PICANet report on SARS-CoV-2 related illness in children admitted to paediatric intensive care

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Introduction

COVID-19 is an infectious disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus. SARS-CoV-2 infection has been linked with a multisystem inflammatory illness in children. This is commonly referred to as paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).

Children described in this report may have presented with:

1) COVID-19 i.e., confirmed SARS-CoV-2 infection without PIMS-TS, which may or may not have been symptomatic/the reason for admission); or

2i) PIMS-TS patients with a positive SARS-CoV-2 polymerase chain reaction (PCR) result); or

2ii) PIMS-TS only (SARS-CoV-2 PCR negative regardless of antibody test results).

1. Data collection

This report presents data on children treated in a paediatric intensive care unit (PICU) in the United Kingdom (UK) or Republic of Ireland (ROI) between **14th March 2020 and 31st January 2022**. These include 1.) Patients with SARS-CoV-2 PCR positive and 2.) Patients with reported PIMS-TS (with or without confirmed SARS-CoV-2 by PCR).

i. Children with confirmed SARS-CoV-2 infection (via polymerase chain reaction (PCR))

These children **may not primarily be in PICU because of COVID-19** but all tested positive to **SARS-CoV-2** either prior to or during their PICU admission. This group **does not include PIMS-TS** as they are reported separately.

This includes:

1. **Patients with COVID-19** (as described above) where this is the **main reason for PICU admission**. This is typically an unplanned admission with infection or respiratory primary diagnosis.
2. Children that are **asymptomatic, i.e.** no symptoms throughout PICU admission. COVID-19 is not the main reason for PICU admission. COVID-19 was detected on screening only and the child was admitted to PICU for reasons that were **unrelated to the SARS-CoV-2**.
3. Children that are **symptomatic** but **this was not the main reason for PICU admission**. Symptoms were potentially of minimal severity, but the infection was not the main reason for PICU admission. For example, where long-stay patients tested positive for SARS-CoV-2 at some point during their PICU stay and were treated, but it was part of the course of a different condition, which needed PICU admission. On its own COVID-19 may not have needed PICU, if the other different condition causing long-stay admission was not present for example. This could have occurred in other short stay admissions also.

ii. Children with recorded PIMS-TS

Children presenting with **PIMS-TS** (both **with and without** a positive SARS-CoV-2 result).

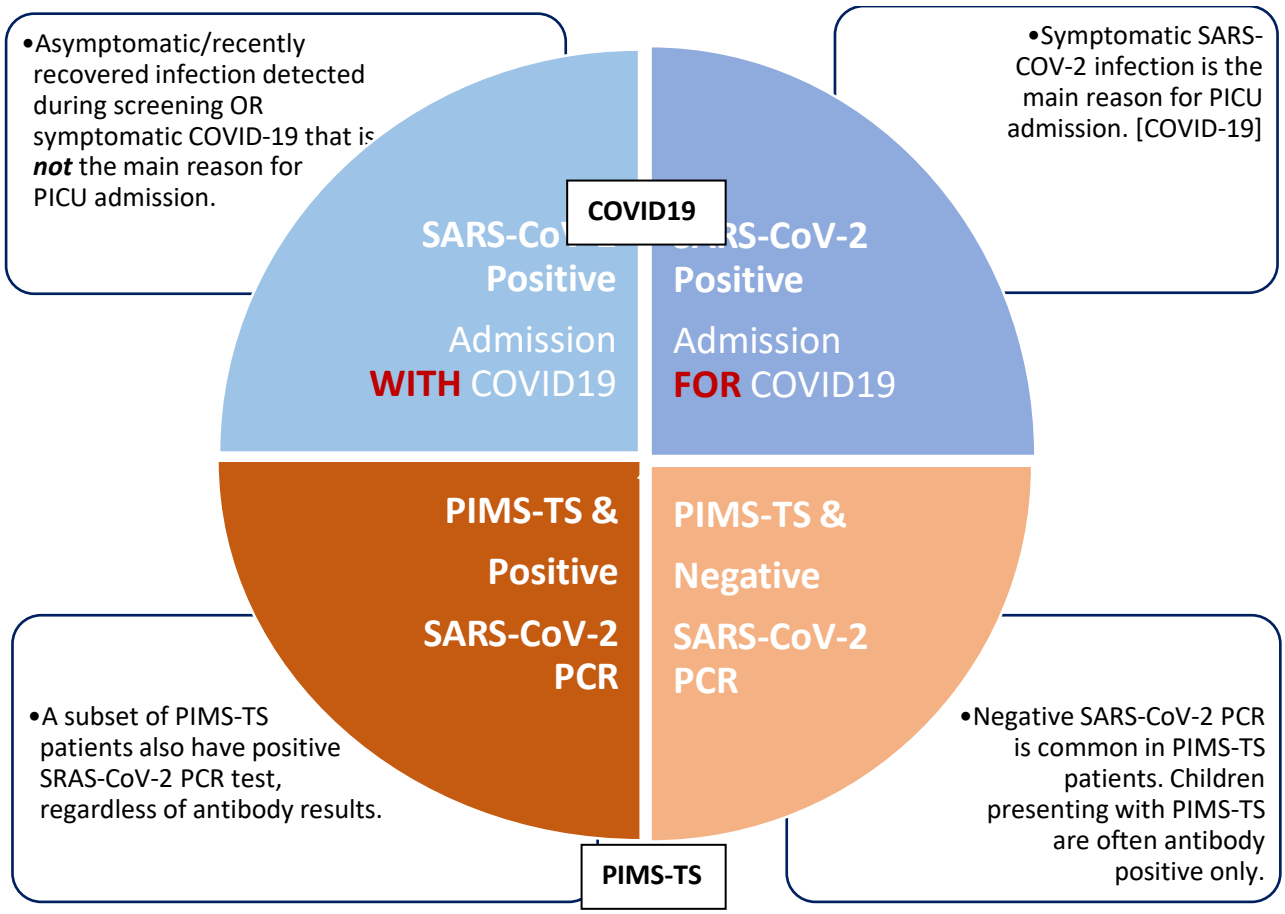

Figure 1. Patterns of SARS-CoV-2 PCR test result and clinical presentations of children presented in this report.

