Anaesthesia 2023 doi:10.1111/anae.16184

Original Article

Risk factors for complications after emergency surgery for paediatric appendicitis: a national prospective observational cohort study

L. A. Sogbodjor, ^{1,2} © C. Razavi, ^{2,3} K. Williams, ⁴ A. Selman, ⁵ S. M. Pinto Pereira, ⁶ M. Davenport, ⁷ CASAP investigators* and S. R. Moonesinghe^{8,9}

- 1 Consultant, Department of Anaesthesia and Pain Medicine, Great Ormond Street Hospital NHS Foundation Trust, London, UK
- 2 Research Fellow, 4 Study Coordinator, Centre for Research and Improvement, Royal College of Anaesthetists, London, UK
- 3 Consultant, Department of Anaesthesia, Guy's and St Thomas' NHS Foundation Trust, London, UK
- 5 Consultant, Department of Anaesthesia, Evelina Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK
- 6 Associate Professor, 8 Professor, Centre for Peri-operative Medicine, Research Department for Targeted Intervention, UCL Division of Surgery and Interventional Science, London, UK
- $7\,Consultant\,and\,Professor,\,Department\,of\,Paediatric\,Surgery,\,King's\,College\,London\,NHS\,Foundation\,Trust,\,London,\,UK\,$
- 9 Director, Central London National Institute for Health Research Patient Safety Research Collaboration, London, UK

Summary

Appendicectomy is a common procedure in children with a low risk of mortality, however, complication rates and risk factors are largely unknown. This study aimed to characterise the incidence and epidemiology of postoperative complications in children undergoing appendicectomy in the UK. This multicentre prospective observational cohort study, which included children aged 1-16 y who underwent surgery for suspected appendicitis, was conducted between November 2019 and January 2022. The primary outcome was 30-day postoperative morbidity. Data collected included: patient characteristics; comorbidities; and physiological status. Multivariable regression analysis was used to identify independent risk factors for poor outcomes. Data from 2799 children recruited from 80 hospitals were analysed, of which 185 (7%) developed postoperative complications. Children from black and 'other' minority ethnic groups were at significantly higher risk of poor outcomes: OR (95%CI) 4.13 (1.87–9.08), p < 0.001 and 2.08 (1.12–3.87), p = 0.021, respectively. This finding was independent of socio-economic status and type of appendicitis found on histology. Other risk factors for complications included: ASA physical status ≥ 3 (OR (95%CI) 4.05 (1.70–9.67), p = 0.002); raised C-reactive protein (OR 95%CI 1.01 (1.00–1.01), p < 0.001); pyrexia (OR (95%CI) 1.77(1.20–2.63), p = 0.004); and perioperative oxygen supplementation (OR (95%CI) 4.20 (1.44-12.24), p = 0.009). In the UK NHS, which is a universally accessible healthcare system, ethnicity, but not socio-economic status, was associated with an increased risk of postoperative complications in children having surgery for acute appendicitis. Further evaluations and interventions are required to address this health inequality in keeping with NHS and international priorities.

Correspondence to: S. R. Moonesinghe Email: ramani.moonesinghe@nhs.net

Accepted: 17 October 2023

Keywords: appendicitis; children; ethnicity; health inequality; peri-operative care

*CASAP Investigators are listed in online Supporting Information Appendix \$1

Presented at the Association of Paediatric Anaesthetists Annual Scientific Meeting, Cardiff 2022; Royal College of Anaesthetists, Anaesthesia, Manchester 2022; British Association of Paediatric Surgeons Annual Scientific Meeting, Birmingham, 2022; National Institute for Academic Anaesthesia, Anaesthesia Research, York 2022.

Twitter/X: @dramakis; @rmoonesinghe

Introduction

Surgery to treat suspected appendicitis is one of the most common emergency operations performed in children. In the UK around 50,000 people are admitted to hospital with suspected appendicitis each year, and it is most prevalent in those aged between 10 and 20 y. As a result around 10,000 appendicectomies are performed in children annually in England [1, 2]. Despite this high prevalence, significant variation has been reported in both the care delivered and outcomes seen in children [3, 4]. It has been highlighted as an area in need of a concerted effort to understand the factors associated with poor outcome to reduce variation in care delivery and promote patient experience and cost-effectiveness [5].

Demographic factors such as age, ethnicity and socioeconomic status have been associated with outcome in children with acute appendicitis in the USA. It is not known whether the same is true in the UK, where healthcare is available to all at the point of need, and independent of one's circumstance [6]. Evidence relating to the impact of deprivation on outcome in other nations providing universal healthcare is conflicting [7, 8]. Understanding the risk factors for poor outcomes after surgery can support clinical decision-making, including when to escalate treatment. While there is a wealth of evidence about the diagnostic predictive power of pre-operative clinical characteristics, such as physiological and pathological findings, much less is known about their association with postoperative morbidity [9]. Identification of these characteristics may contribute to pre-operative planning and improve postoperative outcomes.

The Children's Acute Surgical Abdomen Programme (CASAP) was established to explore risk factors associated with adverse outcomes in children undergoing emergency abdominal surgery. This first analysis of the CASAP cohort describes the incidence and epidemiology of morbidity associated with surgery for suspected acute appendicitis in children in the UK.

