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## Management of Intussusception in Children: A Systematic Review

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## Abstract

**Objective:** The goal of this systematic review by the American Pediatric Surgical Association Outcomes and Evidence-Based Practice Committee was to develop recommendations for the management of ileocolic intussusception in children.

**Methods:** The [ClinicalTrials.gov](https://clinicaltrials.gov), Embase, PubMed, and Scopus databases were queried for literature from January 1988 through December 2018. Search terms were designed to address the following topics in intussusception: prophylactic antibiotic use, repeated enema reductions, outpatient management, and use of minimally invasive techniques for children with intussusception. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were followed. Consensus recommendations were derived based on the best available evidence.

**Results:** A total of 83 articles were analyzed and included for review. Prophylactic antibiotic use does not decrease complications after radiologic reduction. Repeated enema reductions may be attempted when clinically appropriate. Patients can be safely observed in the emergency department following enema reduction of ileocolic intussusception, avoiding hospital admission. Laparoscopic reduction is often successful.

**Conclusions:** Regarding intussusception in hemodynamically stable children without critical illness, pre-reduction antibiotics are unnecessary, non-operative outpatient management should be maximized, and minimally invasive techniques may be used to avoid laparotomy.

**Type of study:** Systematic Review of level 1–4 studies

**Level of Evidence:** level 3–5 (mainly level 3–4)

## Keywords

intussusception; enema; outpatient; surgery

## Introduction

Ileocolic intussusception is one of the most common abdominal emergencies in children less than three years old [1]. The reported incidence is 0.33–0.71/1000 person years [2,3]. Most cases of intussusception in children have a benign etiology without a pathological lead point; therefore, surgical resection is necessary only in the minority of cases [4]. Practice patterns in the management of intussusception can vary by institution. Key areas of variability include prophylactic antibiotic usage prior to radiologic reduction, protocols for radiologic reduction of intussusception, care and disposition of the child post-reduction, and operative approaches when radiographic reduction has failed.

This study systematically reviewed the most recent literature regarding the management of intussusception in children. Topics of interest defined *a priori* included antibiotic stewardship, radiologic management, emergency department (ED) discharge, and use of minimally invasive techniques. The findings from the systematic review were summarized to create an evidence-based management algorithm that is suitable for routine practice in a variety of hospital settings.

## Methods

### 1.1 Research questions

The American Pediatric Surgical Association (APSA) Outcomes and Evidence-Based Practice (OEBP) committee defined the following topics and questions for this systematic review:

1. Antibiotic use and surgeon availability:
  - a. Should prophylactic antibiotics be given prior to radiological reduction of intussusception?
  - b. If antibiotics are to be given, what spectrum of antibiotics is appropriate?
  - c. Are surgeons required to be present at time of radiographic reduction?
2. Radiology:
  - a. What clinical parameters allow for safely reattempting radiologic reduction of intussusception when the first attempt fails?
  - b. What is the optimal time interval between reduction attempts?
3. Post-reduction care:
  - a. What is the difference in rate of complications (ED returns, readmissions, recurrent intussusception) between discharge from the ED compared to inpatient observation?
  - b. How long should patients be observed in the emergency room?
4. Operative care:

- a. What is the difference in rate of complications (ED returns, readmissions, recurrent intussusception) between techniques for operative reduction - open, laparoscopically assisted, or laparoscopic only?
- b. Should the appendix be removed if the procedure is laparoscopic or laparoscopically assisted?

## 1.2 Search Methods

Literature searches were conducted in [ClinicalTrials.gov](https://www.clinicaltrials.gov), Embase, PubMed, and Scopus by a medical librarian. The searches used a combination of terms derived from the literature and discussion with content experts in conjunction with controlled vocabularies and keywords (Appendix A). Searches were conducted through January 24, 2019, with the exception of the PubMed database which was indexed through up to December 22, 2018. All non-English papers, animal studies, case reports, abstracts without manuscripts, and clinical trial protocol papers were excluded. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed [5].

## 1.3 Study Selection

Figure 1 outlines the PRISMA flow of the literature search and exclusion. A list of 4256 titles and/or abstracts were generated by the search outlined above. These were reviewed independently by four authors (L.K., L.A., R.W., and A.K.). Overall, 3931 titles were excluded as they were published before 1988, were not in English, or did not address the study questions. Of note, studies performed in resource-limited settings were excluded from this review as children in those centers presented later with intussusception leading to increased morbidity and mortality. This resulted in the omission of several studies using hydrostatic ultrasound as the primary means of reduction. Full manuscript review of the remaining 325 papers was performed, with each paper assigned to the relevant questions(s). Some manuscripts included for analysis addressed several questions.

## 1.4 Full Review Process

Manuscripts were assessed based on level of evidence as outlined by the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence [6]. A total of 83 manuscripts met inclusion criteria. Consensus statements summarizing recommendations in response to the study questions were developed. Finally, a clinical management algorithm was created based on the results of the analysis.

# Results

## Prophylactic Antibiotics and Surgeon Availability

Many hospitals caring for children with intussusception have pre-procedural protocols regarding antibiotic use and surgeon availability at time of reduction. Antibiotics may be given prior to an attempt at reduction to treat a transient bacteremia associated with reduction and/or to decrease morbidity associated with bowel perforation during reduction. Presence of a surgeon at time of reduction is thought to facilitate immediate treatment of

pneumoperitoneum in case of high-pressure enema perforation and therefore decrease morbidity. Literature addressing both concerns was reviewed.