1.1 Pandemic waves

We present data according to waves of the COVID-19 pandemic. Children in the COVID-19 group (without PIMS-TS) were categorised into one of four waves based on the date of the first positive confirmation of SARS-CoV-2 via PCR:

1. Other (14st March 2020 – 31st December 2020)
2. Alpha (1st January 2021 – 16th May 2021) (Variant B.1.1.7)
3. Delta (17th May 2021 – 12th December 2021) - includes 'Other Delta' and 'Delta' (AY.4.2/AY.4.2.x)
4. Omicron (13th December 2021 – 31st January 2022) (Variant BA.1/BA.1.x and BA.2))

These dates were used to define waves for the whole of the UK for the analyses in Section 2.

For instances where a child had multiple recorded admissions to PICU, they were categorised into a wave based on the date of the first positive confirmation of SARS-CoV-2 infection via PCR, during their first recorded admission to PICU. Date of first PICU admission was used as a proxy for date of first positive confirmation of SARS-CoV-2 via PCR where this information was not recorded.

2. COVID-19 (without PIMS-TS)

This section focuses on children who were positive for SARS-CoV-2 (as defined in Section 1) but did not present with PIMS-TS. Focusing on children with COVID-19-only allows for robust comparisons of patient characteristics across the four waves of the COVID-19 pandemic.

- This report contains data on **733 PICU care episodes for 714 children** (<16 years) with a confirmed COVID-19 diagnosis (without PIMS-TS). Of the 714 children included in this report covering the period between 14th March 2020 and 31st January 2022, 585 had a date recorded for when they first tested positive for SARS-CoV-2 infection via PCR test.

- Peak weekly admissions occurred during the Omicron wave in the week commencing 03/01/2022. There were 23 PICU admissions in the week commencing 10/01/2022, 22 admissions for the week beginning 17/01/2022 and 23 for the week beginning 24/01/2022 (Figure 2).

- 135 admissions (133 children) did not have a date of the first positive confirmation of SARS-CoV-2 infection via PCR recorded by 22nd July 2022 (data cut-off date).

2.1 COVID-19 and SARS-CoV-2 positive PICU admissions in England

Based on the aggregated total number of SARS-CoV-2 infections in the age-equivalent population of England (0-15 years) between March 2020 and January 2022 [1-2]:

- For every 20,000 SARS-CoV-2 infections recorded there was approximately one SARS-CoV-2 positive admission to a PICU in England.

- Peak monthly admissions to PICUs in England were broadly in line with SARS-CoV-2 infection transmission and incidence reported in the general population (Figure 3).