Methods

This national prospective observational multicentre cohort study is reported in accordance with the STROBE statement.

Ethical approval was granted by the Health Research Authority and Health and Care Research Wales. Our study protocol and patient information sheets were reviewed by the NIHR Young Person's Advisory Group in the West Midlands.

The Quality Audit and Research Coordinator network managed by the Health Services Research Centre at the Royal College of Anaesthetists facilitated hospital engagement. All NHS hospitals which conduct emergency surgery on children were identified via a nationally distributed survey and invited subsequently to enrol as a study site. Patient recruitment took place between 22 November 2019 and 31 January 2022. All children aged 1-16 y requiring non-elective abdominal surgery were eligible to be recruited provided their legal quardian was willing and able to provide consent. We did not study children in whom the pre-operative indication for surgery was urological, gynaecological or traumatic in nature and those with non-English speaking legal guardians. Patients were identified prospectively by the local study team once a decision was made to proceed to surgery. Children whose indication for surgery was suspected appendicitis were identified subsequently from this CASAP dataset and included in the analysis.

All data were collected prospectively by local clinicians and research staff on a case record form, which was available in paper and online format (see online Supporting Information Appendix S2, p.35). The online case record form included only non-identifiable data; these data were uploaded onto REDCap, a web-based portal, through the study recruitment period. Identifiable data from participants in England and Wales were uploaded by sites to the University College London (UCL) Data Safe Haven, and included: NHS number; sex; date of birth; postcode; and dates of admission, surgery and discharge. Sex was the only patient identifiable dataset variable collected for Scottish patients. The two datasets were linked using the unique CASASP study identification number assigned to each participant. Data were collected either directly from patients or from their patient record and included: patient characteristics; comorbidities; physiological parameters recorded on initial assessment in the hospital where surgery

took place; pathology results; and postoperative care and outcome data. The primary outcome was postoperative morbidity, treated as a binary variable and defined as the occurrence of complications. Complications of interest were those classified as ≥ 2 using the Clavien-Dindo scoring system (see online Supporting Information Appendix S2, p.4). This system was developed for adult surgery but has also been used widely in children as a means of standardising reporting of postoperative complications [10, 11]. Scores are allocated based on the severity of the complication and range from 1 (any deviation from the normal postoperative course not requiring surgical, endoscopic or radiological intervention but allowing for certain therapeutic regimes) to 5 (death of the patient). On postoperative day 30, local investigators conducted a follow up review of the patient if still an inpatient or the medical notes if discharged.

Ethnicity was classified in line with the Office for National Statistics' Census 2021 [12]. Index of multiple deprivation scores, adjusted to allow comparisons between countries in the UK, were identified for each participant in England and Wales using their postcode and presented as quintiles in line with methods published previously [13]. Index of multiple deprivation scores for Scottish patients were identified by local principal investigators using open-source government data [14]. The index of multiple deprivation scores were then sent to the central CASAP team for inclusion in the analysis. Implausible physiological values within the dataset were removed and treated as missing values. Temperature and haemoglobin were categorised into hyperthermic/normal/ hypothermic and high/normal/low, respectively, and heart rate and plasma creatinine levels were categorised similarly and stratified by age (see online Supporting Information Appendix S2, p.2). White cell count and C-reactive protein were not categorised but instead were analysed as continuous variables in their raw form. Histological reports were classified into simple appendicitis; complicated appendicitis; negative; or 'other'. Complicated appendicitis was defined by the presence of a perforated or gangrenous appendix, while simple appendicitis was identified by the presence of an acute inflammatory process in the appendix specimen.

Patients without a documented primary outcome were not analysed. Multiple imputation with chained equations were used to impute missing predictor variables assuming data were missing at random. Variables included in the imputation model were the same as those included in the substantive model. Ten complete datasets were inputed owing to the very low average proportion of missing data for the included variables.

Bivariate analysis was undertaken using the unpaired ttest or and Wilcoxon rank-sum test for parametric data and non-parametric data, respectively. Categorical variables were compared using either the Pearson's χ^2 or Fisher's exact test. The association with postoperative duration of stay was analysed using the Spearman's rank correlation test for continuous or interval variables and Mann-Whitney U test or Kruskal-Wallis test for categorical variables. Multivariable binary logistic regression was performed on each complete dataset and the results pooled. Variables, including potential confounders, to be entered into the multivariable model were identified either because of their bivariate association with outcome or previous clinical knowledge. In addition, a linear regression model was fitted to review the association between the predictor variables and postoperative duration of stay. Associations between risk factors and outcomes are presented as odds ratio (OR) with 95%CI. Subgroup analysis was conducted in patients with a reported histological outcome. Analyses were conducted using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

In total, 3107 children were recruited from 80 study sites across the UK including England, Wales and Scotland, and 2799 children with a pre-operative indication for surgery of suspected appendicitis were identified. There were missing outcome data for 31 children, resulting in 2768 being included in this analysis (Fig. 1 and Table 1). Data completeness, excluding histological diagnosis, was 98%, with no other variable returning more than 6% missing data (see online Supporting Information Appendix S2, p.2).

