

## Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK

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1 **Intensive Care Admissions Of Children With Paediatric Inflammatory Multi-system Syndrome**  
2 **Temporally Associated with SARS-CoV-2 Pandemic (PIMS-TS) In The United Kingdom**

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34 The corresponding author confirms that he had full access to all the data in the study and has final responsibility  
35 for the decision to submit for publication

36

1 **Research in context**

2 **Evidence before this study**

3 Recent reports of a novel inflammatory syndrome in children resembling Kawasaki disease and toxic shock  
4 syndrome from many parts of the world represent an important and poorly understood aspect of the evolving  
5 pandemic. An initial case definition has been published for this syndrome, called Paediatric Inflammatory  
6 Multi-system Syndrome temporally associated with SARS-CoV-2 (PIMS-TS), in the United Kingdom.

7 We searched PubMed up to 18 June, 2020, without date limits or language restrictions, with different  
8 combinations of the search terms “paediatric inflammatory multi-system syndrome”, “multisystem  
9 inflammatory syndrome in children”, “atypical Kawasaki”, “inflammatory syndrome”, “intensive care units,  
10 “critical care” OR “critical illness” OR “intensive care”, “ICU” OR “PICU”.

11 Published reports of PIMS-TS cases so far represent single-centre case series and convenience samples,  
12 precluding a detailed analysis of clinical presentations and outcomes, especially in the sickest subset of children  
13 requiring critical care.

14 **Added value of this study**

15 This is the largest cohort of critically ill children with PIMS-TS reported so far, the first nationwide report, and  
16 the first to describe longitudinal data.

17 Coronary artery abnormalities were seen in one third of cases. Comparison with historical data indicate at least a  
18 ten-fold increase in intensive care admissions for children with an inflammatory syndrome during a six-week  
19 period in April/May 2020.

20 **Implications of all the available evidence**

21 There are small but important numbers of children requiring critical care admission for an unexplained  
22 multisystem inflammatory syndrome that may be associated with the COVID-19 pandemic.

23 Uncertainties regarding the underlying basis of this syndrome and lack of evidence regarding optimal treatments  
24 and follow up have led to considerable variation in clinical management.

25 Urgent efforts to recruit patients to robust clinical trials of potential treatments to reduce longer term morbidity  
26 (eg coronary artery aneurysm formation and evolution) are needed to inform clinical practice.

27

28

1 **Abstract**

2 **Background**

3 Clinicians observed a cluster of children with unexplained inflammation requiring admission to United  
4 Kingdom (UK) paediatric intensive care units (PICU) in April 2020. We aimed to describe the clinical  
5 characteristics, course, management and outcomes of intensive care patients with this condition, now known as  
6 Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS).

7 **Methods**

8 Multicentre observational study of children (<18 years), admitted to UK PICUs between 1 April and 10 May  
9 2020, fulfilling the case definition of PIMS-TS. Routinely collected, deidentified data was analysed. PICU  
10 admission rates of PIMS-TS were compared with historical trends of PICU admissions for other inflammatory  
11 conditions.

12 **Findings**

13 78 children with PIMS-TS were reported by 21/23 UK PICUs. Historical data for similar inflammatory  
14 conditions showed a mean of 1 (95% CI 0·85-1·22) admissions/week, compared to a peak of 32/week for PIMS-  
15 TS. Median age was 11 (IQR 8-14) years. Males (52, 67%) and ethnic minorities (61, 78%) were over-  
16 represented. Fever (78, 100%), shock (68, 87%), abdominal pain (48, 62%), vomiting (49, 63%) and diarrhoea  
17 (50, 64%) were common. Longitudinal data over the first 4 days of admission showed serial reduction in CRP,  
18 D-Dimer, and Ferritin, while lymphocyte count increased to  $>1\cdot0 \times 10^9/L$  by day 3 and troponin increased over  
19 the four days. 36 (46%) were invasively ventilated and 65 (83%) needed vasoactive infusions; 57 (73%)  
20 received steroids, 59 (76%) intravenous immunoglobulin, and 17 (22%) biologic therapies. 28 (36%) had  
21 evidence of coronary artery abnormalities (18 aneurysms, 10 echogenicity). Three children needed  
22 Extracorporeal Membrane Oxygenation, and two children died.