### **1.1 Should prophylactic antibiotics be given prior to radiological reduction of intussusception?—**

Three papers compared clinical outcomes based on the administration of antibiotics before enema reduction [7–9]. A single-center prospective cohort study conducted in Israel identified 27 infants with intussusception and did not administer pre-procedural antibiotics [8]. Blood cultures were obtained before and after enema administration and none demonstrated enteric bacteremia. In a two-hospital retrospective cohort comparison with 97 children, there was no difference in post-reduction fever, length of stay, or time to oral feeds between children who received antibiotics prior to reduction compared to those who did not [7]. Finally, a recent single-center retrospective cohort study of 188 children treated for intussusception in China revealed no difference in rates of upper respiratory tract infection or enteritis based on antibiotic administration prior to enema reduction [9]. However, in this study children who received antibiotics did stay several hours longer in the hospital compared to children who did not receive antibiotics prior to reduction (27h vs 21h,  $p=0.003$ ). Whether prolonged hospital stay was due to duration of antibiotic infusion was not reported. Given that the literature did not support the use of prophylactic antibiotics, no recommendation was made regarding the ideal spectrum of prophylactic antibiotics to be used.

**Recommendation:** Administration of prophylactic antibiotics prior to enema reduction does not appear to decrease post-reduction complications and is therefore unnecessary. (*Grade C recommendation, Level 3–4 evidence;*)

### **1.2 Should surgeons be present at time of radiographic reduction?—**

According to a single-institution retrospective cohort study of 433 US children undergoing enema reduction of intussusception, 1.4% experienced hemodynamic instability that required needle decompression and cardiopulmonary resuscitation [10]. All achieved hemodynamic stability with these maneuvers. The authors state that surgeon presence at the time of enema reduction may not be necessary if the radiology attending is facile with percutaneous decompression and surgical care is readily available if needed. In a survey of European pediatric radiologists, 46% of respondents reported that a surgeon was present at the time of radiologic reduction [11]. However, no studies compared outcomes after enema reduction based on the presence or absence of a surgeon at the time of enema reduction.

**Recommendation:** A physician capable of abdominal decompression of pneumoperitoneum and cardiopulmonary resuscitation should be present at the time of reduction. Facilities performing reduction should have emergent pediatric surgical capability available within the hospital system. (*Grade D recommendation, Level 5 evidence*).

## **Delayed Repeat Enemas**

Delayed repeat enemas (DRE) refers to the re-application of reduction enemas after a first unsuccessful attempt. There were 25 papers included in the literature search that addressed the use of (DRE) in the treatment of intussusception. Our search revealed one level 3

database cohort study and 23 level 4 studies (5 single center prospective case series, 18 single center retrospective trials), and one level 5 survey that reviewed the role of DREs in the treatment of intussusception.

**2.1. What clinical parameters allow for safely reattempting radiologic reduction of intussusception if the first attempt fails?**—Based on our review, the most common clinical criteria used to select patients felt to be safe to undergo DRE were: 1) progressive movement of the intussusceptum on the prior reduction attempt; 2) patient stability during interval between enemas; and 3) absence of peritonitis. Eleven of the 25 studies (44%) used these three criteria to define patients who were eligible to attempt DRE. Two other studies only performed DRE on patients who had a failed enema at an outside, non-children's hospital [12,13]. In a 1992 report by Stein et al, delayed barium enemas on all 22 patients who failed initial air enemas did not achieve any successful reductions [14]. Another center reported taking all 31 of the 62 patients who failed an initial hydrostatic enema to the operating room and performing a DRE under anesthesia with 21/31 (68%) patients being successfully reduced prior to undergoing surgical treatment [15]. A small 2011 study noted that in 10/11 cases in which air was seen encircling the intussusceptum, DRE was unsuccessful, suggesting that this radiographic finding may be a contraindication to attempting DRE [16]. Ten of the 25 studies did not have any definitive criteria for performing DRE.

**2.1.1 Outcomes of patients undergoing DRE:** The overall success rate of DRE was reported in 21 of the 25 studies reviewed. Of all patients undergoing DRE, 57.2% were successfully reduced (624 successes out of 1091 attempts). Only 15 of these studies also reported the overall success rate of all enema reductions (76.8%, 7029/9150 attempts), of which DRE comprised 545 (6.0%) of all successful reductions. When looking specifically at the studies with the defined eligibility criteria of progressive movement of the intussusceptum on previous enema, hemodynamic stability, and lack of peritonitis, a similar success rate of DRE, 54.3% (132/243), was noted (Table 1). The overall success rate of all enema reductions could be determined in 7 of 11 of these studies as 81.1% (953/1151) with 110 (9.6%) successful DRE. Therefore, an additional 9.6% of all patients presenting with intussusception in these studies (110/1151) avoided surgery due to a successful attempt of a DRE using the defined eligibility criteria of patient stability, lack of peritonitis, and progressive movement of the intussusceptum on previous enema attempt. When considering all studies reviewed, 545 children of 1151 children avoided surgery by attempts at delayed reduction rather than proceeding directly to surgery after a single failed enema.

The outcomes of patients undergoing DRE were similar to the outcomes of all patients with successful enema reduction at the first attempt. Patients who failed DRE required surgical resection for either ischemia or pathologic lead points 29.2% of the time (91/311 patients), underwent manual reduction 69.8% of the time, and had spontaneous reduction at surgery 1.0% of the time. The overall rate of surgical resection after all failed intussusception reductions was nearly identical with 664 out of 2291 patients (29.0%) requiring resection and the remainder manually reduced at surgery.