Histopathology results were available for 2134 (77%) of the children who had surgery for suspected appendicitis. Of these, 1261 (59%) were found to have simple appendicitis and 558 (26%) had complicated appendicitis. Thirty-two (15%) children were found to have alternative pathologies, 11 (34%) of which were a malignancy and 9 (28%) were a Meckel's diverticulum (see online Supporting Information Appendix S2, p.5). Overall, 283 (13%) children had a normal appendix.

One hundred and eighty-five children (7%) developed Clavien-Dindo grade 2 or above complications within 30 days of their procedure. Most complications were infective in nature with surgical site infections reported in 80 (3%) children and lower respiratory tract infections in 6 (< 1%). An additional 23 (1%) children received empirical treatment for infection despite a source not being identified. Eight children (< 1%) developed postoperative bowel obstruction and 53 (2%) required a secondary

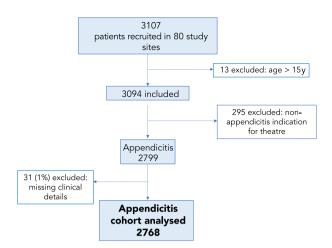


Figure 1 Study flow diagram.

procedure (surgical or radiological) under general anaesthesia. No deaths were reported in this cohort.

Patient COVID-19 status was added to our dataset during the first wave of the pandemic in July 2020, and this information was available for 1855 (67%) of the complete cohort. Thirty-six (2%) children tested positive during their hospital stay (26 pre-operatively and 10 postoperatively) and one of these children developed a complication (Clavien-Dindo grade 2). Bivariate analysis identified significant relationships between: age; ethnicity; ASA physical status; heart rate; temperature; oxygen supplementation; haemoglobin concentration; white cell count; C-reactive protein; creatinine; and postoperative complications (Table 2).

Multivariable analysis was conducted on the complete multiply-imputed datasets and pooled to determine the independent pre-operative risk factors associated with complications (Table 3). Complicated appendicitis and having 'other' histological findings were independently with greater odds of postoperative complications (see online Supporting Information Appendix S2, p.6). However, the pre-operative factors associated with complications remained broadly similar, with similar magnitudes, even when adjusting for the type of appendicitis found on histology. Black ethnicity, ASA physical status, need for oxygen supplementation and raised C-reactive protein remained independent risk factors for complications. Hyperthermia was the only pre-operative variable which was no longer significant on adjusting for histological findings.

On bivariate analysis, factors significantly associated with increased duration of stay were: younger age; sex; ethnicity; index of multiple deprivation score; ASA physical status; heart rate; temperature; haemoglobin

concentration; white cell count; C-reactive protein; and creatinine (Table 4). On multivariable linear regression, the factors most strongly associated with an increased duration of stay were: younger age; greater ASA physical status; complicated appendicitis on histology; and encountering postoperative complications. Additionally, children who were anaemic and presented with an acutely inflamed picture, as evidenced by the presence of tachycardia, pyrexia or an elevated C-reactive protein, also experienced longer hospital stays. Ethnicity was not associated with prolonged hospital stay after adjustment for histological diagnosis and postoperative morbidity, but deprivation was, with those from the lowest quintile remaining in hospital for longer.

Discussion

We report the largest prospective study of children undergoing surgery for suspected appendicitis in the NHS, and two previously unreported findings. First, almost 7% of children in our cohort developed Clavien-Dindo grade 2 or higher postoperative complications. The majority were infective complications treated with antibiotics. Of these, 75% were related to the wound and 25% either respiratory, urinary, line-related or of unknown origin. Second, one of the biggest risk factors associated with postoperative complications was black or 'other' minority ethnicity, with a four-fold increase in the odds of developing complications for black children and a doubling of the odds for those in the 'other' minority group. Other risk factors associated with complications included significant long-term health conditions (indicated by ASA physical status \geq 3), preoperative signs of inflammation and the need for oxygen

Appendicitis remains the most common paediatric surgical emergency with over 10,000 appendicectomies performed in the UK every year [1]. It is recognised to be a significant contributor to paediatric morbidity and has been identified as a potential high yield area for comparative effectiveness research [5]. Postoperative morbidity and extended hospital admissions have broader implications in the paediatric population for whom families can experience significant financial penalties due to the cost of travel, accommodation and the time parents are away from work to be with their children in hospital [15]. Additionally, it is recognised that parental and sibling psychological morbidity can occur due to the stress associated with prolonged hospital stays, even for mild acute illnesses, and that the emotional fallout from these experiences can persist beyond discharge [16, 17].

Table 1 Baseline patient characteristics of children undergoing appendicectomy. Unless otherwise stated, physiological parameters were all recorded at the time of initial assessment. Values are median (IQR [range]), number (proportion) or mean (SD).