23 **Interpretation**

24 During this study period, rate of PICU admission with PIMS-TS was 11-fold higher than historical trends of  
25 similar inflammatory conditions. Clinical presentations and treatments varied. Coronary artery aneurysms are an  
26 important complication. Although immediate survival is high, the long term outcomes of PIMS-TS are  
27 unknown.

28 **Funding**

29 None

## 1 **Introduction**

2 The coronavirus disease 2019 (COVID-19) pandemic caused by Severe Acute Respiratory Syndrome  
3 Coronavirus 2 (SARS-CoV-2) has been associated with nearly 4.5 million infections and over 300,000 deaths  
4 worldwide by the 15th May 2020<sup>1</sup>. While approximately 3-5% of infected adults need critical care admission<sup>2,3</sup>,  
5 children appear to be relatively spared both in frequency and severity of illness<sup>4-7</sup>. Data published so far indicate  
6 that the main reason for intensive care admission in children with COVID-19, similar to adults, has been  
7 respiratory disease, particularly in children with co-morbidities<sup>8</sup>.

8 Over the second half of April 2020, a cluster of children presenting to Paediatric Intensive Care Units (PICUs)  
9 in the United Kingdom (UK) with an unexplained multi-system inflammatory syndrome triggered an alert by  
10 NHS England and the UK Paediatric Intensive Care Society<sup>9</sup>. Children with this illness appeared to have  
11 overlapping features of Kawasaki disease (KD), Toxic Shock Syndrome (TSS) and Haemophagocytic  
12 Lymphohistiocytosis (HLH)/Macrophage activation syndrome (MAS)<sup>10</sup>. Since then, similar cases have been  
13 reported from the United States<sup>11</sup> as well as Europe<sup>12</sup>, with reports in the lay media<sup>13</sup>. On 1<sup>st</sup> May 2020, the  
14 Royal College of Paediatrics and Child Health (RCPCH) published a case definition and guidance related to this  
15 multi-system illness<sup>10</sup>, defining it as a child presenting with persistent fever, inflammation, and evidence of  
16 single or multi-organ dysfunction, with exclusion of any other microbial cause, with or without polymerase  
17 chain reaction (PCR) evidence of SARS-CoV-2. In the UK this has become known as Paediatric Inflammatory  
18 Multi-system Syndrome Temporally Associated with SARS-CoV-2 Pandemic (PIMS-TS), and in the United  
19 States with a more restrictive case definition as Multisystem Inflammatory Syndrome in Children (MIS-C)<sup>11</sup>.  
20 Details regarding some PIMS-TS cases have been recently published from the UK and Italy. The majority of  
21 children had a negative PCR test for SARS-CoV-2 antigen, but had evidence of antibodies, indicating past  
22 infection<sup>14,15,16</sup>. Some of the patients reported in these cohorts were cared for in intensive care and are therefore  
23 included in this paper, although previous reports have either been from single centres or convenience samples,  
24 and have not detailed longitudinal data to assist in better understanding the trajectory and outcome of this  
25 condition..

26 The fact that PIMS-TS has overlapping features with KD, TSS, and HLH/MAS has triggered debate as to  
27 whether this is a new condition, or whether it is an unusual, more severe variant of these previously well-known  
28 conditions requiring critical care management<sup>17</sup>. Comparison with previous admission rates of inflammatory  
29 syndromes to critical care is important to ensure that this condition does not reflect an inadvertent reanalysis of  
30 the background rate of an already known pathology. Improved knowledge of the clinical course in the subset of  
31 children with PIMS-TS needing PICU admission is important to raise awareness and to identify significant areas  
32 of variation in current clinical management. In this report, we aimed to describe the clinical characteristics,  
33 treatments and outcomes of a cohort of children admitted to UK PICUs with PIMS-TS over a 40-day period in  
34 April/May 2020.