Of the 25 included studies, 22 papers reported the number of attempts made at radiologic reduction. Eleven studies reported 2 radiographic reduction attempts (one delayed reduction), 4 studies reported 3 total attempts (2 DREs), 4 studies reported 4 overall attempts (3 DREs), and 3 studies reported attempting reduction 5 times (4 DREs). Success rates for DREs did not appear to be related to the number of attempts made but may lose efficacy with repeated attempts. Ten of the studies using a single DRE reported a 53.2% success rate, 3 studies using 2 DRE reported a 62.5% success rate, 2 studies using 3 DRE reported a 50.9% success rate, and the 3 studies reporting 4 DRE attempts reported a 35.4% success rate. This suggests that there may be a decrease in benefit with more than 3 attempts of DRE, but this would need a prospective, standardized approach to demonstrate safety and efficacy.

**2.1.2 Adverse Events with DRE.:** Perforation rates associated with DRE were reported in 18 studies. The overall perforation rate was 1.1% (4 patients out of the 373 attempts). When evaluating only the studies with defined criteria for performing DRE as listed above, the rate was slightly less at 0.8% (2/243 attempts). The overall perforation rate for all attempted enemas was reported in 15 studies as 0.5% (37/7542 attempts).

**Recommendations:** Based on available evidence, DRE appears to increase the overall success rate of radiologic reduction by almost 10%, with nearly half of all patients, who fail initial enema reduction avoiding surgery due to the delayed reduction attempt(s). The surgical resection and perforation rates for patients undergoing DRE are similar to those reported for all patients undergoing enemas. While there are no definitive protocols for DRE, the available evidence indicates that safe criteria for selecting patients appropriate for DRE are 1) a medically stable patient, 2) without peritonitis, and 3) whose previous enema achieved a partial reduction. (*Grade C recommendation, Level 4 evidence*)

**2.2 What is the optimal timing between reduction attempts?**—There are no studies that specifically examined the optimal timing between reduction attempts. Of the 25 papers included in our search, 15 reported time intervals between enema attempts. The shortest time reported was 10 minutes and the longest time reported was 24 hours. The highest success rate of DRE (82.3% =19/23 attempts) was reported in a study using a 45–60 minute interval between enemas [17]. Sandler et al reported 2 perforations out of 8 patients undergoing DRE with intervals of 6 and 10 hours in an initial retrospective arm of their study and subsequently switched to a 2–4 hour interval for the remainder of their study and had no further perforations [18]. Kopelwitz et al was the only other study to report a DRE-associated perforation, which occurred after a 4-hour interval [16]. A survey of 456 radiologists (30% response rate), reported that 64% of the respondents performed DRE [19]. Of those respondents, 37% waited 0–15 minutes, 20% waited 15–30 minutes, 22% reported waiting 30–120 minutes, and 22% waited greater than 2 hours between enemas.

**Recommendation:** Waiting for an interval between 30 minutes and 4 hours is likely to be a safe for repeated attempts at delayed enema reduction, but further study must be done to determine if there is an optimal time frame between reduction attempts. (*Grade D recommendation, level 5 evidence*)

## Discharge from the Emergency Room compared to Inpatient Observation

Though patients with intussusception have traditionally been admitted to the hospital for treatment, recent studies have suggested patients may be treated with an enema reduction of the intussusception and safely discharged home from the Emergency Department (ED). However, there is concern for recurrent intussusception and potential need for return to the hospital. Thirteen studies addressed the concept of emergency room observation rather than inpatient admission for patients with intussusception.

**3.1 What is the difference in rate of complications (ED returns, readmissions, recurrent intussusception) between discharge from the emergency room compared to inpatient observation?**—Twelve studies addressed differences in complication rates between patients discharged from the ED compared to those who were observed as inpatients [20–31]. In the largest series, in which 547 patients with intussusception had successful enema reduction, 53% were discharged after a median observation time in the ED of 7.2 hours [32]. Although there was a difference in recurrence rates after discharge [19/239 (8%) ED versus 8/329 (2%) inpatient observation,  $p = 0.004$ ], operative reduction rates [2/239 (1%) ED vs 2/329 (0.6%) inpatient observation] and overall recurrence rates (8.8% ED vs 8.5% inpatient observation) were equivalent. Return to ED and readmission were not reported in this study. Only 2 studies suggested need for continuing observation outside the ED after successful enema reduction [33,34]. In a retrospective analysis of 360 patients with successful air enema reduction with 32 recurrences, multivariable logistic regression identified that the only predictor of recurrence was age greater than 2 years, with a median time to recurrence of 25 hours between ultrasound studies [33]. They suggest admission for patients greater than 2 years of age. Most studies examining ED discharge had eligibility criteria including failure of enema reduction, persistent symptoms after reduction (vomiting, lethargy, pain), or difficulty returning to ED after discharge due to transportation or distance from the hospital [21,22,26,27,29]. Finally, in Lessenich's retrospective review of a single center, tertiary hospital of 464 patients, 19% required an intervention within 24 hours of radiologic reduction [34]. Major interventions, including management of recurrent intussusception with repeat enema or surgery, occurred in 6% of patients. Minor interventions, including ultrasound to evaluate for recurrent intussusception or administration of analgesic or antiemetic, were more common (13%). While this final study did not stratify by ED versus inpatient discharge, it did identify intussusception located proximal to the hepatic flexure as associated with need for a major intervention; the authors suggested that this perhaps counterintuitive finding could be explained by increased bowel wall edema preventing more distal migration of the intussusceptum, and that a more distally-migrated intussusceptum might be less edematous and more easily reduced. Overall, the reviewed studies report recurrent intussusception in 7.5–15% of patients following successful enema reduction of an ileocolic or colocolic intussusception, with early recurrence (< 24–48 hours) ranging from 0.6–2.45% (Table 2) [22,35–38].