	Whole cohort n = 2768	Simple appendicitis n = 1261	Complicated appendicitis n = 558
Age; y	11 (8–13 [2–15])	11 (813 [2–15])	10 (8–13 [2–15])
1–5	216 (8%)	80 (6%)	77 (14%)
6–12	1691 (61%)	799 (63%)	332 (60%)
13–15	861 (31%)	382 (30%)	149 (27%)
Sex; female	1067 (39%)	452 (37%)	215 (39%)
Ethnicity			
White	2308 (84%)	1053 (84%)	472 (85%)
Asian	188 (7%)	81 (7%)	38 (7%)
Black	48 (2%)	16(1%)	12 (2%)
Mixed	69 (3%)	36 (3%)	14(3%)
Other	126 (5%)	65 (5%)	21 (4%)
Index of multiple deprivation quintile			
1 – most deprived	507 (19%)	222 (18%)	116 (21%)
2	520 (19%)	246 (20%)	101 (19%)
3	568 (21%)	244 (20%)	117 (22%)
4	555 (21%)	277 (23%)	102 (19%)
5 – least deprived	537 (20%)	236 (19%)	109 (20%)
ASA physical status			
1–2	2675 (99%)	1221 (99%)	537 (98%)
3–5	33 (1%)	11(1%)	13 (2%)
Comorbidities			
Respiratory	248 (9%)	117 (9%)	41 (7%)
Cognitive/non-neurotypical/developmental	163 (6%)	77 (6%)	37 (7%)
Gastrological	74(3%)	30 (2%)	11 (2%)
Neurological	72 (3%)	29 (2%)	10 (2%)
Cardiac	39(1%)	16(1%)	7 (1%)
Haematological	27 (1%)	12(1%)	6 (1%)
Renal	20(1%)	8 (1%)	2 (< 1%)
Acute respiratory disorder	19 (1%)	10(1%)	5 (1%)
Diabetes mellitus	16(1%)	6 (1%)	4(1%)
Metabolic	13 (1%)	5 (< 1%)	2 (< 1%)
Nutritional support (PEG/NG)	8 (< 1%)	4 (< 1%)	0 (0%)
Malignancy	7 (< 1%)	4 (< 1%)	2 (< 1%)
Heart rate; min ⁻¹	105 (21.6)	104 (20.1)	114 (20.5)
Age-adjusted heart rate categories			
Normal	1779 (65%)	816 (66%)	333 (60%)
Bradycardic	177 (7%)	72 (6%)	13 (2%)
Tachycardic	764 (28%)	344 (28%)	209 (38%)
Temperature; °C	37.1 (0.8)	37.1 (0.8)	37.4(0.9)
Oxygen supplementation on arrival for anaesthesia and surgery	25 (1%)	9 (1%)	3 (1%)
Haemoglobin; g.l ⁻¹	133 (12.2)	133 (12.2)	134(13.1)

(continued)

Table 1 (continued)

	Whole cohort n = 2768	Simple appendicitis n = 1261	Complicated appendicitis n = 558
Haemoglobin categories*			
Low	96 (4%)	43 (4%)	22 (4%)
High	673 (25%)	284 (23%)	156 (29%)
White cell count; 10 ⁹ .l ⁻¹	14 (11–18 [1–65])	15 (11–18 [3–65])	16 (13–20 [1–37])
C-reactive protein; mg.l ⁻¹	38 (9-100 [0-541])	31 (9-80 [0-541])	92 (43–159 [1–473])
Creatinine; µmol.l ⁻¹	48 (14.5)	47 (13.5)	48 (17.3)
Age-adjusted creatinine categories*			
Low	142 (5%)	68 (6%)	37 (7%)
High	176 (7%)	66 (6%)	54 (10%)

^{*}See online Supporting Information, Appendix S2, p.2 for definitions.

This is the first study to show a relationship between ethnicity and poor outcome in children with suspected appendicitis in the UK, where residents have universal health coverage through the NHS. We have also highlighted inter-minority differences in peri-operative risk. Black children experienced far greater odds of developing complications than Asian children. The Asian minority ethnic group is the largest, representing 9% of the population, and is also one of the most diverse, including both south and east Asian ethnicities [12]. Differential risk profiles may exist within this broad category, which when combined may compound or dilute any aggregated outcome.

Disparity in postoperative outcomes for children, dependent on ethnicity, have been reported previously in other healthcare systems, and several contributing factors proposed. However, ours is the first study to demonstrate the relationship between ethnicity and poor outcome in children with suspected appendicitis in the UK. Multiple studies in North America have demonstrated worse outcomes in children undergoing appendicectomy from minority ethnic groups [6, 18]. There is substantial evidence to suggest that black children in the USA have higher rates of complicated appendicitis, and it has been postulated that this may in part be related to delays in diagnoses [6, 19]. The rate of complicated appendicitis was higher in children from a black minority ethnic group in our cohort (25% vs. 20% for white children), but the difference was not significant, potentially representing a type 2 error. However, ethnicity remained an independent risk factor for postoperative morbidity even when adjusting for histological diagnosis.

In keeping with published literature, we also report that adjusting for the impact of socio-economic scores on outcome does not mitigate the increased rates of morbidity

seen in minority ethnic children [6]. Similar findings have also been reported in relation to postoperative mortality in the USA, with children from black minority ethnic groups experiencing significantly higher odds of mortality compared with their white counterparts [20], a relationship which also appears to be independent of socio-economic scores [21]. In adult emergency abdominal surgery conducted within the NHS, the reverse is true. Socioeconomic scores are associated with outcome whereas ethnicity is not [22]. However, the adult cohort is more complex, with multiple different pathologies of different aetiologies, which may lead to diagnostic challenges and contribute to differential outcomes. Children with acute appendicitis constitute a particularly useful cohort in which to review the impact of ethnicity on health and healthcare outcomes, due the homogeneity of the clinical condition all children present with the same suspected pathology. The 'free at the point of delivery' NHS healthcare model should reduce the impact of inequitable access to healthcare which may partly explain differential outcomes in other health systems [23]. However, while access to services may be universally available, the utilisation and delivery of services may still differ. A review of the processes of care is needed to understand whether the quality of care provided is comparable for all.