35

## 36 **Methods**

37 Study design and participants:

38 This is a multi-centre observational study of children less than 18 years of age, admitted to UK PICUs over a  
39 40-day period (1st April 2020 to 10th May 2020), who fulfilled the case definition of PIMS-TS<sup>10</sup>, and the first  
40 national report of these patients. The project was classified as a service evaluation by the Nottingham Research  
41 and Innovation team (Nottingham Clinical Effectiveness Team ref: 20-235C), and ethics approval was not  
42 required. The study team analysed routinely collected de-identified data submitted by clinicians from the  
43 individual PICUs as a local service evaluation. Clinicians obtained informed parental consent if required locally.  
44 Data were submitted for central analysis using a secure, web-based survey tool (SurveyMonkey, USA) and  
45 included demographic details, presenting clinical features, underlying co-morbidities, laboratory markers,  
46 echocardiographic findings, interventions, treatments, and outcome (survival to PICU discharge, length of PICU  
47 stay). Serology information was collected if available.

1 We classified co-morbidities as minor if primary care management would ordinarily be sufficient (eg mild  
2 asthma), and major if hospital-based management would ordinarily be required (eg sickle cell disease). Ethnicity  
3 was described using UK Government standard groups and compared with reported population rates<sup>18</sup>. We  
4 calculated the ratio of observed weight to expected weight (based on the 50th centile weight for age and sex).  
5 Characterisation of shock into vasodilated or vasoconstricted shock was based on treating clinician's judgement.  
6 There were no interventions as part of this study. Investigations and patient management were as per the  
7 discretion of the relevant responsible medical teams. All patients had SARS-CoV-2 antigen tests performed by  
8 reverse transcriptase polymerase chain reaction (PCR). Serology for SARS-CoV-2 was performed where  
9 available.

10 The Paediatric Intensive Care Audit Network (PICANet) dataset contains prospectively collected patient  
11 diagnoses for patients admitted to PICUs in the UK. Anonymised summary data were provided for a five-year  
12 period (1 Jan 2015 to 31 Dec 2019) for all patients admitted to all 23 UK PICUs with a primary diagnosis of  
13 four similar inflammatory conditions (KD, TSS, HLH and MAS)<sup>19</sup>. The database was searched for Read(CTV3)  
14 codes Y70QV, XUauZ, G7510, A3Ayl, X70Il, X20E8, XUwry, X20E7, and XUgRm. PICANet report all  
15 incidences below 5 as "<5".

## 16 17 Statistical Analysis

18  
19 Results are presented as numbers and proportions for categorical data and medians and inter-quartile range for  
20 continuous data. Data analyses were performed using Microsoft Excel (Microsoft Corporation, USA).

21 Role of the funding source:

22 This study was unfunded. The corresponding author had full access to all of the data and the final responsibility  
23 to submit for publication.

## 24 Results

25 During the study period, data on 78 patients admitted to PICUs and meeting case definition for PIMS-TS were  
26 submitted. Initial presenting features of 29 of these patients have been reported in a recent paper focusing on the  
27 definition of this novel condition (8 of whom had previously been reported in correspondence)<sup>14,16</sup>. Cardiac and  
28 renal features in 6 and 23 patients respectively have also been presented in single centre reports<sup>20,21</sup>. Detailed  
29 presentation, intensive care course, evolution in treatment over time, and longitudinal laboratory data in a  
30 national cohort have not been published previously. Of the 23 National Health Service (NHS) Hospital Trusts  
31 with PICUs in the UK, 15 submitted PIMS-TS patient data (median per unit 3, range 1-24), 4 reported zero  
32 patients and 2 were not admitting any children during the study period (having been converted to adult ICUs  
33 during the COVID-19 surge). The two closed units were cardiac units, and their paediatric patients were  
34 admitted to neighbouring PICUs. Two PICUs did not share data. The total number of PICU admissions of  
35 PIMS-TS cases by week (and cumulative number of admissions) are shown in Figure 1. The cumulative  
36 expected number of admissions derived from historical UK PICANet data with similar inflammatory conditions  
37 requiring PICU admission is also shown, demonstrating an increase of cases above the expected from the week  
38 beginning 20th April.

