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Impact of the COVID-19 pandemic on management and outcomes of children with appendicitis: The Children with AppendicitiS during the CoronAvirus panDEmic (CASCADE) study

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ABSTRACT

Aim: To report the impact of the SARS-CoV-2 pandemic on management and outcomes of paediatric appendicitis in the UK and Ireland.
Methods: Prospective, multicentre observational cohort study at general surgical and specialist paediatric surgical centres in the United Kingdom and Ireland from 1st April to 31st July 2020. Primary outcome was treatment strategy used for acute appendicitis.
Results: This study includes 2002 children treated for acute appendicitis of a median age of 10 (range 1–15) years and 605 children from a similar data set pre pandemic from 2017. In the pandemic cohort 560/2002(28%) were initially treated non operatively of whom 125/560(22%) proceeded to appendicectomy within initial hospital admission. Non operative treatment wasn't used in the pre pandemic cohort. Diagnostic imaging use was greater during the pandemic compared to pre pandemic (54*vs*31%; $p < 0.00001$) but overall use of laparoscopy was similar during both time periods (62.4*vs*66.6%). Hospital readmission rate was lower (8.7*vs*13.9%; $p = 0.0002$) during the pandemic than pre pandemic and *Re*-intervention rate was similar (2.9*vs*2.6%;$p = 0.42$). In cases treated operatively negative appendicectomy rate was lower during the pandemic than pre pandemic (4.4*vs*15.4%; $p = 0.0001$), and during the pandemic was amongst the lowest ever reported in the UK.
Conclusion: COVID-19 has had a significant impact on the management of children with appendicitis in the UK and Ireland. The rate of imaging and the use of non operative management increased, whilst the negative appendicectomy rate reduced. Overall, patient outcomes have not been adversely impacted by change in management during the pandemic.
Level of evidence: Level I.
Type of study: Prognosis study.

What is currently known about this topic?

- The SARS-CoV-2 pandemic brought about changes in management of appendicitis including increasing use of non operative treatment.
- The impact of these changes are uncertain.
- Until this time non operative treatment for paediatric appendicitis in the UK has been limited to trials.

What new information is contained in this article?

- Patient outcomes have not been adversely impacted by change in management during the pandemic, rather some important outcomes have improved.
- The negative appendicectomy rate at 4.4% is one of the lowest ever reported in the UK.
- The widespread, real world use of non operative treatment in general and specialist settings resulted in acceptable patient outcomes.

1. Introduction

Acute appendicitis is the most common surgical condition in children and in the United Kingdom (UK) treatment of children

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with appendicitis is shared between general surgeons (GS) in district general hospitals and specialist paediatric surgeons (SPS) at specialist paediatric centres [1]. Typically treatment is surgical with the majority of cases undergoing urgent appendicectomy; non operative treatment of acute appendicitis in children is not widespread in the UK.

The SARS-CoV-2 (COVID-19) pandemic caused widespread disruption to the provision of all healthcare but to surgical care in particular, for a wide variety of reasons including staff redeployment, operating theatre availability and concerns about transmission of SARS-CoV-2 from patients to healthcare staff [2]. Guidance during the first few weeks of the pandemic from the Royal College of Surgeons of England suggested that laparoscopy should only be used in procedures where the risk of an open procedure to the patient outweighed the potential risk to staff in theatre, as laparoscopy was believed to be an aerosol generating procedure (AGP) [2]. It was also recommended that non operative treatment should be used to avoid surgery for all conditions, including appendicitis, if it was considered an acceptable alternative treatment option [3]. As the pandemic progressed, emerging data revealed that surgery in adults infected with Covid-19 was associated with adverse outcomes, including increased mortality [4]. All of these factors had significant impact on the management of children with appendicitis and early reports from the pandemic observed a shift from operative to non operative treatment, and from laparoscopic to open appendicectomy [5].