**Recommendation:** Given that there is no evidence for a difference in the rate of complications between patients observed in the ED and patients admitted to the hospital following enema reduction of an ileocolic intussusception, patients may be discharged from



the ED. Parents of children greater than 2 years of age should be counseled regarding a possible slight increased risk of recurrence compared to those less than 2 years of age. Additionally, parents should be educated on recurrent symptoms and the importance of returning to the ED while physicians should assess the family's local resources and ability to represent to the ED if needed. (*Grade C recommendation, level 3–4 evidence*).

**3.2 How long should patients be observed?**—Five studies addressed length of observation for patients discharged from the ED. Raval et al developed a guideline which included a standardized radiologic report, an observation period of 3–4 hours, and both absolute and relative criteria for hospital admission [29]. Though 7 patients returned to the ED, only 1 had a recurrent intussusception; no other complications were reported. A more recent study that implemented an ED observation guideline in which patients were not fed for 2 hours and then observed for 2 hours after eating, showed a decrease in hospital length of stay and no difference in recurrence rate [27]. A similar single-institution study measured outcomes after 4 hours of observation and found no difference in recurrence rates, time to recurrence, or adverse outcomes [22]. The most recent study examining 64 patients with oral intake provided 2–4 hours after reduction followed by discharge 5–8 hours after reduction demonstrated only one recurrence requiring repeat enema within the first week after discharge and no adverse events [28].

**Recommendation:** The optimal length of observation after enema reduction of ileocolic intussusception appears to be 4 hours, based on the current data. (*Grade C recommendation, level 3–4 evidence*).

## Open versus Laparoscopic Surgical Management

**4.1.1 What is the difference in rate of complications (ED returns, readmissions, recurrent intussusception) between operative reduction techniques – open, laparoscopically assisted, or laparoscopic only?**—Table 3 provides specific details from 20 selected studies that addressed conversion rates, intussusception recurrence, complications, length of stay, and readmissions based on operative technique. All included studies were retrospective reviews of pediatric patients diagnosed with intussusception who either failed enema reduction or were taken directly to the operating room without attempts at radiographic reduction. All but two studies included a proportion which were performed laparoscopically [39,40]. In many institutions laparoscopic reduction was considered the standard of care for all pediatric patients with intussusception not reducible by enema alone [41–46]. Conversion rates were highly variable, ranging from 0% to 79%, with more recent studies trending toward lower conversion rates. Laparoscopic cases that required an extension of the umbilical incision only were still analyzed in the laparoscopic group, as the majority of papers included the umbilical extension patients in the laparoscopic group. The overall conversion rate for the combined studies was 17%. Surgeries that were converted from laparoscopic to open were associated with a higher rate of bowel resection. Reasons for conversion to open included inability to reduce the intussusception, bowel ischemia, pathological lead point, perforation, and inadequate visualization due to bowel dilation.

## Length of stay

Description of length of stay (LOS) was not reported in a uniform fashion across studies, which made comparisons difficult. The overall length of stay was highly variable but was significantly shorter in the laparoscopic groups for seven of the eight studies that directly compared the two groups. [41,44,47–51]. The longer LOS in open surgeries may be partially confounded by the indication for open operative intervention, including a higher likelihood of pathological lead points, bowel edema, bowel ischemia, need for bowel resection, and/or presence of peritonitis in patients who underwent open procedures. For uncomplicated intussusception requiring operation, the longer LOS for open procedures is likely driven by pain control and wound management.

## Recurrence rates after surgical treatment of intussusception

Recurrence rates for intussusception after surgical treatment ranged from 0–14%. In the twelve studies that had a comparison of the recurrence rates for intussusception following laparoscopic compared to open procedures, no study demonstrated a statistically significant difference between the two techniques.

Two studies additionally reported the rate of intussusception recurrence with and without ileopexy. In a study of 278 children who underwent open operations, there was no difference in the rate of intussusception recurrence in 186 patients with open reduction with ileopexy versus 67 with simple open reduction without ileopexy (4.9 vs 4.3%, respectively) [52]. In a 2015 retrospective case series, there was no reduction in intussusception recurrence with ileopexy, whether the procedure was completed laparoscopically or open [50]. The authors recommended a laparoscopic approach without ileopexy. However, a few authors have commented on the utility of ileopexy in a select group of patients who have had multiple episodes recurrent intussusception without a pathological lead point [53,54].

## Complications

Early complications were defined as those that occurred prior to hospital discharge. These included a wide variety of complications including perforation, sepsis, wound infections, urinary tract infection, enterotomy, viral infection, abscess formation, and death. Late complications were defined as those that occurred after discharge and included bowel obstruction, hernia, and volvulus. There were similar complication rates following laparoscopic and open operative management of intussusception.

**Recommendation:** No evidence is currently available to identify superiority of laparoscopic vs. open surgery regarding recurrence rate or complications after management of intussusception not reducible by enema. However, an initial laparoscopic approach should be considered given the associated shorter length of stay and equivalent complication rates. (*Grade C recommendation, level 3–4 evidence*).

