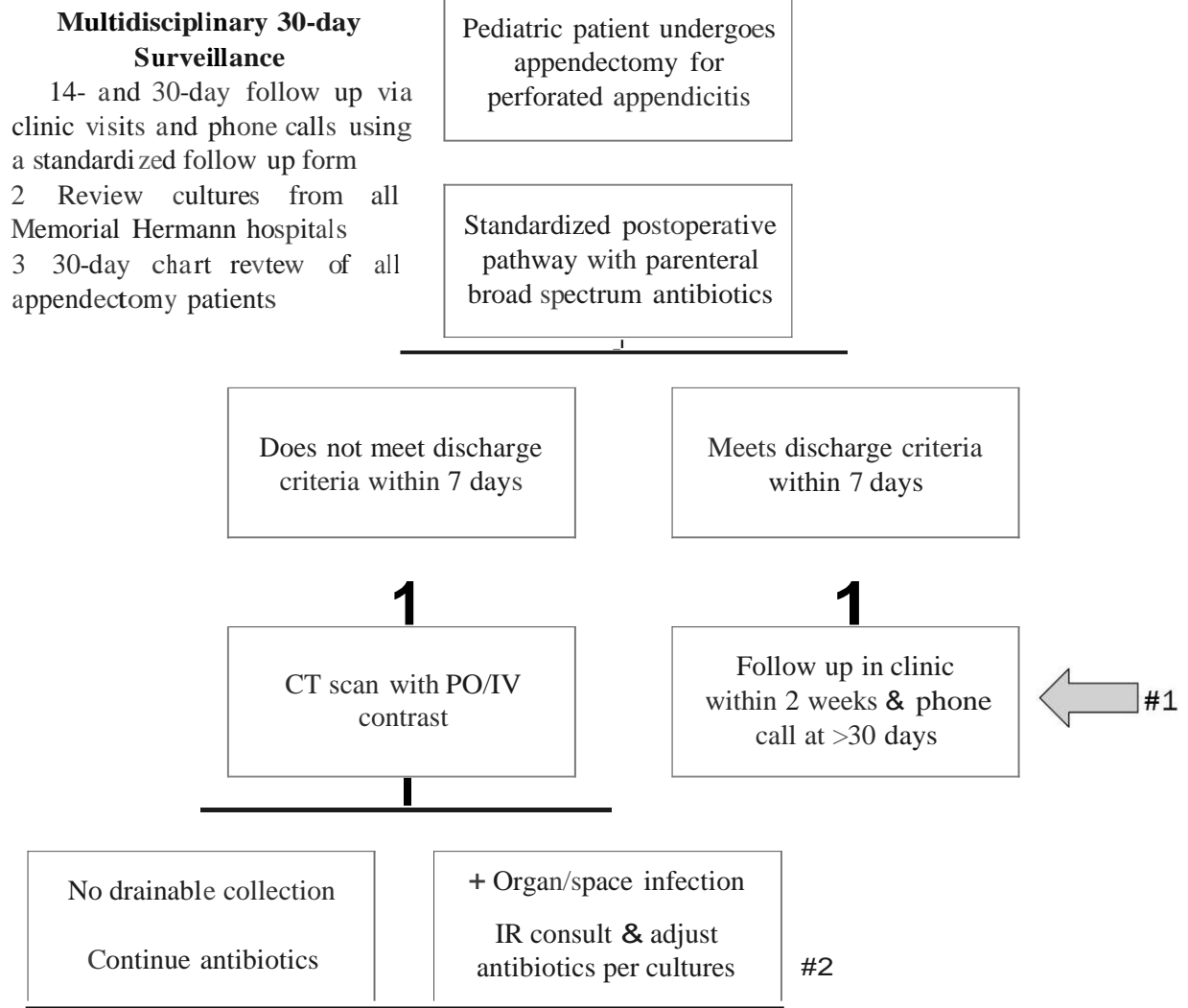
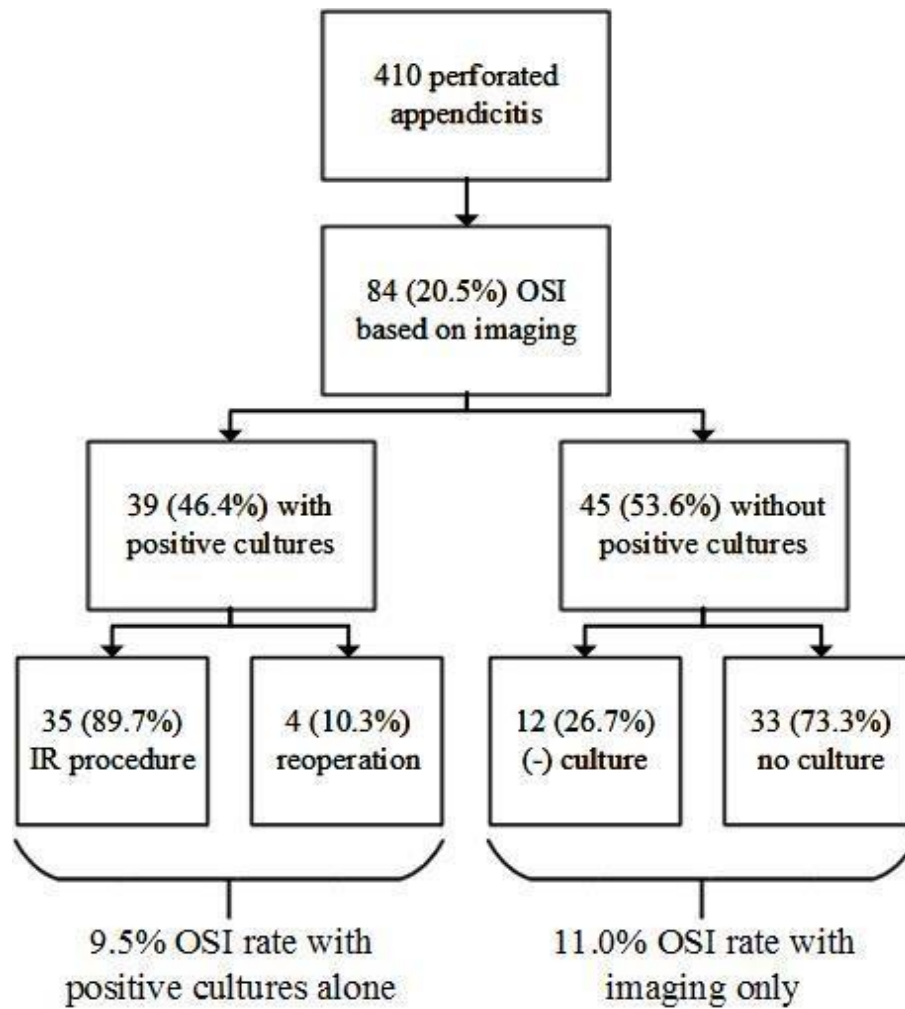


Fig 2





**Fig 3**