The potential impact of these widespread changes in healthcare delivery for children with appendicitis were unknown. Amidst this uncertainty and concern that patient outcomes may be negatively affected, the CASCADE study (Children with AppendicitiS during the CoronAvirus panDEmic) was initiated in late March 2020 to capture data relating to the impact of the pandemic on the management and outcomes of children with appendicitis. Initially, paediatric and adult surgeons in the UK who treat children with appendicitis were surveyed to understand the anticipated impact of the pandemic on management of children with appendicitis [5]. This was followed by an observational cohort study during the first wave of the pandemic in the UK and Ireland. Initial data from the first 2 months of this study have previously been published [5]. This report details the findings of the full 4 months of study and by comparing data to a pre-pandemic cohort aims to investigate the impact of the pandemic on patient management and important outcomes.

2. Methods

2.1. Cohort study design

A prospective multicentre observational cohort study of children aged less than 16 years at time of hospital admission who were diagnosed with and treated for acute appendicitis in the UK and Ireland was performed. Participating hospitals, including district general hospitals and specialist paediatric surgery centres, were not required to alter diagnostic or treatment pathways and no changes were made to patient care as part of this study.

2.2. Centre recruitment and patient identification

Hospitals providing acute surgical care to children were invited to participate in this study via a number of channels including targeted emails, newsletters, social media and websites of surgical and paediatric national organisations including the British Association of Paediatric Surgeons, the Royal College of Surgeons of England, and the Royal College of Paediatrics and Child Health. Children were included in the study if they were diagnosed with and treated for acute appendicitis in hospital. Diagnosis was based on clinical and/or radiological criteria. Children who presented with abdominal pain but not felt to have appendicitis were excluded, however those treated for appendicitis initially but then given an alternative diagnosis were included. This study includes all children with an initial admission date between April 1st 2020 and July 31st 2020. Follow-up was censored at 30 days post hospital discharge from initial admission. Data were collected at 72 hospitals in the UK and 2 in Ireland of which 29 were specialist paediatric surgery centres and the remainder were district general hospitals where children were treated by general surgeons.

2.3. Ethical considerations

This study was registered at each site as a service evaluation, as defined by the health research authority guidance, as this was an observational study only collecting routine anonymised data with no change to clinical care pathways.

2.4. Outcomes

The primary outcome was the initial treatment strategy for acute appendicitis, defined as surgical or non operative. Secondary outcomes related to patient management included number and proportion of operative cases performed open and laparoscopically, use of diagnostic imaging and variation in patient management over time, as the pandemic progressed. Clinical outcomes were success rate of non operative treatment (defined as no appendicectomy within initial hospital inpatient episode in a case in whom the initial treatment strategy was non operative), need for hospital readmission, wound infection, bowel obstruction, intra-abdominal collection, further intervention, length of hospital stay, negative appendicectomy and mortality. *Re*-intervention was defined as an invasive procedure, either surgical or radiological intervention such as drainage of collection. Negative appendicectomy was defined as absence of pathology on, histological assessment of the appendix. These outcomes were all reported to 30 days following initial hospital admission and were selected as important outcomes from a core outcome set for paediatric appendicitis [6].

2.5. Pre COVID-19 pandemic cohort

In order to compare outcome and management to a pre-COVID-19 cohort the complete dataset from the Right Iliac Fossa Treatment (RIFT) study was obtained with permission [7]. This study included patients of all ages who were admitted to hospital during a pre-specified four-week period between 13th March and 18th June 2017 with right iliac fossa pain. Data were collected at 130 hospitals in the UK and 9 in Ireland of which 17 were specialist paediatric surgery centres and the remainder were district general hospitals where children were treated by general surgeons. Patients were only included in a comparison cohort if they were <16 years old and were treated for suspected appendicitis in the UK and Ireland. Those treated for other diagnoses were excluded.

Comparisons were made, where possible, between the primary and secondary outcomes of the pre-pandemic and pandemic cohorts.