**4.1.2 Should simultaneous laparoscopy and enema be used for the reduction of intussusception if enema alone was not effective?** While this was not one of our initial study questions, during our review we encountered several studies that describe success with this technique. Six studies describe the use of laparoscopy combined with saline or air

enema reduction when primary enema reduction has failed (Table 4) [45,49,55–58]. For these patients, standard enema reduction was first attempted, but was not deemed successful. Of the reported 62 patients, 10 (16%) already had complete reduction of the intussusception at laparoscopy, all of which occurred at centers that allow for delayed repeat enemas [57,58]. For the combined 52 patients with persistent intussusception, simultaneous laparoscopy and enema facilitated reduction of the intussusception in 87% (range 30–100%) of the patients. This technique may limit the amount of laparoscopic bowel manipulation required to complete reduction, theoretically decreasing the risk of injury to the bowel and provides the added benefit of visual confirmation that the intussusception is completely reduced.

**Recommendation:** The simultaneous use of air or saline enema may help facilitate laparoscopic reduction of intussusception. (*Grade C recommendation, level 4 evidence*).

#### **4.2 Should the appendix be removed if laparoscopic or laparoscopically assisted surgery is performed?:**

The role of appendectomy in the surgical management of intussusception remains controversial. Some surgeons advocate for removal of the appendix as it may serve as a lead point for recurrent intussusception [43,54]. Of the manuscripts reviewed, eleven addressed appendectomy. Only one study specifically addressed whether an incidental appendectomy should be performed during the operative treatment for intussusception (excluding patients undergoing bowel resection) [59]. In this 2008–2015 analysis of the Pediatric Health Information System (PHIS) database, 13.5% of 748 patients with surgery for intussusception with appendectomy (SWA) vs. 15.8% of 564 patients with surgical reduction alone (SRA) presented for re-evaluation within 30 days. Both mean length of stay (3.0 vs. 2.5 days) and adjusted total cost (\$10,594 vs. \$8938) were significantly higher in the patients who had an appendectomy. Readmission for recurrent intussusception was similar in both groups (SWA 5.5% vs. SRA 6.7%,  $p=0.34$ ) at one-year follow-up, while 10 patients (1.3%) in the SWA and two patients (0.35%,  $p=0.06$ ) in the SRA group returned with a small bowel obstruction. However, a comparative study found no significant difference in the rate of intussusception recurrence at an average of 71-months follow-up with 3 (8%) recurrences following appendectomy and 4 (12%) recurrences without appendectomy during the operative management of intussusception [60]. In two studies, surgeons removed the appendix only in the case of ischemia or inflammation [45,55]. Only one manuscript specifically reported appendectomy to prevent later confusion if the patient presented in the future with abdominal pain [61]. In the remaining four manuscripts, a portion of patients did have appendectomy, but there was no specific reason for removal of the appendix or report on patient outcomes [49,50,62,63].

**Recommendation:** There are inadequate data to support prophylactic removal of the appendix during surgical management of intussusception. While appendectomy does not seem to reduce the rate of recurrent intussusception, removal of the appendix can be considered in the setting of inflammation or ischemia. (*Grade D recommendation, level 4 evidence*).

## Discussion

Overall, the present literature review on management of intussusception in the pediatric patient highlights opportunities for improved healthcare utilization while maintaining best outcomes. Notably, the data support avoiding antibiotic administration prior to reduction, that repeating attempts at radiologic reduction decrease the need for surgery, safety of discharging patients with radiographically reduced intussusceptions after a period of observation in the ED, and utility of minimally invasive surgical techniques as the first-line operative approach. In addition, this review reinforces general clinical principles guiding management of intussusception in children, mainly that recurrence is not common after surgical or radiologic reduction techniques and that children aged >2 years may be a distinct clinical group warranting closer observation. These salient points from the literature were summarized to create a management algorithm (Figure 2). Of note, this management algorithm should only be applied in children who are hemodynamically stable without critical illness.

The pathophysiology of the majority of pediatric intussusception is thought to be secondary to a transient viral illness leading to temporary lymphatic engorgement creating a lead-point and resultant intussusception [64,65]. Most children with intussusception are otherwise healthy and do well after enema reduction or surgery, making poor outcomes such as perforation, sepsis, or hospital readmission after management of intussusception rare. Resolution of the intussusception coupled with recovery from a viral illness likely removes future risk of recurrence. Currently, there is a lack of Level 1 and Level 2 evidence for any of the questions addressed in this manuscript to inform clinical management. Many published studies are limited to small, single center reports of retrospective studies or quality improvement initiatives. Several larger cohort studies using administrative claims data such as the PHIS dataset were included in our analysis but are limited by the retrospective and non-clinical nature of data collected for billing purposes.

Future studies using large datasets that track patients over time through different hospitalizations and emergency room visits would be helpful to more accurately assess healthcare utilization. As many of the clinical management practices outlined in the present literature are now standard practice at many institutions, enrollment in randomized control trials may be challenging due to concerns about equipoise among physicians and surgeons. However, outpatient management of pediatric intussusception may be an ideal target for a randomized controlled trial as both discharge from the emergency room and inpatient monitoring appear to be no more than minimal risk but have significant implications for healthcare utilization. Our review identified several other topics that may benefit from additional study, including safety, efficacy and timing of delayed repeated enemas for radiographic reduction, novel reduction techniques including on-table, laparoscopic-assisted enema reduction or ultrasound-guided enema reduction, and the long-term risks/benefits of concomitant appendectomy during operative reduction of intussusception.