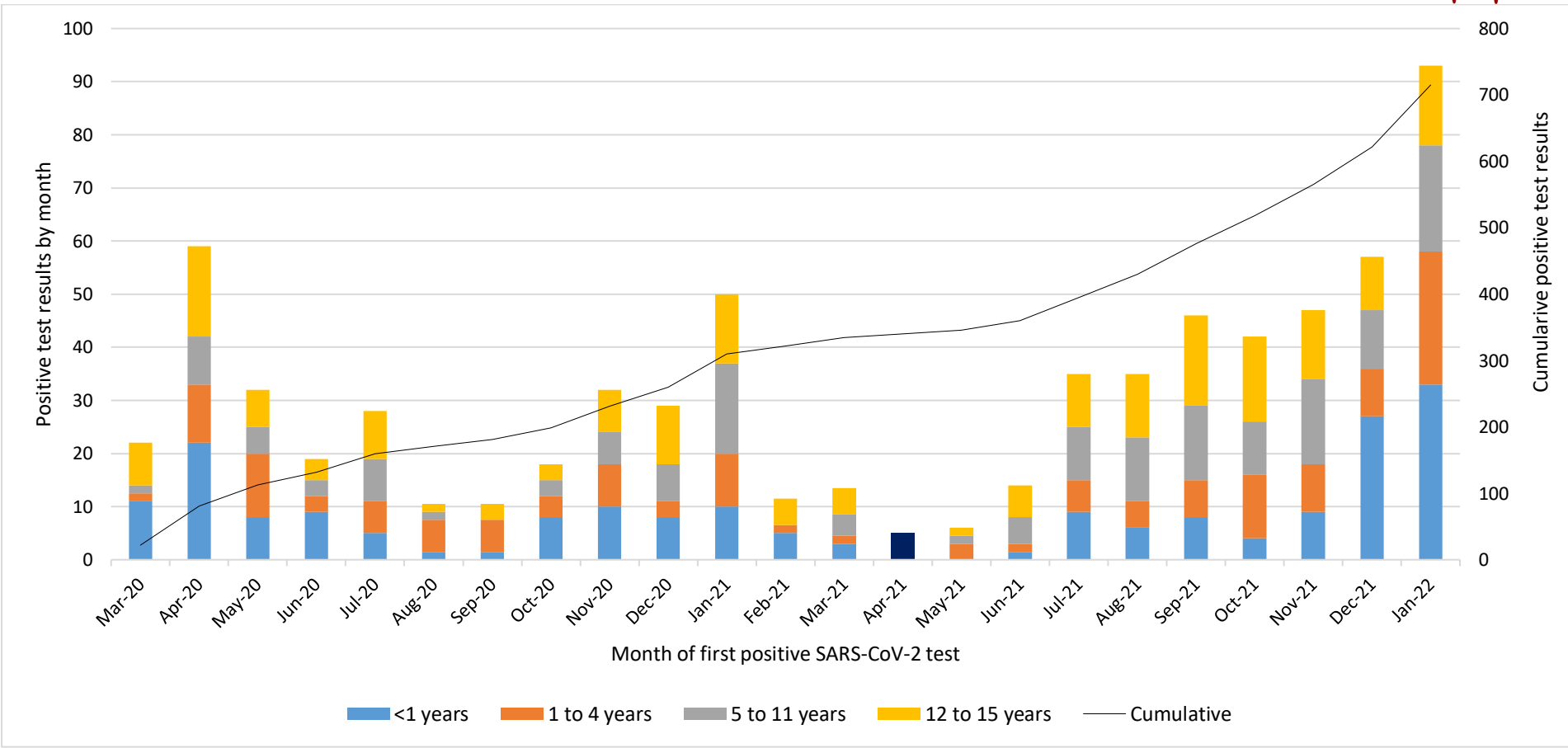

Figure 2. PICU admissions for SARS-CoV-2 positive children (without PIMS-TS) by month of first positive confirmation of SARS-COV-2 infection via PCR and age group (years).

The number of children admitted to **UK and ROI** PICUs where the child was first confirmed as SARS-CoV-2 infection positive between 14th March 2020 and 31st January 2022, presented by week based on date of first positive test (or date of first PICU admission where this information is not recorded). Statistical disclosure control has been applied where fewer than five admissions occurred for a given month.

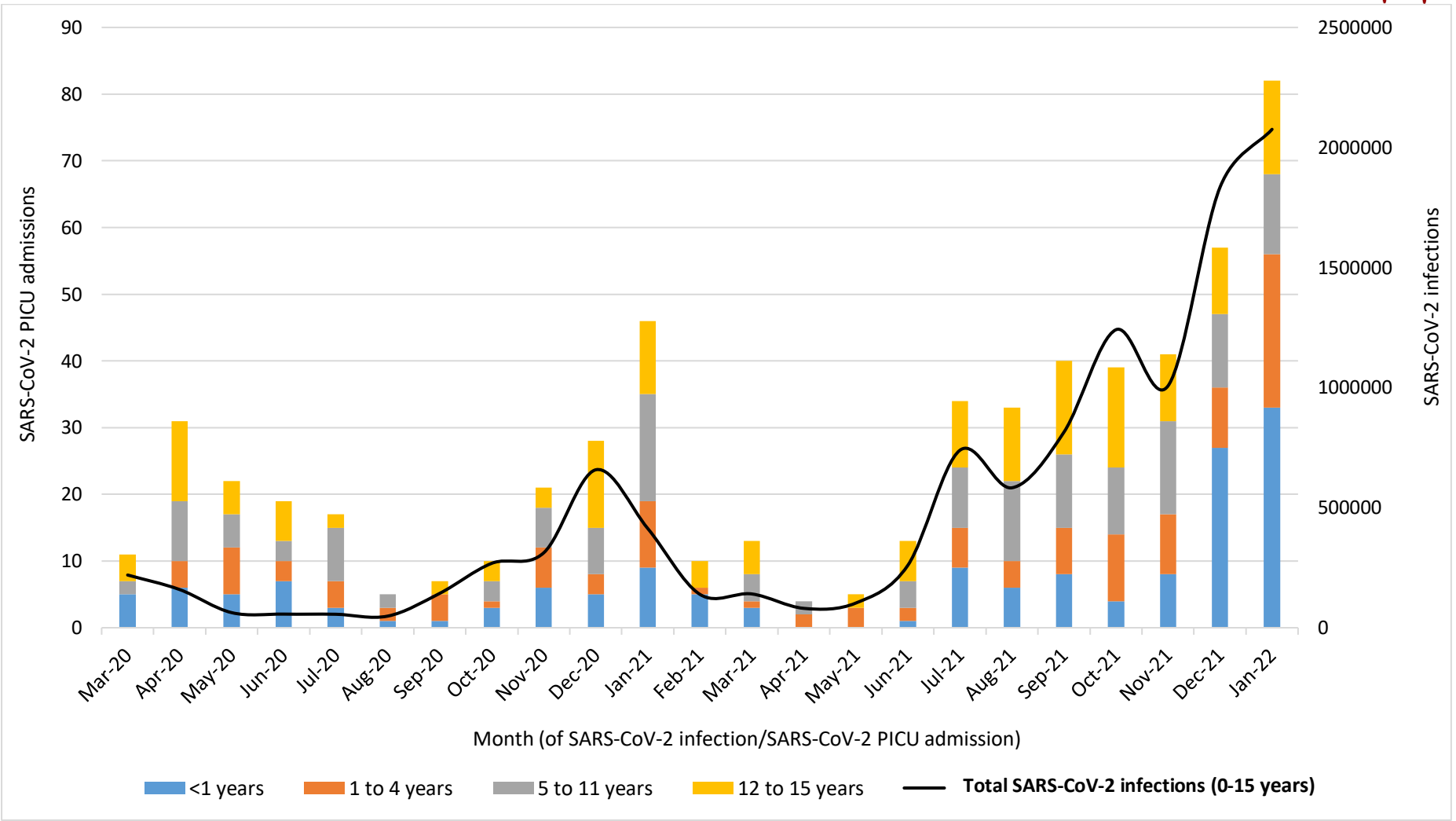

Figure 3. Total monthly number of recorded SARS-CoV-2 infections for children aged 0-15 years in England and the number of SARS-CoV-2 positive admissions to English PICUs, by month of first confirmation of SARS-CoV-2 positive via PCR and age group. Comparator data on real-time pandemic monitoring and the number of new SARS-CoV-2 infections in England was obtained from UK Health Security Agency [1-2].

2.2 Overview of SARS-CoV-2 PCR positive children (without PIMS-TS)

Characteristics of the 714 children with a confirmed SARS-CoV-2 infection included in this report are presented in Table 2.