2.6. Data collection and analysis

Anonymous data were collected by local study teams within each hospital and submitted to the study team monthly. Data were checked for duplication since we were aware that some cases were transferred from one hospital to another during the study period (typically from a district general hospital to a local specialist paediatric surgery centre) and we wished to avoid duplication. Duplicated data records were identified and excluded if all of age, sex,

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Table 1
Clinical characteristics and management of children treated prior to and during the COVID-19 pandemic.

		Pre-pandemic (n = 605)	Pandemic (n = 2002)
Age (years)		11 (9–13)	10 (8–13)
Male (n,%)		341 (56.4)	1210 (60.4)
Speciality (n,%)	GS	470 (77.7)	818 (40.9)
	SPS	135 (22.3)	1184 (59.1)
Admission bloods	WCC – x10^9/L	14.4 (9.8–18)	14.9 (11.6–18.1)
	CRP - mg/L	25 (5–75.5)	42 (12–105)
US performed (n,%)		182 (30.1)	985 (49.2)
CT/MRI performed (n,%)		8 (1.3)	97 (4.9)
Non operative management (n,%)		0 (0)	560 (28.0)
Laparoscopic appendicectomy$ (n,%)		403 (66.6)	898 (62.4)

GS – general surgeon; SPS – specialist paediatric surgeon; WCC – white cell count; CRP – C-reactive protein; L – litre; mg – milligrams; US – ultrasound; CT – computer tomography; MRI – magnetic resonance imaging. $-initial operative management. Continuous data are median (IQR).

CRP and WCC at admission were identical or if flagged as a child that was transferred between centres and therefore appeared in the dataset more than once.

Statistical analysis was performed using StataSE v15 (StataCorp LLC, Texas, USA) and the figures were produced using GraphPad Prism v8 (GraphPad Software, La Jolla California USA). Data are presented as median (IQR or range) and/or number/total (%) as appropriate. Fisher's exact test or chi-squared test, as appropriate, were used for comparison of categorical data and the Mann Whitney-U test was used for non parametric continuous data. A p value of less than 0.05 was considered as statistically significant. The study was conducted according to Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines for observational studies [8].

2.7. Funding

The study did not receive any funding. The corresponding author had full access to all study data and responsibility for publication.

3. Results

3.1. Children included and diagnostic investigations

In the pandemic cohort, there were 2002 children treated for appendicitis between April 1st and July 31st 2020 in 74 centres with a median age of 10 (range 1–15) years. Clinical characteristics and diagnostic investigations used are shown in Table 1. At the point of diagnosis 1464 children (73.5%) were suspected by the treating surgeon to have simple acute appendicitis, 458 (23.0%) complicated appendicitis and 71 (3.6%) an appendix mass (data missing in 9 cases). At time of diagnosis of acute appendicitis the COVID-19 status was known positive in 5 (0.3%) children, known negative in 440 (22.0%) children, tested awaiting result in 1117 (55.8%) children and 440 (22.0%) children were untested. Three children (0.1%) were initially treated for appendicitis but subsequently were diagnosed with Paediatric Multisystem Inflammatory Syndrome (PIMS-TS), of these 2 children were treated non operatively whilst one child underwent laparoscopic appendicectomy.

The pre-pandemic cohort (Table 1) comprised 605 children treated for appendicitis at 139 centres between 13th March and 18th June 2017 with a median age of 11 (range 1–15) years. In the pandemic cohort a greater proportion of cases were treated by SPS compared to GS than pre-pandemic and diagnostic imaging was used more frequently than pre-pandemic (54 vs 31%; $p < 0.00001$).