The timing of this study included the COVID-19 pandemic, and it is conceivable that this may have influenced the results we report. This is true both for children with and without COVID-19, due to lockdowns and the potential for patient or family reluctance to attend hospital with presentation delayed. The impact of COVID-19 on disease severity at presentation is conflicting with the narrative differing between countries [24–27]. Higher rates of complicated appendicitis, possibly due to delays in

Table 2 Frequencies and bivariate associations between pre-operative risk factors and peri-operative complications. Values are median (IQR [range]), number (proportion) or mean (SD).

	No major complications n = 2583	Major complications n = 185	p value
Age; y	11 (8–13 [2–15])	10 (8–13 [2–15])	0.009
1–5	188 (7%)	28 (14%)	< 0.001
6–12	1581 (61%)	110(60%)	
13–15	814 (32%)	47 (25%)	
Sex			
Female	996 (39%)	71 (39%)	0.886
Male	1531 (61%)	113 (61%)	
Ethnicity			
White	2169 (85%)	139 (76%)	< 0.001
Asian/Asian British	172 (7%)	16 (9%)	
Black/African/Caribbean/Black British	38 (2%)	10 (5%)	
Mixed/multiple ethnic groups	63 (3%)	6(3%)	
Other	113 (4%)	13 (7%)	
Index of multiple deprivation quintiles			
1 – most deprived	472 (19%)	35 (20%)	
2	474 (19%)	46 (26%)	0.202
3	532 (21%)	36 (20%)	
4	522 (21%)	33 (18%)	
5 – least deprived	508 (20%)	29 (16%)	
ASA physical status			
1–2	2507 (99%)	168 (95%)	< 0.001
3–5	24(1%)	9 (5%)	
Heart rate; min ⁻¹	104(21.1)	115 (21.5)	< 0.001
Temperature; °C	37.1 (0.8)	37.5 (0.9)	< 0.001
Oxygen supplementation on arrival for anaesthesia and surgery	19 (0.7)	6 (3.2)	0.002
Level of consciousness			
Alert	2455 (99%)	174 (99%)	0.413
Voice	2 (< 1%)	1 (1%)	
Pain	3 (< 1%)	0	
Unresponsive	1 (< 1%)	0	
Haemoglobin categories ⁻¹ *	133 (12.0)	131 (15.0)	0.109
Low	81 (3%)	15 (9%)	0.001
High	630 (25%)	43 (25%)	
White cell count; 10 ⁹ .l ⁻¹	14 (11–18 [1–65])	16 (12–20 [3–36])	< 0.001
C-reactive protein; mg.l ⁻¹	35 (9–93 [0–541])	109 (39–191 [0–434])	< 0.001
Age-adjusted creatinine categories*	46 (39–55 [4–262])	44 (36–56 [14–105])	0.191
Low	127 (5%)	15 (9%)	0.002
High	156 (6%)	20 (12%)	

^{*}See online Supporting Information, Appendix S2, p.2 for definitions.

presentation, have been reported in some populations, but this was not replicated universally. These differences in the severity of appendicitis seen may highlight behavioural differences across cultural sub-groups relating to presentation and healthcare access. This could therefore provide some insight into why we saw different results in children of different ethnic groups. However, we found ethnicity to remain an independent risk factor even when

7

Table 3 Multivariable analysis of pre-operative predictors of postoperative complications. Values are odds ratio (95%CI).

	OR (95%CI)	p value
Age; y		
13–15	-	-
6–12	1.17 (0.79–1.75)	0.432
1–5	1.63 (0.90–2.96)	0.098
Ethnicity		
White	-	-
Asian/Asian British	1.25 (0.70–2.23)	0.459
Black/African/ Caribbean/Black British	4.13 (1.87–9.08)	< 0.001
Mixed/multiple ethnic groups	1.22 (0.49–3.05)	0.663
Other	2.08 (1.12–3.87)	0.021
Sex		
Female	-	-
Male	1.05 (0.75–1.48)	0.760
ASA physical status 1–2		
3–5	4.05 (1.70–9.67)	0.002
Index of multiple deprivation of	quintile	
1 – most deprived	1.05 (0.61–1.80)	0.863
2	1.54 (0.93-2.57)	0.097
3	1.18 (0.70-2.01)	0.530
4	1.11 (0.65–1.91)	0.704
5 – least deprived	-	-
Age-adjusted heart rate catego	ories*	
Normal	-	-
Bradycardic	0.49 (0.17–1.39)	0.182
Tachycardic	1.04 (0.72–1.52)	0.825
Temperature		
Normothermic	-	-
≥ 38 °C	1.77 (1.20–2.63)	0.004
< 36 °C	0.63 (0.18–2.18)	0.469
Oxygen supplementation on arrival for anaesthesia and surgery		
No	-	-
Yes	4.20 (1.44–12.24)	0.009
White cell count 10 ⁹ .l ⁻¹	1.02 (1.00–1.05)	0.091
C-reactive protein mg.l ⁻¹	1.01 (1.00–1.01)	< 0.001
Haemoglobin categories *		
Normal	-	-
Low	1.60 (0.83–3.10)	0.158
High	1.19 (0.79–1.80)	0.407
Age-adjusted creatinine categ	ories **	
Normal	1 47 (0 00 0 74)	0.040
Low	1.47 (0.80–2.71)	0.213
High	1.48 (0.85–2.57)	0.166