- The **median age** of SARS-CoV-2 positive children when first admitted to PICU was **six years** (interquartile range (IQR): 1-12 years).
- **58%** of the children were **male (n=411)**.
- **407** children were **White (57%)**, 112 **were Asian (16%)** and 68 were **Black (10%)**. Data on ethnicity were **unavailable** for 9% of children.
- **404 (57%)** of children were admitted to PICU **for infections or respiratory conditions** with a further 7% for endocrine/metabolic reasons and 14% for neurological problems.
- **90% (n=644)** of the initial admissions for these children were **unplanned admissions** to PICU (where the admission was not expected and therefore was an emergency admission).

2.2.1 Co-infections

Data identifying the simultaneous presence of one or more other viral and bacterial respiratory pathogens detected during testing was available for children admitted during the first three waves (n=584). Testing for pathogens may occur during or immediately prior to this paediatric intensive care admission.

Of these 584 children:

- 16% (n=94) of children had a co-infection recorded.
- Another viral pathogen was detected in 10% of children (n=60).
- 6% (n=37) of children had a bacterial respiratory co-infection.

2.3 SARS-CoV-2 patient characteristics (by wave)

Characteristics of the **714 children** in the SAR-CoV-2 group are presented by wave of the pandemic in Table 2

- 38% of children (n=270) were first admitted to PICU with SARS-CoV-2 or had a date of first positive confirmation of SARS-CoV-2 during the Other wave.
- The age distribution of children admitted to PICU with confirmed SARS-CoV-2 differed considerably across waves. The median age at admission was 9 years (IQR: 2-13) for admissions during the Delta wave compared to 2 years for the Omicron wave. Admissions for children under 1 year accounted for around 30%, 24% and 18% of admissions, respectively, during the first three waves compared to just over 40% for Omicron admissions (median age at admission: 2 years (IQR: 0.4-8.6)).
- The proportion of **males** was 6-10% higher for admissions during the Other (60%) and Omicron (63%) wave compared to the Alpha (54%) and Delta (53%) waves.
- Neurological/developmental and congenital heart/cardiac disease **co-morbidities were most common.** Children admitted to PICU during the Omicron wave were more likely to have recorded co-morbidities. 62% of children admitted to PICU during the Omicron wave had recorded co-morbidities, compared to around 34% of children admitted during the other three waves.
- Children were **sicker at presentation** (according to the PIM3 score) when admitted to PICU during the Delta wave (2.1, IQR: 1.2-4.4), compared to children admitted during the other three waves where the estimated probability of death for children was between 1.6% and 1.7%, taking into account their sickness levels at admission.

2.4 SARS-CoV-2 positive: symptomatic & asymptomatic

86% of SARS-CoV-2 positive admissions were unplanned not following surgery (n=616). Of these n=165 (26%) had primary diagnostic group of infection and n=223 of respiratory (35%). 77% of children were symptomatic for SARS-CoV-2 where admission type was unplanned. 83% of children were asymptomatic when the SARS-CoV-2 positive admission was planned following surgery.

Table 1. Description of primary diagnosis group and symptoms recorded relating to admissions *for* versus *with* COVID-19 for the 581 children admitted to PICUs in UK and ROI with positive confirmation of SARS-CoV-2≠

	Admission Type (n, %)									
	Planned - following surgery (n=46, 6.4%)		Unplanned - following surgery (n=28, 3.9%)		Planned – other (n=24, 3.4%)		Unplanned (n=616, 86.3%)		**Total (n=714, 100.0)**	
Primary Diagnosis Group†										
Infection	<5	<10%	-	-	<5	21%	165	26%	**176**	**24%**
Respiratory	-	-	<5	<17%	-	-	223	35%	**238**	**32%**
Endocrine	0	0%	0	0%	0	0%	53	8%	**53**	**7%**
Neurological	5	11%	<5	10%	<5	21%	94	15%	**106**	**14%**
Cardiovascular	13	28%	-	-	-	-	35	6%	**54**	**7%**
Gastrointestinal	6	13%	10	33%	0	0%	14	2%	**30**	**4%**
Other	16	34%	6	20%	8	31%	46	7%	**76**	**10%**
Symptoms recorded										
Symptomatic	8	17%	8	27%	18	69%	482	77%	**516**	**70%**
Asymptomatic*	39	83%	22	73%	8	31%	148	23%	**217**	**30%**

≠ Including date of first positive confirmation of SARS-CoV-2 via PCR.
*No symptoms recorded throughout PICU stay
†Where a child has had multiple admissions information is presented for the first recorded event.
- Statistical disclosure control applied

2.5 Management of SARS-CoV-2

A range of interventions were reported in this cohort. Table 2 displays information on interventions given during the child's first PICU care episode.

- **Respiratory support was required in most children (80%)**. Children admitted during the Delta wave were most likely to receive respiratory support, with 86% of children (n=207) requiring some form of respiratory support.
- **Over half (62%,** n=444) received the highest level of respiratory support (**invasive ventilation)**. The proportion of children whom were invasively ventilated was similar across the waves. In **the Other and Alpha waves,** children **required on average 3 fewer days of invasive ventilation** than in **the Delta wave** (median of 4 days vs 7 days).
- Overall, just under one-third of children received vasoactive support during their first PICU care episode (32%). The proportion of children requiring **vasoactive interventions** decreased steadily from the Other (36%) to the Omicron wave (24%)**.**
- The **length of vasoactive support** provided was longest during the Delta wave, with a **median of 4 days** (IQR: 2–6 days) compared with 3 days for those diagnosed during the Other and Alpha (IQR: 2-5 days) wave. Length of vasoactive support provided was shortest for those on PICU during the Omicron wave (median 2 days (IQR: 2-5 days)).
- Very small numbers of children received renal support. The proportion of children requiring renal support was highest in the Alpha wave (n=12, 7%) and lowest during the Omicron wave (2%). The highest proportion of children requiring extracorporeal membrane oxygenation (ECMO) was during the Delta wave (5%).
- **PICU length of stay** was **shortest** for those diagnosed during the **Alpha wave** (median 4 days, IQR: 2.0-11.0 days) and greatest for those diagnosed during the Delta wave (5 days, IQR: 2-11 days). Median length of stay overall was just under 5 days (4.7, IQR: 2.0-10.4 days).
- **39 children** (5%) in the COVID-19 only cohort **died whilst on PICU**. Mortality was roughly consistent across the waves. It is possible that the cause of death in some children is unrelated

to SARS-CoV-2 infection. Where children died during the Omicron wave (n=6), fewer than three deaths were recorded as being related to COVID-19.