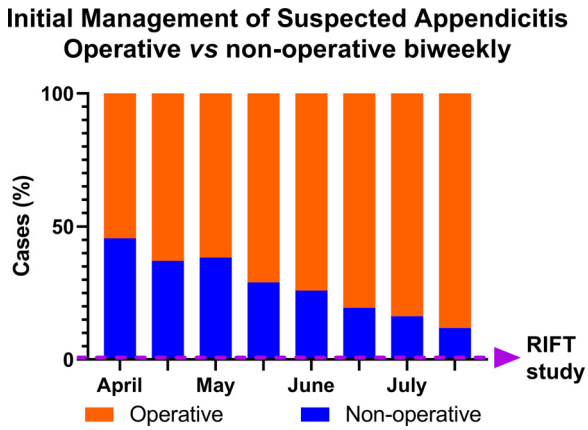

Fig. 1. Initial management strategy of appendicitis biweekly, operative vs non operative. The red bars represent operative treatment and the blue bars represent non operative treatment. The purple line represents practice prior to COVID19 pandemic from RIFT study data. During the first two weeks of April 2020 the proportion of cases initially treated non operatively was 46% which reduced to 12% in the last two weeks of July 2020.

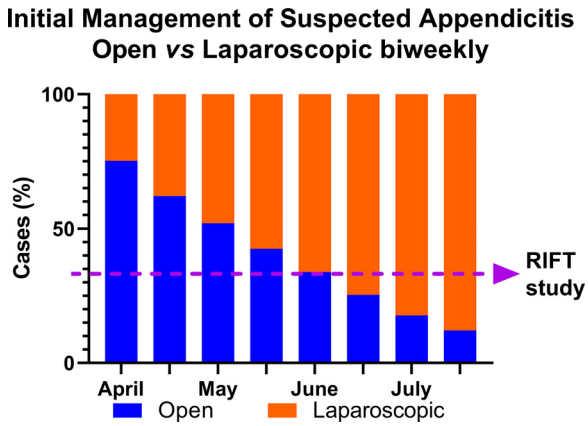

Fig. 2. Initial operative management strategy of appendicitis biweekly, open vs laparoscopic. The red bars represent laparoscopic appendicectomy and the blue bars represent open appendicectomy. The purple line represents practice prior to COVID19 pandemic from RIFT study data. During the first two weeks of April 2020, 75% of cases were treated by open appendicectomy and this reduced to 12% in the last two weeks of July 2020.

Across both cohorts, diagnostic imaging was used more frequently by SPS than GS (pandemic: 55 *vs* 46%, $p < 0.001$; pre-pandemic: 38 *vs* 29%, $p = 0.04$).

3.2. Management strategy

During the pandemic there was a significant shift towards non operative management such that 28% of cases were initially managed non operatively during the pandemic compared to none in the pre-pandemic cohort. As the pandemic progressed there was a gradual reversal of this shift back toward surgical management (Fig. 1). Where operative management was undertaken, the rate of laparoscopic, versus open appendicectomy, overall was similar in the pandemic and pre-pandemic cohorts. In the pandemic cohort there was evidence of a change in practice over time with an increase in proportion of cases performed laparoscopically over the 4 months period (Fig. 2).

3.3. Patient outcomes

Overall outcomes amongst the two cohorts are shown in Table 2. At 30-days there were no reported deaths. Regardless of

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Table 2
Outcomes of children treated prior to and during the COVID-19 pandemic.

		Pre pandemic ($n = 605$)	Pandemic ($n = 2002$)	p
Length of stay, days (IQR)		3 (2–4)	3 (2–5)	**0.03**
Readmission (n,%)		84 (13.9)	175 (8.7)	**0.0002**
Re-intervention[$] (n,%)		15 (2.6)	41 (2.9)	0.42
Histology for cases treated surgically (n,%)	Normal	93 (15.4)	58 (4.4)	**0.0001**
	Simple	260 (43.1)	720 (54.7)	
	Complicated	216 (35.8)	494 (37.5)	
	Other	34 (5.6)	44 (3.3)	

Histology not available in 2 children in pre pandemic cohort and 123 children in pandemic cohort. $-initial operative management. Continuous data are median (IQR).

treatment method, the readmission rate was higher in the pre pandemic cohort compared to the pandemic cohort however the *Re*-intervention rate was similar. Readmission rate was similar between children treated by GS and SPS (9.4 *vs* 8.3%, $p = 0.38$). Findings were similar at only SPS centres compared to the whole cohort of children (supplementary table).