^{*}See online Supporting Information, Appendix S2, p.2 for definitions.

the severity of the underlying pathology was adjusted for, thus limiting the impact of this argument. It has also been recognised that care delivery was influenced by the pandemic with a greater use of pre-operative imaging reported and more children being managed conservatively [26, 28]. The negative appendicectomy rate was noted to reduce in the UK during the first wave, but overall we report a negative appendicectomy rate in keeping with historical pre-pandemic data [28].

Our findings highlight that children from minority ethnic groups represent a population for whom we must better understand and address inequity in outcome. The NHS England CORE20PLUS5 initiative, set up to address healthcare inequalities in the UK has recently launched an agenda to focus on the paediatric population [29]. This initiative targets the most deprived 20% of the population in addition to specific inclusion groups who are known to experience poorer access to healthcare, experience and/or outcomes – these include ethnic minority groups. The NHS Race and Health Observatory cites socio-economic deprivation and structural racism both inside and outside healthcare as potential drivers of health inequalities [30]. We did not find deprivation status to be a risk factor for postoperative complications in our cohort. Therefore, we must consider the possibility that structural inequality in society and/or the health service underpins these adverse outcomes for black children. Children of black and Asian ethnicity have higher rates of childhood obesity than white children [31], although this is at least in part thought to be due to deprivation. Small, single-centre studies have reported different findings regarding associations between obesity and outcome after appendicitis surgery in children. [32, 33] Inside healthcare, concerns have been raised about the accuracy of pulse oximetry in patients with darker skin, with studies of adult patients reporting a higher risk of occult hypoxaemia in black individuals than white [34]. In children, in whom accurate pulse oximetry readings may be more difficult to ascertain for multiple reasons, there is the potential for this problem to be exacerbated. In our population, a pre-operative requirement for oxygen therapy was also a predictor of postoperative complications. This and other potential underlying causes of structural inequality require investigation.

Our study has limitations. Although this is the largest prospective study in children undergoing appendicectomy reported from the UK, with participants recruited from across England, Wales and Scotland, females (39%) and children from ethnic minorities (16%) are slightly underrepresented [12]. However, there is evidence to suggest that children from black minority groups present

 Table 4
 Multivariable analysis of independent predictors of prolonged length of stay.

	Regression coefficients	Regression (95%CI)	coefficients	
		Lower	Upper	p value
Age; y				
13–15	-			-
6–12	0.05	-0.27	0.38	0.751
1–5	1.09	0.50	1.69	< 0.001
Ethnicity				
White	-			-
Asian/Asian British	0.48	-0.06	1.02	0.080
Black/African/Caribbean/Black British	0.37	-0.72	1.46	0.508
Mixed/multiple ethnic groups	0.44	-0.38	1.26	0.296
Other	-0.40	-1.03	0.24	0.222
Sex				
Female	-			-
Male	0.18	-0.11	0.47	0.215
ASA physical status				
1–2				
3–5	1.39	0.11	2.68	0.033
Index of multiple deprivation quintile				
1 – most deprived	0.44	0.00	0.87	0.049
2	0.43	0.01	0.85	0.045
3	0.20	-0.22	0.61	0.349
4	0.31	-0.11	0.73	0.142
5 – least deprived	-			-
Age-adjusted heart rate categories*				
Normal	-			-
Bradycardic	-0.05	-0.64	0.54	0.867
Tachycardic	0.38	0.04	0.71	0.028
Temperature				
Normothermic	-			-
≥ 38 °C	0.53	0.12	0.94	0.012
< 36 °C	-0.15	-0.97	0.66	0.710
Oxygen supplementation on arrival for anaesthesia and surgery	-			-
Yes	-0.68	-2.28	0.93	0.409
White cell count 10 ⁹ .l ⁻¹	0.00	-0.02	0.03	0.747
C-reactive protein mg.l ⁻¹	0.01	0.01	0.01	< 0.001
Haemoglobin categories*				
Normal	-			-
Low	0.79	0.05	1.54	0.037
High	0.22	-0.11	0.54	0.188
Age-adjusted creatinine categories*				
Normal	-			-
Low	-0.40	-0.97	0.17	0.172
High	0.16	-0.37	0.70	0.545

(continued)

9

Table 4 (continued)

	Regression coefficients	Regression (95%CI)	coefficients		
		Lower	Upper	p value	
Histology					
Complicated appendicitis	1.09	0.60	1.58	< 0.001	
Simple appendicitis	0.21	-0.21	0.63	0.331	
Other	0.64	-0.50	1.79	0.272	
Complications					
Yes	4.79	4.25	5.33	< 0.001	