39 Patient characteristics are shown in Table 1. The median age was 11 (IQR 8-14) years, and two thirds of the  
40 patients (52/78, 67%) were male. Only two patients had major co-morbidities, with 61/78 (78%) having none.  
41 Afro-Caribbean and Asian ethnicities were over-represented in this cohort. The proportion of children aged 10-  
42 14 from an Asian background is 6.9%, and Afro-Caribbean 7.8% in the UK<sup>18</sup>, in contrast to 22/78 (28%) and  
43 37/78 (47%) of the patients in this cohort respectively. The observed percentages are well outwith the 95%  
44 confidence intervals. 3 patients had co-infections, 1 viral and two bacterial. None were judged to be clinically  
45 causative.

46 Shock (68/78, 87%), usually vasodilated, (55/78, 71%), abdominal pain (48/78, 62%), diarrhoea (50/78, 64%)  
47 and vomiting (49/78, 63%) were common presenting features. 70/78 (90%) of patients presented with at least  
48 one abdominal symptom. Rash (35/78, 45%), and conjunctivitis (23/78, 29%) were also seen. Of those tested for

1 SARS-CoV-2 IgG serology, 33/35 were positive, and one of the two negative serology patients was PCR  
2 positive. All MIS-C criteria were definitely met in 45/78 (58%), Details are shown in supplementary table 1.

3 Longitudinal data on the first four days of admission are presented in Table 2. Data was available for all 78  
4 patients for day 1, and for 46 patients throughout the first four days. Only data of patients still on intensive care  
5 are displayed. Patients presented with elevated CRP (median [IQR]: 264 [192-316] mg/L) and ferritin (1042  
6 [538-1746] µg/L), and lymphopaenia (median [IQR]: 0.70 [0.42-1.1]  $\times 10^9/L$ ). Longitudinal data over the first  
7 four days of admission showed a reduction in CRP, D-Dimer, and Ferritin. Neutrophil count was static, and  
8 Creatinine and ALT remained normal. Lymphocyte count increased and the median rose above  $1.0 \times 10^9$  by day  
9 3. Troponin increased over the four days.

10 Historical data on the incidence of PICU admission for the four similar inflammatory conditions (KD, TSS, and  
11 HLH/ MAS) between 2015 and 2019 showed that the average number of admissions to all UK PICUs combined  
12 with the four inflammatory conditions was 1 admission per week (95% confidence interval: [0.8-1.22]), with an  
13 annual total number of admissions ranging from 44 to 67. Toxic Shock Syndrome (119) and Haemophagocytic  
14 Lymphohistiocytosis/ Macrophage Activation Syndrome (114) had the highest number of total national  
15 admissions over the five years, with Kawasaki's Syndrome less common (between 30-40 in total, exact numbers  
16 not available due to small numbers as detailed above). Full details are in Supplemental table 2. During the  
17 study, the average number of weekly admissions to UK PICUs with PIMS-TS was 14 (at least 11.2 times greater  
18 than expected for similar conditions), peaking at 32 (at least a 26-fold increase).

19 Critical care interventions, treatments and outcomes are shown in Table 3. Overall, 36/78 (46%) children were  
20 invasively ventilated, and 3/78 (3.8%) required Extracorporeal Membrane Oxygenation (ECMO). A variety of  
21 therapies were given, with 59/78 (76%) receiving intravenous immunoglobulin and 57/78 (73%) steroids. 17/78  
22 (22%) received biologic immunomodulation agents (8 Anakinra, 7 Infliximab, 3 Tocilizumab, 1 Rituximab).  
23 Two patients received two biologics. Only one child was treated with antiviral therapy (Remdesivir). Treatments  
24 were varied and inconsistent, however over the study period, the percentage of patients being given each therapy  
25 increased over time (Figure 2). The percentage of patient on vasoactive infusions remained constant (between  
26 81 and 84% in weeks 3-6), however the proportion of patients invasively ventilated dropped from 5/6 (83%)  
27 (week 3) to 2/17 (12%) by week 6. Three (3.8%) patients had significant thrombi, with no pulmonary emboli.  
28 Seven (9.0%) patients received therapeutic anticoagulation, either due to thrombi or due to concerns regarding  
29 diffuse microthrombi.