3.4. Outcomes of operative treatment

In cases treated operatively, outcomes were stratified by surgical findings (Table 3) since severity of appendicitis is well recognised to predict post operative management and clinical course (note cases of appendix mass are excluded from this comparison). Macroscopic appearance of the appendix at operation was either normal ($n = 63$, 4.4%), inflamed ($n = 748$, 52.8%), gangrenous ($n = 143$, 10.1%), perforated ($n = 421$, 29.7%) or appendix mass ($n = 43$, 3.0%). For further analysis in this section and Table 3, simple and no appendicitis have been grouped together and, gangrenous and perforated appendicitis has been grouped (complicated appendicitis) together since the post operative management is typically stratified by operative findings in this way.

Appendix histology reports were available for 1316/1439 (91%) children that initially underwent operative management. The findings were simple appendicitis in 720 (55%), gangrenous appendicitis in 205 (16%), perforated appendicitis in 289 (22%) and other pathology in 44 (3.3%) children. Other pathology included 6 (0.45%) neuro endocrine tumours (NET). The negative appendicectomy rate was 4.4% ($n = 58$) in the pandemic cohort and 15.4% ($n = 93$) in the pre pandemic cohort.

As in previous reports [9], the negative appendicectomy rate was lower in children treated by SPS compared to GS (3.4 *vs* 5.9%, $p = 0.03$). The negative appendicectomy rate was similar in both sexes (52% [male] vs 48% [female], $p = 0.15$).

3.5. Non operative management

No children in the pre pandemic cohort underwent non operative management. In the pandemic cohort clinical, laboratory and radiological characteristics for cases treated surgically and non operatively are shown in Table 4. Cases treated non operatively received antibiotic therapy and typically had less advanced appendicitis with lower CRP and white cell count at diagnosis and were more likely to have suspected simple (as opposed to complicated) appendicitis. A higher proportion of cases treated non operatively had an ultrasound scan than of cases treated surgically. The majority of cases selected for non operative treatment were suspected to be simple appendicitis at the time of diagnosis although a small number of suspected complicated cases were also treated non operatively.

3.6. Non operative treatment outcomes

Of the 560 cases treated non operatively, 125 (22% [95%CI 19–26%]) children failed non operative treatment during the initial admission and proceeded to appendicectomy. This was approached via an open procedure in 49 (39%) cases and a laparoscopic procedure in 76 (61%) cases. Where available (missing $n = 1$), intra-operative findings in those who failed initial non operative treatment were normal appendix in 6 (4.8%) children, simple appendicitis in 50 (40%), complicated appendicitis in 61 (49%) children and appendix mass in 7 (5.7%) children.

Overall the 30-day readmission rate was 11% (47/435) for non operative treatment in those that were discharged home without an operation. Reasons for readmission in the group which underwent non operative treatment without appendicectomy prior to discharge were abdominal collection/abscess ($n = 1$), abdominal pain ($n = 37$) and fever ($n = 5$). In some cases there were multiple reasons for readmission or the reason was not specified. Of those readmitted, 15% (7/47) of children had an appendicectomy within 30-days of initial hospital admission.

Appendix histology reports were also available for 110 of the 125 (88%) children that failed non operative management. The findings were simple appendicitis in 51 (46%), gangrenous appendicitis in 19 (17%), perforated appendicitis in 28 (25%), other pathology in 4 (3.6%) and normal appendix in 8 (7.2%) children. There were no neuroendocrine tumours.