^{*}See online Supporting Information, Appendix S2, p.2 for definitions.

less frequently with appendicitis [19]. For practical and pragmatic reasons, we did not study children whose parents were unable to speak or understand English sufficiently to provide informed consent to participate. It is possible that this presents some bias in our cohort and our findings, particularly as this cohort of patients may be vulnerable to poor experiences of healthcare due to marginalisation resulting from difficulties with communication. We did not include weight, height or BMI in our final dataset as a review of data quality after the first 800 patients were recruited indicated that these data were recorded poorly. The study began before the Core Outcome Set for paediatric appendicitis was published [35], and we omitted three of the recommended outcomes from our reporting framework (patient stress/psychological distress, time away from full activity and quality of life). However, a strength is that we have reported the other 11 variables. Finally, we only included children who had surgery and therefore we have not evaluated the outcomes of children who were managed conservatively.

In summary, acute appendicitis is a common condition in children, causing morbidity at scale. In the NHS, black children had a significantly higher risk of postoperative morbidity than other children, even after adjusting for household socio-economic status, acute physiology and long-term health. This health inequality requires urgent further investigation, and development of interventions aimed at resolution.

Acknowledgements

The study was registered with ClinicalTrials.gov (NCT04602429). We thank the Health Services Research Centre at the Royal College of Anaesthetists for supporting this study, including project management support and access to the Quality Audit and Research Coordinator network. We thank all our local investigators (see online

Supporting Information Appendix S1) and the Children's Acute Surgical Abdomen Programme's steering group: M. Peters; S. Courtman; M. Davenport; R. Stewart; S. Walker; and D. Hargreaves. Our project grant was funded by the Association of Paediatric Anaesthetists of Great Britain and Ireland and awarded by the National Institute for Academic Anaesthesia. Additional funding provided by the Royal College of Anaesthetists and the UCL/UCLH Surgical Outcomes Research Centre, supported by the University College London Hospitals (UCLH) National Institute for Health Research (NIHR) Biomedical Research Centre (BRC). SRM is supported by the NIHR Central London Patient Safety Research Collaboration based at UCLH/UCL and the UCLH NIHR BRC. SMPP was funded by a UK Medical Research Council Career Development Award.

References

- Kenny SE. NHS England and NHS Improvement; Getting It Right First Time: Paediatric Surgery GIRFT Programme National Specialty Report. 2021. https://gettingitrightfirsttime.co.uk/wpcontent/uploads/2022/09/PaediatricSurgeryReport-Sept21w. pdf (accessed 06/09/2023).
- Baird DLH, Simillis C, Kontovounisios C, Rasheed S, Tekkis PP. Acute appendicitis. British Medical Journal 2017; 357: j1703.
- Giuliani S, Cecil EV, Apelt N, Sharland M, Saxena S. Pediatric emergency appendectomy and 30-day postoperative outcomes in district general hospitals and specialist pediatric surgical centers in England, April 2001 to march 2012: retrospective cohort study. *Annals of Surgery* 2016; **263**: 184– 90.
- Rice-Townsend S, Barnes JN, Hall M, Baxter JL, Rangel SJ. Variation in practice and resource utilization associated with the diagnosis and management of appendicitis at freestanding children's hospitals: implications for value-based comparative analysis. *Annals of Surgery* 2014; **259**: 1228–34.
- Cameron DB, Graham DA, Milliren CE, et al. Quantifying the burden of interhospital cost variation in pediatric surgery implications for the prioritization of comparative effectiveness research. *Journal of the American Medical Association:* Pediatrics 2017; 171: e163926.
- Zwintscher NP, Steele SR, Martin MJ, Newton CR. The effect of race on outcomes for appendicitis in children: a nationwide analysis. *American Journal of Surgery* 2014; 207: 748–53.