30 One third (28/78, 36%) of patients were found to have coronary artery abnormalities on echocardiography  
31 during PICU admission. 18 had evidence of aneurysms, and 10 had coronaries which were characterised as  
32 unusually echogenic. They were no obvious differences between the demographics, presenting features, or level  
33 of invasive therapies between those with any coronary artery abnormality and those with normal coronaries, or  
34 those who were invasively ventilated or not invasively ventilated (Table 4). Similarly, no clear differences were  
35 found between those patients invasively ventilated and those not invasively ventilated.

36

## 37 **Discussion**

38 Our report describes the characteristics and outcomes of the largest cohort of PICU admissions to date with the  
39 newly described unexplained multi-system inflammatory syndrome named PIMS-TS in the UK. This report is  
40 the first to describe a national cohort, give full details of the presentation, clinical course on intensive care, and  
41 treatments, as well as demonstrate longitudinal laboratory results.

42 We found that the number of UK PICU admissions with PIMS-TS during a 40-day study period in 2020  
43 (following the surge of COVID-19 infections in the UK) significantly exceeded the historical numbers of  
44 admissions of four inflammatory conditions with overlapping clinical features. These patients were critically  
45 unwell with multi-system disease. Although this increase in the number of patients was unexpected, it is still a  
46 small proportion of the usual expected national 250 unplanned paediatric intensive care admissions per week<sup>19</sup>.

1 As of the 10<sup>th</sup> May, around 220,000 people in the UK had tested positive for SARS-CoV-2. Previous data has  
2 shown a paediatric infection rate of around 2% of the total, which would equate to 5,000 children infected. This  
3 means that PIMS-TS would have an incidence of 1.5%.

4 The emergence of this condition in children may have social impact also. Children have been thought of as at  
5 negligible risk from Covid-19 until now: even though the risk is still low, there are implications for health care  
6 resources and balancing the need for adult and paediatric intensive care units. Our data also has significant  
7 implications for any future peaks of PIMS-TS, especially if this coincides with a winter surge of other viral  
8 infections.

9 Viral sepsis with SARS-CoV-2 has been well described in adults<sup>22</sup>. Such patients meet clinical criteria for  
10 shock, are generally SARS CoV-2 positive on PCR from respiratory secretions and have predominantly  
11 pulmonary, renal, hepatic, and cardiac involvement. Coagulopathy is a feature in adults. In comparison,  
12 although D-Dimers are high in PIMS-TS patients, other coagulation tests were usually normal. The notable  
13 absence of severe pulmonary and renal symptoms in PIMS-TS is a further differentiation between the  
14 presentations.

15 In children, although the four inflammatory conditions (KD, TSS, and HLH/MAS) are well known, they cause  
16 illnesses which rarely require PICU admission<sup>19,23</sup>. The presenting features of these four conditions partially  
17 overlap with the presenting features of PIMS-TS; however, none of them were fully consistent with the clinical  
18 presentation and natural history seen in our report. Although the case definition for PIMS-TS is broad, there are  
19 some definitive blood markers which were largely shared by the cohort. We used the published case definition,  
20 which may include some cases which would previously have been diagnosed with one of KD, TSS, or  
21 HLH/MAS. Kawasaki disease has been known to have some seasonality<sup>24</sup>, with peaks in presentation up to 2.5  
22 times the background expected rate, including a known association with other coronavirus infections<sup>25</sup>; this is  
23 unlikely to account for the fluctuation seen in this study. Kawasaki shock syndrome shares the main features of  
24 the clinical presentations detailed in this report including shock; however, the younger age, longer duration of  
25 fever, more consistent mucosal involvement and a lack of abdominal symptoms, distinguish it from PIMS-TS<sup>26</sup>