Table 2. Characteristics of 714 children treated in UK PICUs who were laboratory confirmed positive for SARS-COV-2 infection (without PIMS-TS) by wave of the pandemic Ω.

	Waves of the COVID-19 pandemic (n, %)									
	Other (n=270, 37.8%)		**Alpha** (n=72, 10.1%)		**Delta** (n=242, 33.9%)		**Omicron** (n=130, 18.2%)		**Total (n=714, 100.0%)**	
Median age (years) at admission (IQR)	4.6	(0.7-11.4)	5.8	(1.2-12.4)	8.9	(1.8-13.1)	1.9	(0.4-8.6)	**5.7**	**(0.9-12.1)**
Age group at admission (years)										
<1	81	30%	17	24%	43	18%	53	41%	**194**	**27%**
1-4	57	21%	14	19%	46	19%	30	23%	**147**	**21%**
5-11	70	26%	22	31%	73	30%	26	20%	**191**	**27%**
12-15	62	23%	19	26%	80	33%	21	16%	**182**	**25%**
Sex										
Male	161	60%	39	54%	129	53%	82	63%	**411**	**58%**
Female	109	40%	33	46%	113	47%	48	37%	**303**	**42%**
Ethnic group										
Asian	47	17%	12	17%	24	10%	29	22%	**112**	**16%**
Black	30	11%	7	10%	15	6%	16	12%	**68**	**10%**
Mixed	8	3%	<5	<7%	5	2%	<5	<4%	**20**	**3%**
White	165	61%	36	50%	147	61%	59	45%	**407**	**57%**
Other	11	4%	7	10%	16	7%	-	-	**41**	**6%**
Unknown	9	3%	-	-	35	14%	16	12%	**66**	**9%**
Primary diagnosis group										
Infection/Respiratory	138	51%	36	50%	157	65%	73	56%	**404**	**57%**
Endocrine**	16	6%	6	8%	20	8%	11	8%	**53**	**7%**

Neurological	47	17%	13	18%	25	10%	17	13%	**102**	**14%**
Cardiovascular	24	9%	<5	<7%	18	7%	-	-	**54**	**8%**
Gastrointestinal	11	4%	-	-	<5	<2%	6	5%	**27**	**4%**
Other	34	13%	7	10%	18	7%	15	12%	**74**	**10%**
Admission type										
Unplanned	233	86%	68	94%	226	93%	117	90%	**644**	**90%**
PIM3 POD (%)										
Median (IQR)	1.6	(0.8-4.5)	1.6	(0.5-3.5)	2.1	(1.2-4.4)	1.7	(0.5-4.4)	**1.7**	**(0.8-4.4)**
Comorbidities										
Neurological‡	40	15%	12	17%	33	14%	29	22%	**114**	**16%**
Cardiac	36	13%	5	7%	14	6%	10	8%	**65**	**9%**
Preterm	18	7%	5	7%	17	7%	14	11%	**54**	**8%**
Genetic	18	7%	<5	<7%	13	5%	6	5%	**40**	**6%**
Malignancy†	<5	<2%	<5	<7%	-	-	-	-	**<5**	**<1%**
Metabolic**	<5	<2%	-	-	6	2%	<5	<4%	**9**	**1%**
Pulmonary	<5	<2%	<5	<7%	10	4%	10	8%	**26**	**4%**
Other β	-	-	<5	<7%	16	7%	<5	<4%	**31**	**4%**
No recorded co-morbidities	179	66%	48	67%	159	66%	50	38%	**436**	**61%**
No symptoms recorded	97	36%	19	26%	47	19%	46	35%	**209**	**29%**
Maximum respiratory support										
None	65	24%	18	25%	35	14%	27	21%	**145**	**20%**
High flow nasal cannula therapy	16	6%	6	8%	30	12%	8	6%	**60**	**8%**
Non-invasive ventilation	16	6%	<5	<7%	31	13%	15	12%	**65**	**9%**
Invasive mechanical ventilation	160	59%	43	60%	116	48%	78	60%	**397**	**56%**
High frequency oscillatory or jet ventilation	13	5%	<5	<7%	30	12%	<5	<4%	**47**	**7%**

Renal support										
No	260	96%	67	93%	230	95%	127	98%	**684**	**96%**
Vasoactive support										
No	174	64%	47	65%	168	69%	99	76%	**488**	**68%**
Yes	96	36%	25	35%	74	31%	31	24%	**226**	**32%**
ECMO										
No	267	99%	70	97%	232	96%	128	98%	**697**	**98%**
Discharge status φ										
Alive	254	94%	69	96%	228	94%	124	95%	**675**	**95%**
Dead	16	6%	<5	<7%	14	6%	-	-	**39**	**5%**
Invasive ventilation (days)										
n (%)	173	64%	45	63%	146	60%	80	62	**444**	**62%**
Median (IQR)	4.0	(3.0-9.0)	4.0	(2.0-12.0)	7.0	(3.0-14.0)	5.0	(2.0-11.5)	**5.0**	**(3-11.5)**
Median days of vasoactive support	3.0	(2.0-5.0)	3.0	(2.0-5.0)	4.0	(2.0-6.0)	2.0	(2.0-5.0)	**3**	**(2.0-6.0)**
Median length of stay (days) ¶	4.2	(1.8-8.9)	3.8	(1.7-3.8)	5.0	(2.1-10.0)	4.6	(2.0-9.3)	**4.6**	**(1.9-9.3)**

Abbreviations: IQR = interquartile range; PIM3 POD = Paediatric Index of Mortality 3 predicted probability of death; ECMO = extracorporeal membrane oxygenation

Ω Waves of the COVID-19 pandemic are defined as follows: Other: 14th March–31st December 2020; Alpha: 1st January 2021 –16th May 2021; Delta: 17th May 2021 – 12th December 2021; Omicron: 13th December – 31st January 2022. Children were assigned to a wave based on date of first positive confirmation of SARS-CoV-2 via PCR. Where this information was missing, children were assigned to one of four waves based on date of admission.