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## Appendix A

### Search Terms for Literature Review:

(((((“Therapeutics”[Mesh] OR “Diagnosis”[Mesh] OR “Recurrence”[Mesh] OR “Patient Readmission”[Mesh]) OR (readmission[Text Word] OR reduce[Text Word] OR reduction[Text Word] OR reduces[Text Word] OR management[Text Word] OR recur[Text Word] OR recurrence[Text Word] OR treating[Text Word] OR treatment[Text Word] OR postreduction[Text Word] OR preimplementation[Text Word] OR postimplementation[Text Word] OR diagnosis[Text Word] OR diagnostic[Text Word] OR therap\*[Text Word] OR decompensat\*[Text Word] ))) OR (readmission[Other Term] OR reduce[Other Term] OR reduction[Other Term] OR reduces[Other Term] OR management[Other Term] OR recur[Other Term] OR recurrence[Other Term] OR treating[Other Term] OR treatment[Other Term] OR postreduction[Other Term] OR preimplementation[Other Term] OR postimplementation[Other Term] OR diagnosis[Other Term] OR diagnostic[Other Term] OR (therap\*[Other Term] ) OR (decrease[Other Term] OR decreased[Other Term] OR decreases[Other Term] OR decreasing[Other Term])) AND (((“Child”[Mesh] OR “Pediatrics”[Mesh]) OR (child[Text Word] OR children[Text Word] OR pediatric[Text Word] OR pediatrics[Text Word] OR boy[Text Word] OR boys[Text Word] OR girl[Text Word] OR girls[Text Word])) OR (child[Other Term] OR children[Other Term] OR pediatric[Other Term] OR pediatrics[Other Term] OR boy[Other Term] OR boys[Other Term] OR girl[Other Term] OR girls[Other Term]))) AND ((“Intussusception”[Mesh] OR (Intussusception[Text Word] OR Intussusceptions[Text Word] OR “Intestinal Invagination” [Text Word] OR “Intestinal Invaginations”[Text Word] OR Intussusception[Text Word] OR Intussusceptions[Text Word])) OR (Intussusception[Other Term] OR Intussusceptions[Other Term] OR “Intestinal Invagination”[Other Term] OR Intussusception[Other Term]))