26 A few days following our study end date, the US Centers for Disease Control and Prevention (CDC) published a  
27 more restrictive case definition for MIS-C, which required evidence of COVID-19 exposure within the 4 weeks  
28 prior to the onset of symptoms. Only one patient who met the PIMS-TS definition would definitely not have met  
29 the MIS-C criteria. It was unclear in 32/78 (41%) of our patients whether they met the stricter MIS-C definition  
30 because at the time of presentation many UK hospitals were not offering SARS-CoV-2 serology. Both criteria  
31 were met in 45/78 (58%) of patients. Emerging evidence that there are asymptomatic carriers of SARS-CoV-2  
32 also suggests that cases may have unknowingly been in contact with SARS-CoV-2<sup>27</sup>. It is unclear whether the  
33 CDC definition is more sensitive or specific than the RCPCH definition in identifying true cases. Comparison  
34 between those who met the CDC criteria, and those in whom it was unclear, did not show any clear differences.

35 There are several clinical implications of our findings. First, the notable absence of significant respiratory  
36 involvement, the low incidence of positive SARS-CoV-2 PCR tests and the presence of SARS-CoV-2  
37 antibodies in 24/25 (96%) patients who were tested following a negative SARS-CoV-2 PCR indicates that  
38 PIMS-TS might represent a post-COVID-19 immunological disease that is clinically distinct from acute  
39 COVID-19 infection in children. The low numbers of patients tested for antibody serology was due to  
40 unavailability of the test in those units at that time. Therefore, the value of antivirals in these cases is unclear.  
41 Only one patient was treated with Remdesivir, who was positive on PCR for SARS-CoV2. Second, the  
42 heterogeneity in clinical presentation seen with PIMS-TS, and variable overlap with previously described  
43 entities such as atypical KD, TSS or HLH/MAS, meant that there was significant variation in the range of  
44 immunomodulatory treatments were offered to these children. There is currently no evidence as to which  
45 treatments are beneficial, highlighting the need for urgent robust clinical trials, such as the RECOVERY trial,  
46 which aims to include PIMS-TS patients<sup>28</sup>. Third, the frequency and extent of multi-system involvement  
47 indicates that a multi-disciplinary team approach (general paediatrics, infectious diseases, cardiology, intensive  
48 care, haematology, immunology, pharmacy, and rheumatology) is very important for managing these patients.  
49 Finally, the lack of long-term follow-up data on these children means that it is difficult to anticipate and plan for



1 their community health care and surveillance needs following recovery. It is unknown whether these patients  
2 may have long term health problems, particularly those with echocardiographic abnormalities of their coronary  
3 arteries. We did not identify any differences in the clinical presentation or laboratory data to indicate potential  
4 prognostic factors for coronary artery abnormalities prediction.

5 There were higher than expected numbers of children with Asian and Afro-Caribbean ethnicities. This is  
6 consistent with the higher rates of adult patients from ethnic minority backgrounds seen with severe clinical  
7 presentations of COVID-19 disease<sup>29</sup>, but higher than expected from previous paediatric intensive care data<sup>30</sup>. A  
8 link between ethnicity, incidence and outcomes is increasingly recognised in the UK<sup>29,31</sup>. The causes behind this  
9 are not clear, however socioeconomic factors, co-morbidities, and differences in the expression of angiotensin  
10 converting enzyme 2 have been implicated<sup>29</sup>. We have used UK data as our comparison denominator in our  
11 study: there are regional differences in ethnic group prevalence; however, the pandemic has affected all regions  
12 of the UK and the regional differences in PIMS-TS incidence may be linked to this.

13 In our study there was a higher proportion of males (67%), in contrast to a recent cross-sectional study of  
14 COVID-19 positive children admitted to 46 North American PICUs, in which 52% of patients were male<sup>9</sup>, but  
15 similar to the experience in adult intensive care<sup>31</sup>.