†† comorbidities not mutually exclusive;

‡ neurological/developmental including epilepsy, cerebral palsy;

**metabolic/endocrine including diabetes;
† malignancy including leukaemia, lymphoma, solid tumours;
β other including autism and attention deficit hyperactive disorder (ADHD)
¶ where a child had multiple admission events the number of days is summed across all events
φ where a child had multiple admission events, the status from the last recorded admission is presented
-statistical disclosure control applied

2.6 Interventions provided for the 714 children who tested positive for SARS-CoV-2 infection (without PIMS-TS)

This section presents information on interventions provided at any point during the PICU care episodes, including interventions given before confirmation of COVID-19 where applicable.

- **Invasive ventilation** (the highest level of respiratory support) was required in **62% of care episodes** (n=444) for a median of 5 days (IQR: 3-12 days).
- **Renal support** was required in 30 of the 714 care episodes **(5%)**.
- The child received a **continuous vasoactive infusion** in 226 care episodes **(32%)**
- **Extracorporeal membrane oxygenation (ECMO)** was received in 17 care episodes **(2%)**.

Table 3. Treatment for 714 children diagnosed as SARS-CoV-2 positive, by wave of the COVID-19 pandemic.

	Waves of the COVID-19 pandemic (n, %)									
	Other (n=270, 37.8%)		**Alpha** (n=72, 10.1%)		**Delta** (n=242, 33.9%)		**Omicron** (n=130, 18.2%)		**Total (n=714, 100.0%)**	
No treatment recorded	98	36%	17	23%	39	16%	67	52%	**221**	**31%**
Antivirals≠	26	10%	13	18%	67	28%	21	16%	**127**	**18%**
Remdesivir±	22	8%	13	18%	67	28%	21	16%	**123**	**17%**
Steroids*	47	17%	29	40%	130	54%	44	34%	**250**	**35%**
Immune modulators†	53	20%	27	38%	125	52%	10	8%	**215**	**30%**

≠ Antivirals include Inhaled interferon beta-1a, Lopinavir with Ritonavir, Oseltamivir and Remdesivir.
± Remdesivir – Veklury –intravenous
* Steroids include oral, IM, and IV Corticosteroids such as Methylprednisolone, Prednisolone, Dexamethasone (excluding administration for extubation).
† Immune modulators include Anakinra, Dexamethasone (excluding administration for extubation), Hydroxychlorquine, Intravenous immunoglobulin, Tocilizumab.

2.7 Treatment for SARS-CoV-2

Table 3 presents information on the treatment(s) used for SARS-CoV-2 positive children.

- **Medication was used to treat 69% (n=493) of SARS-CoV-2 patients.** 31% of children (n=221) **did not receive any of the treatments** listed or specified in the PICANet COVID-19 customised data collection, and had no other antiviral or immune modulator medications recorded.
- The use of immune modulators, steroids and to treat children with SARS-CoV-2 in PICU increased from the Other to Delta wave.
- Medication was used to treat 84% (n=203) of SARS-CoV-2 positive children in PICU during the Delta wave compared to 48% of children diagnosed with SARS-CoV-2 during the Omicron wave (n=63).
- Use of antiviral medication to treat SARS-CoV-2 was lowest during the Other wave, where 10% of SARS-CoV-2 children (n=26) received antiviral medication.

2.8 SARS-CoV-2 PCR positive patient outcomes

- **39 children died in PICU (5%)**: 41% were neonates or infants (aged less than 1 year), 21% were aged 5-11 years and 26% were aged 12 years or above. 49% had other pre-existing health conditions/co-morbidities recorded. Where cause of death was available from death certificates (n=6/39), this indicated that around half of these fatalities were directly attributable to COVID-19
- The overall **median length of stay** for the 39 care episodes in these 39 children was **11 days** (IQR: 5-29 days).
- The median length of stay for children who died in PICU was a week longer than that for children who were discharged alive from PICU (discharged alive: median length of stay = 4 days, IQR 2-9).

2.9 Comparisons of the SARS-CoV-2 positive cohort with other PICU admissions

In Table 4, we present information based on the SARS-CoV-2 positive cohort of 714 children alongside information relating to all children admitted to PICU during the equivalent period (14th March 2020 – 31st January 2022) without a confirmed SARS-CoV-2 diagnosis or recorded PIMS-TS. This cohort represents a SARS-CoV-2 negative PICU case-mix comparator group.

- Median age at admission for SARS-CoV-2 positive children was 6 years (IQR: 1-12) compared to 1 year for the SARS-CoV-2 negative PICU population (IQR: 0-7).
- Children with a confirmed SARS-CoV-2 were **sicker at presentation** according to the PIM3 score at admission to PICU (1.7% (IQR: 0.8-4.4)), compared to all SARS-CoV-2 negative children admitted to PICU during the equivalent time period (1.2% (IQR: 0.4-3.3)).
- Respiratory support was required for 80% of SARS-CoV-2 positive children compared to 70% of SARS-CoV-2 negative children.
- Length of stay was almost doubled for SARS-CoV-2 positive patients (4.6 days (IQR: 1.9-9.3)) compared to the SARS-CoV-2 negative cohort (2.4 (IQR: 1.0-5.5)).

