

**The 'great unknowns' in management of appendicitis in children.**

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Acute appendicitis is the commonest surgical emergency in children [1]. The lifetime risk of developing appendicitis in the developed world is 7-9% with a peak incidence in the early teenage years [2]. As such over 10,000 children in the United Kingdom alone develop appendicitis annually [3]. Given the abundance of cases and the frequency with which surgeons and other clinicians encounter children with appendicitis one might think that we know with certainty how to best to assess and treat young people suspected of having this condition. It is something of a surprise therefore given the cumulative experience of (primarily) surgeons in managing children and young people with appendicitis that there are so many uncertainties about best practice [1]. In this article I will highlight some of the key uncertainties that exist in the way appendicitis is managed in the hope that by highlighting these they will be the target of future research efforts.

Two recent publications have drawn attention to some of these uncertainties. The Getting It Right First Time (GIRFT) abdominal pain pathway was published in 2022 and provides a comprehensive a set of clinical guidelines for the management of children with abdominal pain who may turn out to have appendicitis [4]. This evidence based review of the existing literature acts as an excellent source for the management of children presenting with abdominal pain and is recommended reading for those providing healthcare in the UK for this patient population. Where recommendations based on existing evidence could not be made the authors highlight areas for future research to address these uncertainties (Table 1). A second recent publication (from 2021) was the results of a research priority setting exercise amongst specialist paediatric and general surgeons who treat children [5]. Amongst the top 10 research priorities in the field of emergency general surgery of childhood, feature 4 topics related to the management of children with appendicitis (Table 2). Taken together these two lists provide a fairly comprehensive summary of what we don't know about assessing and treating children and young people with appendicitis and provide a useful list of topics to be investigated in research.

Yet amongst all this residual uncertainty, there is positive news. Thanks to previous research endeavours current practice is more evidence based than ever. A range of interventions supported by research evidence make up clinical pathways for management of children and young people with appendicitis in most centres. As a result the laparoscopic approach to appendicectomy is now routine and negative appendicectomy rates are gradually falling. Furthermore, these uncertainties present abundant opportunity for further collaborative research, ideally joint endeavours between specialist paediatric surgeons and general surgeons to ensure generalisability of findings, wide engagement and a clear path towards implementation of trial findings.

One uncertainty that is well underway to being addressed is the safety and efficacy of non-operative management compared to appendicectomy in children with simple appendicitis. At least two small initial trials (one pilot, one feasibility) have been completed [6, 7] and several full scale randomised controlled trials are well underway [8, 9] including the CONTRACT-2 study in the United Kingdom [10]. Whilst recruitment is not yet complete, progress is being made and there is hope that before too long research findings will be available to implement into clinical practice. The challenge is on to continue to seek answers to what we don't truly know. Only by doing so that we can ensure practice is evidence based and all children and young people in our care have access to the best possible outcomes.

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**Table 1 - Knowledge gaps identified during the GIRFT process (adapted from [4])**

Optimal method of local anaesthetic delivery during surgical procedure
Optimal appendicitis scoring system for use in clinical practice
Utility of additional blood tests (biomarkers), particularly pro-calcitonin
Utility of physiological parameters in the emergency department to differentiate between children with a surgical and non-surgical cause of abdominal pain.
The role of diagnostic imaging in the assessment of children with abdominal pain
Safety and efficacy of non-operative management of children with simple appendicitis
The impact of delay between diagnosis and appendicectomy for children
Optimum antibiotic regime for children with complex appendicitis
The optimum management of post-appendicectomy intra-abdominal collections
What are the patient and family reported outcomes following appendicectomy in children?

**Table 2 – Emergency research priorities related to appendicitis (adapted from [5])**

In children undergoing appendicectomy, to what extent does duration, type and administration route of antimicrobial treatment affect outcomes? Do any specific organisms (e.g. Streptococcus milleri) require variations in therapy (e.g. longer course of treatment)?
In children with uncomplicated acute appendicitis, does appendicectomy or non-operative treatment with antibiotics result in better outcomes?
In children with complicated appendicitis, does appendicectomy or non-operative treatment (with or without drain) result in better outcomes compared with no appendicectomy? Are there clinically distinct subgroups (e.g. mass, abscess, neither) that influence this?
In children with a postappendicectomy collection, how might intervention (percutaneous drain or open drain) improve outcome compared with antibiotics alone? Are there factors, such as age or size of collection, that influence this?

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