4. Discussion

This report of the management of children with appendicitis during the first 4 months (first wave) of the SARS-CoV-2 pandemic in the UK and Ireland demonstrates a clear increase in the use of non operative treatment and open appendicectomy for appendicitis in children compared to a pre COVID19 cohort. This sudden change of practice coincided with the guidance published by the Royal College of Surgeons of England advising non operative treatment wherever possible and cautioning against the use of laparoscopy [2]. As the pandemic progressed, guidance evolved and towards the end of July clinical practice was reverting back towards that seen in the pre COVID dataset. Interestingly, 12% of children were still being initiated on non operative treatment at the end of July 2020. This may be owing to ongoing concerns of operative treatment, local policy or a permanent shift in practice owing to increased surgeon familiarity with this treatment method. Importantly, despite this sudden and widespread change in practice there does not appear to have been a negative impact on patient outcomes. In fact it appears there is evidence of improved outcomes that are worthy of discussion and consideration of how to realise these benefits on an ongoing basis.

Undoubtedly the most significant shift in practice was the use of non operative treatment which occurred without any pre defined case selection criteria or treatment protocol. Despite this, the success rate of non operative management was as high as 78% even though 13% of children treated non operatively were suspected to have complicated appendicitis. Non operative treatment has been used here outside the criteria used to date in formal research studies in which it has been evaluated and hence with tighter case selection outcomes may be even better [10–12]. These data demonstrate that surgeons are willing to consider non operative treatment (although we note that practice reverted towards operative management over time) and also suggest that non operative treatment may be considered as an effective treatment modality and an alternative to appendicectomy. Whilst we believe that further evaluation of the comparative outcomes of non operative treatment and appendicectomy should be under-

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Table 3
Comparative operative outcomes between pandemic and pre pandemic cohorts stratified by operative findings.

	Simple or No appendicitis			Complicated appendicitis		
	Pandemic (n = 811[$])	Pre pandemic (n = 390[&])	p	Pandemic (n = 564[$])	Pre pandemic (n = 214[&])	p
Re admission (n,%)	30 (3.7)	40 (10.3)	**<0.0001**	80 (14.2)	43 (20.1)	**0.04**
Re-intervention (n,%)	4 (0.5)	5 (1.4)	0.13	33 (5.9)	10 (5.0)	0.52
Length of stay (days, median and IQR)	2 (1–3)	2 (2–3)	**<0.0001**	5 (3–7)	4 (2–6)	**<0.0001**

$ Operative findings missing in 25 cases. & Operative findings missing in 1 case.

Table 4
Clinical, laboratory and radiological characteristics of cases treated initially non operatively or operatively (data for pandemic cohort only).

		Non operative (n = 560)	Operative (n = 1439)	p
Age (years)		10 (8–13)	10 (8–13)	0.21
Male (n,%)		330 (58.9)	879 (61.1)	0.39
Duration of symptoms (hours)		36 (24–72)	48 (24–72)	0.42
Speciality (n,%)	GS	229 (40.9)	589 (40.9)	1.00
	SPS	331 (59.1)	850 (59.1)	
Admission bloods	WCC – x10^9/L	14.2 (10.5–17.5)	15.0 (12.0–18.2)	**0.0003**
	CRP - mg/L	32 (7.7–87)	45 (14–114)	**<0.0001**
US performed (n,%)		358 (63.9)	624 (43.3)	**<0.0001**
CT/MRI performed (n,%)		34 (6.0)	62 (4.3)	0.76
Suspected severity at diagnosis (n,%)	Simple	437 (78.3)	1027 (71.7)	**<0.0001**
	Complicated	71 (12.7)	385 (26.9)	
	Appendix mass	50 (9.0)	20 (1.4)	

GS – general surgeon; SPS – specialist paediatric surgeon; WCC – white cell count; CRP – C-reactive protein; L – litre; mg – milligrams; US – ultrasound; CT – computer tomography; MRI – magnetic resonance imaging. Continuous data are median (IQR).

taken, non operative treatment of appendicitis in children in the UK outside of a clinical trial is no longer without precedent.