Table 4. Characteristics of children who were with laboratory confirmed positive for SARS-CoV-2 infection (without PIMS-TS) alongside those children admitted to PICU without recorded SARS-CoV-2.

	SARS-CoV-2 positive (n=714)		Other PICU admissions* (n=22,492)	
Median age (years) at admission (IQR)	5.7	(0.9-12.1)	1.4	(0.2-7.4)
Age group at admission (years)				
<1	194	27%	10,129	45%
1-4	147	21%	5,867	26%
5-11	191	27%	3,731	17%
12-15	182	25%	2,766	12%
Sex				
Male	411	58%	12,629	56%
Female	303	42%	9,858	43%
Unknown	0%	0%	5	<1%
Ethnic group				
Asian	112	16%	2,223	10%
Black	68	10%	1,075	5%
Mixed	20	3%	789	3%
White	407	57%	14,212	63%
Other	41	6%	849	4%
Unknown	66	9%	3,344	15%
Primary diagnosis group				
Infection/Respiratory	404	57%	6,106	27%
Endocrine/metabolic**	53	7%	937	4%
Neurological	102	14%	2,570	11%
Cardiovascular	54	8%	6,557	29%
Gastrointestinal	27	4%	1,589	7%
Other	74	10%	4,733	21%
Admission type				
Planned	70	10%	8,958	39%
Unplanned	644	90%	13,527	60%
Unknown	0	0%	7	<1%
PIM3 POD (%)				
Median (IQR)	1.7	(0.8-4.4)	1.2	(0.4-3.3)
Co-morbidities				
Neurological‡	114	16%	1,987	9%
Cardiac	65	9%	2,594	12%
Preterm	54	8%	2,044	9%
Genetic	40	6%	793	4%
Malignancy†	<5	<1%	89	<1%
Metabolic **	9	1%	104	<1%
Pulmonary	26	4%	546	2%
Other β	31	4%	563	3%
No recorded co-morbidities	436	61%	6,542	29%
No symptoms recorded	209	29%	0	0%

Maximum respiratory support				
None	145	20%	6,683	30%
High flow nasal cannula therapy	60	8%	1,072	5%
Non-invasive ventilation	65	9%	1,070	5%
Invasive mechanical ventilation	397	56%	13,140	58%
High frequency oscillatory or jet ventilation	47	7%	527	2%
Renal support				
No	684	96%	21,767	97%
Yes	30	4%	725	3%
Vasoactive support				
No	488	68%	14,915	66%
Yes	226	32%	7,577	34%
Days of vasoactive support (median (IQR))	3	(2.0-6.0)	3.0	(2.0-6.0)
ECMO				
No	697	98%	22,197	99%
Yes	17	2%	295	1%
Discharge status φ				
Alive	675	95%	21,631	96%
Dead	39	5%	853	4%
Unknown≠	0	0%	8	<1%
Median days of invasive ventilation	444	62%	13,667	61%
n (%)	5.0	(3-11.5)	3.0	(2.0-6.0)
Median length of stay (days) ¶	4.6	(1.9-9.3)	2.4	(1.0-5.5)

Abbreviations: IQR = interquartile range; PIM3 POD = Paediatric Index of Mortality 3 predicted probability of death; ECMO = extracorporeal membrane oxygenation

*Children with recorded PIMS-TS also excluded from the SARS-CoV-2 negative comparator population.

†† comorbidities not mutually exclusive;

‡ neurological/developmental including epilepsy, cerebral palsy;

**metabolic/endocrine including diabetes;

† malignancy including leukaemia, lymphoma, solid tumours;

β other including autism and attention deficit hyperactive disorder (ADHD)

¶ where a child had multiple admission events the number of days is summed across all events;

φ where a child had multiple admission events, the status from the last recorded admission is presented

≠8 children were still in PICU at the time of data extraction and so do not have discharge status available

3. PIMS-TS

This report contains data on **823 PICU care episodes for 818 children** (<16 years) who presented to PICUs in the UK and ROI (between 14th March 2020 and 31st January 2022) with PIMS-TS regardless of whether they had been confirmed SARS-CoV-2 PCR positive or not. A child was defined to have PIMS-TS based on clinical judgement of the reporting PICU clinicians.

3.1 PIMS-TS overview

- There were **823 PICU care episodes for 818 children** (<16 years) where a child was admitted with PIMS-TS.
- Among these, 264 (32%) were noted to have a positive SARS-CoV-2 PCR during this admission episode.
- Almost **47%** of children (n=382) presenting with **PIMS-TS** were admitted to PICUs in London, with a further **43%** (n=355) admitted to PICUs in the rest of England, whilst **6%** (n=49) of children were admitted to PICUs in the Scotland, Wales and Northern Ireland and the remaining 4% (n=32) were admitted to PICUs in ROI.
- 27 of 32 PICUs in total had at least one child admitted with PIMS-TS.