16 The strengths of our study include the multi-centre data coverage (data was submitted by the vast majority of  
17 PICUs in the UK) and depth of clinical detail captured. Comparison with reliable, historical data from PICANet  
18 allowed us to demonstrate a step-change in the need for PICU admission for inflammatory conditions during the  
19 COVID-19 pandemic. The main limitation is the retrospective nature of data collection; however, given the  
20 relatively short study period, the time interval between PICU admission and data collection was minimal. We  
21 are unable to offer any conclusions regarding the immunological basis behind PIMS-TS, or provide long-term  
22 data on these patients, although our study was not designed to do so. We used PICANet data as the denominator  
23 as it has a robust mechanism to obtain national critical care related information and is audited to ensure  
24 consistency. It was not possible to ensure 100% case ascertainment and therefore the numbers may be an under-  
25 estimate of PICU admissions. The selection of conditions covered by the PICANet search may not have covered  
26 all inflammatory conditions, and it is likely that a small number of patients with undiagnosed multi-system  
27 inflammatory illnesses were not included in our PICANet search. Moreover it is likely that a large population of  
28 patients affected did not need critical care admission and we may be underestimating the true incidence of  
29 PIMS-TS in the hospital population. Recently launched national initiatives (PICANet and British Paediatric  
30 Surveillance Unit<sup>32</sup>) to study this condition will gather ongoing data. It is unlikely that clinical practice was  
31 influenced by the RCPCH alert, as 51/78 patients predated the alert. The true incidence of coronary artery  
32 aneurysms and other complications will become clearer with longer term follow-up data. We did not capture the  
33 rationale for specific therapies used. Additional therapies that may have been provided after discharge from  
34 PICU may not have been captured.

35 We were unable to find clear correlations between presenting features, laboratory tests, and treatments, with the  
36 risk of having coronary artery abnormalities or being invasively ventilated. This has implications for those  
37 patients not unwell enough to need to come to the intensive care unit. We advise caution and close follow up for  
38 all PIMS-TS patients.

39

## 40 **Conclusion**

41 In this large cohort of children requiring critical care admission for the novel inflammatory condition known as  
42 PIMS-TS, we saw significant short-term morbidity in terms of the need for critical care interventions, but  
43 mortality was low. Nearly a third of patients had coronary artery abnormalities, although the long-term  
44 outcomes for these findings are unclear. While an increasing proportion of patients received immunomodulatory  
45 therapies, there is, as yet, no evidence to support any specific treatment, and supportive intensive care remains  
46 important. Further evidence from clinical trials and long term follow up studies is crucial to inform clinical  
47 practice.

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## Conflict of Interest Statement

All authors have completed the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest, and have no conflicts of interest to disclose.

## Data sharing statement

Requests for data sharing to the corresponding author.

## Contribution statement

1 Literature Search

2 Figures

3 Study Design

4 Data Collection

5 Data Analysis

6 Data interpretation

7 Writing

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1 Figure 1: PIMS-TS admissions per week to UK Paediatric Intensive Care Units 1<sup>st</sup> April to 10<sup>th</sup> May 2020, with  
2 the cumulative total, and the expected UK cumulative total of similar conditions (Kawasaki's disease, Toxic  
3 Shock Syndrome, and Haemophagocytic Lymphohistiocytosis/Macrophage activation syndrome from the  
4 previous 5 years.

5 Table 1: Demographics and clinical features of PICU admission for 78 PIMS-TS patients presenting to UK  
6 Paediatric Intensive Care Units.

7 Table 2: Laboratory results for the first 4 days of PICU admission: median [interquartile range]Table 3:  
8 Interventions on PIMS-TS patients on the intensive care unit

9 Figure 2: Number of patients with PIMS-TS admitted to UK Paediatric Intensive Care units, and percentage  
10 receiving individual treatments over time. Weeks with <3 patients were excluded. IVIG: Intravenous  
11 Immunoglobulins. Biologic: any of Anakinra, Infliximab, Tocilizumab, Retiximab.

12 Table 4: Comparison between the demographics, highest or lowest laboratory tests over the first four days of  
13 admission, presenting features, and therapies of those patients with any coronary artery abnormalities  
14 (aneurysms or echogenicity) and those with normal coronary arteries, and between those not invasively  
15 ventilated and those invasively ventilated.

16 Supplementary table 1: Comparison between those patients meeting US CDC MIS-C definition, and those who  
17 may not have met US CDC MIS-C definition

18 Supplementary table 2:  
19 UK PICU admissions per year for inflammatory conditions 2015-2019, from submissions to PICANet.  
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