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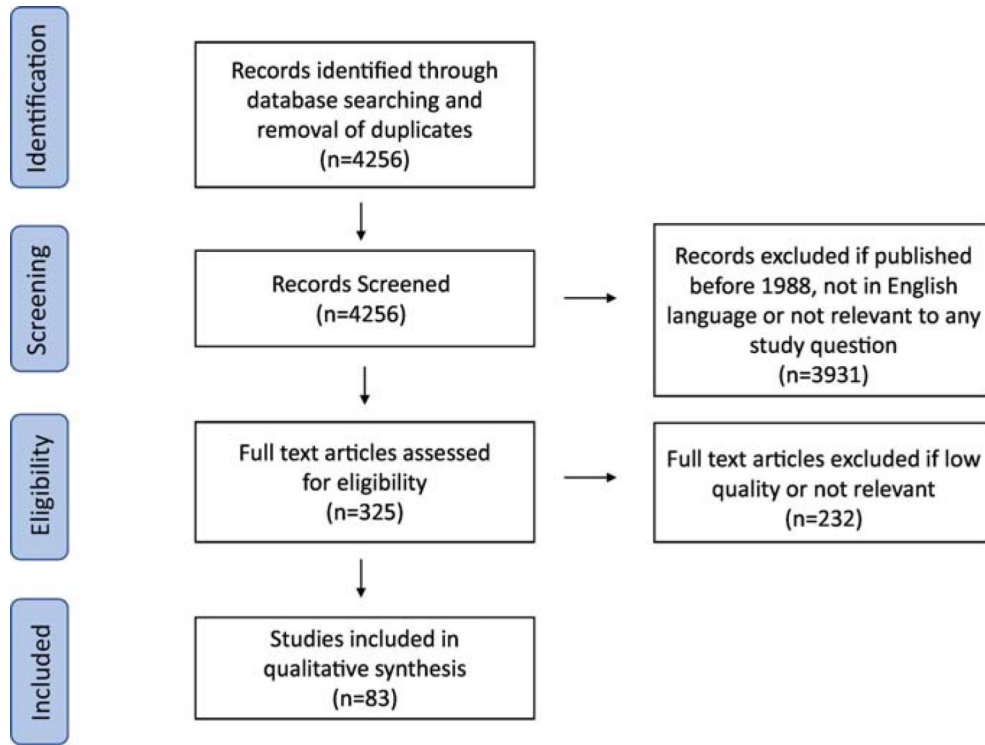
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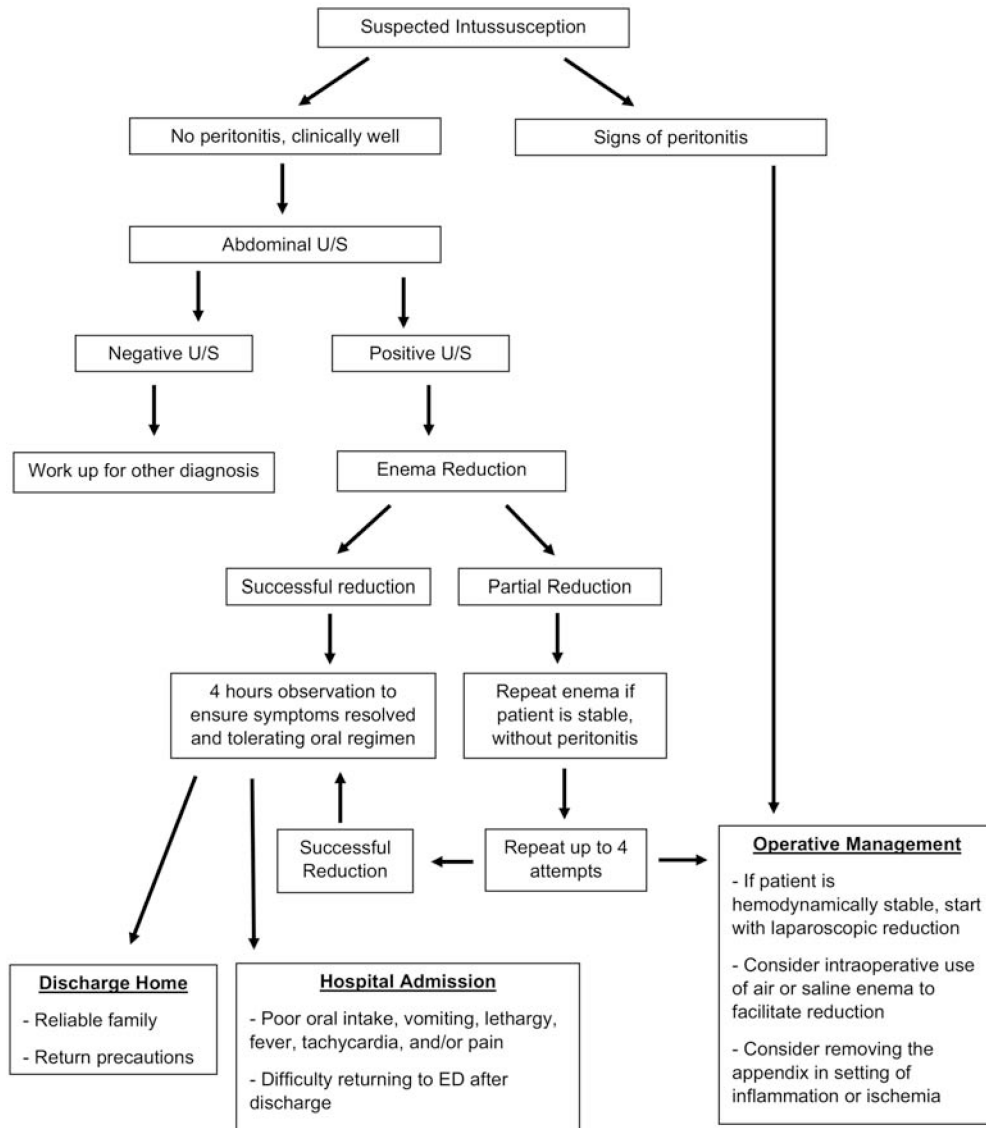
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**Figure 1.** PRISMA flow diagram of literature search and exclusion



**Figure 2.**  
Intussusception Management Algorithm

**Table 1.**

Outcomes for Delayed Repeat Enema (DRE) using standardized criteria\* for patient enrollment

Study	DREN (%)	Enema	Time to DRE	Attempts	Success N (%)	Perforation N (%)	LOE
Saxton 1994	21/143 (15)	Air	30 min to 3 h	2	11/21 (52)	0/21 (0)	4
Gorenstein 1998	23/44 (52)	Air	45–60 h	3	19/23 (83)	0/13 (0)	4
Gonzalez-Spinola 1999	65/194 (34)	Hydrostatic with US	30 min to 24 h	2	30/65 (46)	0/65 (0)	4
Sandler 1999	17**	Air	2–4 h	5	10/17 (59)	2/17 (12)	4
Navarro 2004	26/219 (12)	Air or Barium	15 min to 12 h	5	13/26 (50)	0/26 (0)	4
Blanch 2007	11/141 (8)	Air	Not Specified	2	7/11 (64)	0/11 (0)	4
Pazo 2010	21**	Air	>2 h	3	12/21 (57)	0/21 (0)	4
Fallon 2013	22/379 (6)	Air or Barium	>2 h	4	22/42 (52)	0/42 (0)	4
Pran 2018	17/60 (28)	Barium	2 to 6 h	4	8/17 (47)	0/17 (0)	4

LOE – Level of Evidence

\* Standardized criteria for DRE is defined as partial reduction of intussusception on first attempt in a medically stable patient without peritonitis.

\*\* Only patients undergoing delayed repeat enema during observation period are reported.