- Cheong LHA, Emil S. Determinants of appendicitis outcomes in Canadian children. Journal of Pediatric Surgery 2014; 49: 777–81
- Omling E, Salö M, Saluja S, et al. Nationwide study of appendicitis in children. *British Journal of Surgery* 2019; 106: 1623–31.
- Benabbas R, Hanna M, Shah J, Sinert R. Diagnostic accuracy of history, physical examination, laboratory tests, and point-ofcare ultrasound for pediatric acute appendicitis in the emergency department: a systematic review and meta-analysis. Academic Emergency Medicine 2017; 24: 523–51.
- Thompson H, Jones C, Pardy C, Kufeji D, Nichols E, Murphy F, Davenport M. Application of the Clavien-Dindo classification to a pediatric surgical network. *Journal of Pediatric Surgery* 2020; 55: 312–5
- Aksenov LI, Granberg CF, Gargollo PC. A systematic review of complications of minimally invasive surgery in the pediatric urological literature. *Journal of Urology* 2020; 203: 1010–5.
- 12. Office for National Statistics. Ethnic group by age and sex, England and Wales: census 2021. https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/ethnicity/articles/ethnicgroupbyageandsexenglandandwales/census 2021#glossary (accessed 02/02/2023).
- Bedford J, Martin P, Crowe S, et al. Development and internal validation of a model for postoperative morbidity in adults undergoing major elective colorectal surgery: the perioperative quality improvement programme (PQIP) colorectal risk model. *Anaesthesia* 2022; 77: 1356–67.
- Scottish Index of Multiple Deprivation 2020. https://simd.scot/ #/simd2020/BTTTFTT/8/-3.9999/55.9000/ (accessed 01/08/ 2023)
- Mumford V, Baysari MT, Kalinin D, Raban MZ, McCullagh C, Karnon J, Westbrook JI. Measuring the financial and productivity burden of paediatric hospitalisation on the wider family network. *Journal of Paediatrics and Child Health* 2018; 54: 987–96
- Wray J, Lee K, Dearmun N, Franck L. Parental anxiety and stress during children's hospitalisation: the StayClose study. *Journal* of Child Health Care 2011; 15: 163–74.
- Commodari E. Children staying in hospital: a research on psychological stress of caregivers. *Italian Journal of Pediatrics* 2010; 36: 40.
- Iantorno SE, Ulugia JG, Kastenberg ZJ, Skarda DE, Bucher BT. Postdischarge racial and ethnic disparities in pediatric appendicitis: a mediation analysis. *Journal of Surgical Research* 2023; 282: 174–82.
- Totapally A, Martinez P, Raszynski A, Alkhoury F, Totapally BR. Do racial/ethnic and economic factors affect the rate of complicated appendicitis in children? Surgery Research and Practice 2020; 2020: 1–9.
- Nafiu OO, Mpody C, Kim SS, Uffman JC, Tobias JD. Race, postoperative complications, and death in apparently healthy children. *Pediatrics* 2020; **146**: e20194113.
- 21. Willer BL, Mpody C, Tobias JD, Nafiu OO. Association of race and family socioeconomic status with pediatric postoperative mortality. *Journal of the American Medical Association:* Network Open 2022; **5**: e222989.
- Poulton TE, Moonesinghe R, Raine R, et al. Socioeconomic deprivation and mortality after emergency laparotomy: an observational epidemiological study. *British Journal of Anaesthesia* 2020; **124**: 73–83.
- 23. Lee SL, Shekherdimian S, Chiu VY, Sydorak RM. Perforated appendicitis in children: equal access to care eliminates racial

- and socioeconomic disparities. *Journal of Pediatric Surgery* 2010: **45**: 1203–7.
- Schäfer FM, Meyer J, Kellnar S, et al. Increased incidence of perforated appendicitis in children during COVID-19 pandemic in a Bavarian multi-center study. Frontiers in Pediatrics 2021; 9: 683607.
- 25. La Pergola E, Sgrò A, Rebosio F, et al. Appendicitis in children in a large Italian COVID-19 pandemic area. *Frontiers in Pediatrics* 2020; **8**: 600320.
- Nassiri AM, Pruden RD, Holan CA, et al. Pediatric appendicitis in the time of the COVID-19 pandemic: a retrospective chart review. *Journal of the American College of Emergency Physicians Open* 2022; 3: e12722.
- 27. Ayyıldız HN, Mirapoglu S, Yıldız ZA, et al. What has changed in children's appendicitis during the COVID-19 pandemic? *Ulusal Travma ve Acil Cerrahi Dergisi* 2022; **28**: 1674–81.
- Bethell GS, Gosling T, Rees CM, Sutcliffe J, Hall NJ. Impact of the COVID-19 pandemic on management and outcomes of children with appendicitis: the Children with Appendicitis during the CoronAvirus panDEmic (CASCADE) study. *Journal* of Pediatric Surgery 2022; 57: 380–5.
- 29. NHS England. Core20PLUS5 An approach to reducing health inequalities for children and young people. https://www.england.nhs.uk/about/equality/equality-hub/national-health care-inequalities-improvement-programme/core20plus5/core 20plus5-cyp/ (accessed 21/05/2023).
- The King's Fund. Ethnic health inequalities and the NHS driving progress in a changing system. 2021. https://www.nhsrho. org/wp-content/uploads/2023/05/Ethnic-Health-Inequalities-Kings-Fund-Report.pdf (accessed 06/09/2023).
- The King's Fund. The health of people from ethnic minority groups in England. 2021. https://www.kingsfund.org.uk/ publications/health-people-ethnic-minority-groups-england# Materna (accessed 04/05/2023).
- Timmerman MEW, Groen H, Heineman E, Broens PMA. The influence of underweight and obesity on the diagnosis and treatment of appendicitis in children. *International Journal of Colorectal Disease* 2016; 31: 1467–73.
- 33. Lorio E, Ballard DH, Guarisco E, Hughes J, Griffen FD, Samra NS. Appendectomy hospital stay: no difference in obese adult or pediatric patient length of stay compared to nonobese patients. *Ochsner Journal* 2021; **21**: 14–8.
- Bangash MN, Hodson J, Evison F, et al. Impact of ethnicity on the accuracy of measurements of oxygen saturations: a retrospective observational cohort study. eClinicalMedicine 2022; 48: 101428.
- Knaapen M, Hall NJ, Moulin D, et al. International core outcome set for acute simple appendicitis in children: results of a systematic review, Delphi study, and focus croups with young people. *Annals of Surgery* 2022; 276: 1047–55.

Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. CASAP Investigator list.

Appendix S2. Missing data, protocols, definitions and further analyses.