The negative appendicectomy rate seen in this dataset, based on histological findings, is extremely low, and is one of the lowest rates reported in the UK [1,7,9]. Alongside this, radiological imaging has been seen more frequently during the COVID-19 dataset compared to the pre pandemic data from 2017. These findings may be directly associated but regardless, this has reduced the burden on stretched healthcare resources whilst protecting children from the risks of surgery when they have not got appendicitis. The high negative appendicectomy rate observed in the UK has been highlighted recently to be of significant public interest [7,13]. The results of this study are therefore encouraging but ongoing work is required to maintain this unanticipated benefit of management during the pandemic. The low negative appendicectomy rate may be explained in this non randomised study by surgeons opting to treat children for appendicitis where there is still some diagnostic uncertainty. Hence, children who didn't have appendicitis may have been treated non operatively. It is also possible that there was overall greater care around making the diagnosis during the pandemic (e.g. greater consultant involvement, greater use of imaging, higher threshold for undertaking surgery owing to COVID risks) and that this has contributed to this positive outcome. Furthermore, there was a greater proportion of children being treated by specialist paediatric surgeons in the pandemic cohort however the statistically significant differences in outcomes comparing these children to the pre-pandemic cohort are the same when just including children treated by SPS (supplementary table). Therefore, these data don't support that children treated by SPS have better outcomes.

Laparoscopic appendicectomy in children has been shown to reduce incidence of wound infection, reduce post operative ileus and shorten inpatient stay compared to open surgery [14,15]. Usage of laparoscopy was high in the cohort of children from the RIFT study however in the first two weeks of the COVID-19 pandemic only 25% were undertaken laparoscopically. This was likely in response to guidance from professional bodies that laparoscopy may increase the risk of SARS-CoV-2 transmission to healthcare staff in positive cases [2]. As the pandemic progressed laparoscopy was utilised more with a shift back to normal practice as guidance from professional bodies was updated and there was a greater understanding about the epidemiology of COVID-19 in children [16]. As many as 88% of children were being treated with laparoscopic appendicectomy at the end of the study (last 2 weeks of July) which is one of the highest rates reported in children. Maintaining this high rate of laparoscopy will mean that children receive appropriate evidence based treatment.

A further positive finding is that the readmission rate for cases treated surgically was lower during the pandemic than in the pre pandemic cohort. These findings hold true for both simple and complicated appendicitis. The reason for this difference is not immediately clear but we postulate that greater consultant involvement in cases may have been contributory and anecdotally we are aware of this practice. Of note this may have been at the expense of a slightly longer hospital stay during the pandemic.

This study is strengthened by the fact that data have been collected prospectively from multiple centres from across the United Kingdom and Ireland. We deliberately did not involve other international centres so as to achieve a region across which there is relative consistency in management of children with appendicitis. This is a pragmatic real world study and provides an overview of real life outcomes outside the confines that would typically be achieved in a clinical trial. Conversely some may view this pragmatism as a weakness since we have not used precise definitions for severity of appendicitis nor have we proposed criteria for different treatment strategies. We recognise that we have only reported outcomes to 30 days and plan further analysis to include longer term follow-up, particularly of the group of children managed thus far without surgery.

The COVID-19 pandemic has had a marked impact on the management of children with appendicitis with clear shifts towards increased use of non operative treatment and open (as opposed to laparoscopic) appendicectomy compared to a pre pandemic cohort in 2017. However, patient-important outcomes have not been

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greatly altered during the pandemic and the negative appendicectomy rate is particularly low. These data should reassure surgeons about the management strategy used during the pandemic in the face of restrictions to normal surgical services, may inform practice in future times of limited surgical capacity and should reassure the public and commissioners that the surgical workforce has continued to deliver high quality care in these difficult times.

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Declaration of Competing Interest

All authors confirm that there are no competing interests.

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CASCADE study steering and writing group

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpedsurg.2022.03.029.

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