**Table 2.**

## Discharge from the Emergency Department

Paper	N	Mean Length of Stay (hours)	ED returns N	Readmissions N	Recurrence N (%)	LOE
LeMasne 1999	54 (ED) 42 (IP)	- 47	-	-	8 (15) 4 (10)	3
Bajaj 2003	51 (ED) 27 (IP)	7.2 22.7	13	5	4 (8) 4 (15)	3
Al-Jazaeri 2006	80 (IP)	38.4	-	-	6 (8) 5* (6)	4
Herwig 2009	6 (ED) 40 (IP)	4.6 25.6	-	-	0 (0) 3 (8)	4
Whitehouse 2010	48 (ED) 138 (IP)	- 38.4	4 10	1 2	4 (4) 10 (7)	3
Gilmore 2011	46 (ED) 10 (IP)	7 33.7	2	2	7 (13) 0 (0)	4
Chien 2013	8 (ED) 90 (IP)	7.1 35.2	-	-	0 (0) 7 (8)	4
Beres 2014	239 (ED) 218 (IP)	7.2 42.6	-	-	21 (9) 28 (9)	3
Raval 2015	30 (ED) 16 (IP)	6.8 -	7 1	-	1 (3) 0 (0)	3
Kwon 2017	45 (ED) 52 (IP)	4.6 25.6	-	-	3 (7) 5 (10)	3
Mallicotte 2017	51 (ED) 79 (IP)	4.9 31.7	-	1 3	(15) (14)	3
Okumus 2018	58 (ED)	6.2	4	0	4 (7)	4

ED – Emergency Department

IP – Inpatient

LOE – Level of Evidence

\* After hospital discharge

**Table 3.**

Comparison of laparoscopic and open surgery for intussusception in children

Manuscript		N	Conversion N (%)	Recurrence %	% Early Complication	% Late Complication	LOS days	Readmission %	LOE
Bailey 2007	Lap	18	5	-	22	-	4.8 ± 3.5*	-	3
	Open	23	(28)	-	26	-	9.1 ± 7.5	-	
Benedict 2018	Lap	63	0	2	11	-	4 (2-5)*	5	3
	Open	18	(0)	0	11	-	5 (4-6)	0	
Bonnard 2008	Lap	69	22	10	5	15	4	15	4
	Open	0	(32)	0	-	-	(2-11)	0	
Burjonrappa 2007	Lap	7	1	-	-	-	(3-10)	-	4
	Open	8	(14)	-	-	-	(3-15)	-	
Chang 2009	Lap	6	0	0	0	0	2-3	0	4
	Open	0	(0)	-	-	-	-	-	
Cheung 2007	Lap	15	1	8	8	-	4.2*	-	3
	Open	18	(7)	0	15	-	8.1	-	
Chua 2006	Lap	0	-	-	-	-	-	-	4
	Open	24	-	4	4	4	4-11	4	
Chui 2007	Lap	14	2	0	0	0	-	-	4
	Open	0	(14)	0	-	-	-	-	
Fraser 2009	Lap	22	2	0	0	9, combined	2.7 ± 1.5	9, combined	4
	Open	0	(9)	0	0	-	combined	-	
Hill 2013	Lap	65	21	5	-	8	1 (1-15)*	8	3
	Open	27	(32)	0	-	7	3 (1-6)	7	
Houben 2015 <sup>^</sup>	Lap	37	13	0	0	3	5 (3-51)*	0	4
	Open	7	(35)	14	43	28	8 (3-14) <sup>^</sup>	15	
Kaiser 2007	Lap	0	-	-	-	-	-	-	4
	Open	120	-	2	21	6	3.9	6	
Kao 2011 <sup>†</sup>	Lap	37	2	9	3	0	2.7 ± 2.2*	9	3
	Open	8	(5)	0	0	0	5.9 ± 1.9 <sup>†</sup>	0	
Kia 2005	Lap	16	2	6	6	-	3.0 ± 1.3*	6	3
	Open	25	(12)	4	4	-	4.5 ± 2.0	4	
Poddoubnyi 1998	Lap	118	36	-	0	0	2-5	-	3
	Open	56	(31)	-	-	-	-	-	
Pujar 2013	Lap	26	4	0	0	-	4.2	0	3
	Open	4	(15)	0	0	-	6.8	0	
Sklar 2014	Lap	5	2	0	20	0	3.8 ± 2.1	0	3
	Open	23	(40)	9	17	4	3.8 ± 2.1	9	
van der Laan 2001	Lap	14	11	-	-	-	-	-	3
	Open	21	(79)	-	-	-	-	-	
Vilallonga 2015	Lap	4	0	-	0	0	2.5 (2-4)	-	4
	Open	0	(0)	-	-	-	-	-	
Wei 2015	Lap	23	1	4	-	-	3.3 ± 1.2*	-	3
	Open	35	(4.3)	3	-	-	4.4 ± 1.6	-	

Lap = Laparoscopic surgical technique, Open = Laparotomy surgical technique

LOS = length of stay, LOE = Level of Evidence

Early complications = before discharge, Late complications = after discharge

\* P &lt; 0.05

<sup>~</sup>Not reported in manuscript

<sup>^</sup>Lap converted to Open included in the OPEN group

<sup>†</sup>Lap converted to Open excluded from outcomes analysis

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**Table 4.**

## Laparoscopic-assisted enema reduction of intussusception

<b>Paper</b>	<b>N</b>	<b>Enema Technique</b>	<b>Reduction Rate (%)</b>	<b>LOE</b>
Geltzeiler 2015	7	Saline enema	2/7 (29%) already reduced 5/7 (71%) complete reduction	4
Chandrasekharam 2011	11	Saline enema	10/11 (91%) complete reduction 1/11 (9%) umbilical extension	4
Kia 2005	5	Saline enema	5/5 (100%) complete reduction	4
Goldstein 2003	4	Air enema	4/4 (100%) complete reduction	4
Hay 1999	12	Saline enema	8/20 (40%) already reduced 6/20 (30%) complete reduction	4
Poddoubnyi 1998	15	Air enema	15/15 (100%) complete reduction	4

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