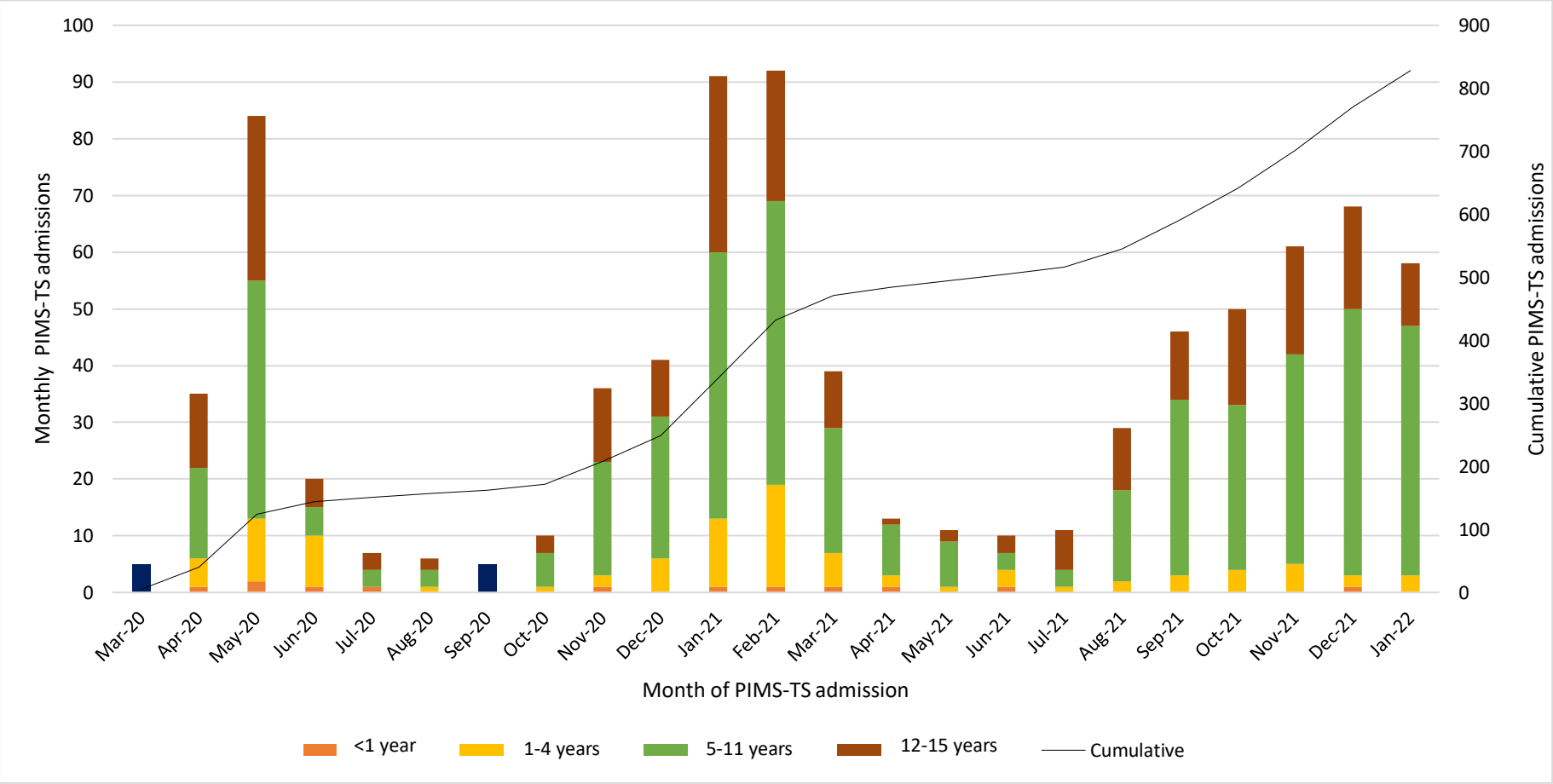

Figure 4. PICU admissions for children with recorded PIMS-TS (with or without confirmed SARS-CoV-2), by month of admission and age group.

The number of children admitted to UK and ROI PICUs between 14th March 2020 and 31st January 2022 with recorded PIMS-TS, presented by week based on date of first PIMS-TS admission. Statistical disclosure control has been applied where fewer than five admissions occurred during a given month.

3.2 PIMS-TS patient characteristics and course

Table 5 compares the characteristics of the 818 children in the PIMS-TS cohort.

- The median age of children in the PIMS-TS cohort when first admitted to PICU was 10 years (IQR: 7 to 13 years). 13% of children (n=99) were aged under 5 years at first recorded PICU admission.
- Around **59%** of the children were **male (n=484)**.
- **332 children were White (41%)**, **164 were Asian (9%)** and **143 were Black (8%)**. Data on ethnicity were **unavailable** for 24% of children in the PIMS-TS cohort overall.
- Given the absence of a specific diagnosis code for this relatively novel condition, a variety of alternatives were chosen by clinicians. The reported primary diagnostic codes mapped to **endocrine or metabolic** diagnostic group in **53%**, **cardiovascular** in 31% and **infection or respiratory group** in 13%.
- **99%** of the initial admissions for these children **(n=812)** were **unplanned admissions** to PICU (where the admission was not expected and therefore an emergency admission).
- **Comorbidities** in the PIMS-TS cohort were recorded infrequently. 68% of children (n=559) in the PIMS-TS cohort had no recorded co-morbidities; the most common types of comorbidities were neurological/developmental (3%) and congenital heart/cardiac disease (4%).

3.3 PIMS-TS patient characteristics (by wave)

Characteristics of the **818 children** in the PIMS-TS group are presented by wave of the pandemic in Table 5.

- The age distribution of children admitted to PICU with PIMS-TS did not differ considerably across waves.
- The proportion of **males** was highest for admissions during the Other (62%) and Omicron (63%) waves compared to the Alpha and Delta (67%) waves.

- There was a reduction in the percentage of children of Black and Asian children ethnicities admitted to PICU with PIMS-TS across the course of the pandemic. Black children accounted for 27% of children admitted during the Other wave and 8% of children admitted during the Omicron wave.
- 77% and 79% of children admitted to PICU with PIMS-TS during the Other and Alpha waves had no recorded co-morbidities compared to 58% and 45% for those admitted during the Delta and Omicron waves, respectively.
- Children were **sicker at presentation** (according to the PIM3 score) when admitted to PICU during the Other wave (1.9%, IQR: 1.4-4.1), compared to children admitted during the other three waves where the estimated probability of death for children was between 1.6% and 1.8%, taking into account their sickness levels at admission.

3.4 PIMS-TS management and outcomes

Table 5 displays information on interventions given during the child's first PICU care episode (n=818 children). Table 6 presents information on the treatment or medication used to treat a child with clinically diagnosed PIMS-TS in PICU.

- Symptoms were present in 99% of children overall (n=814). Symptoms were not reported/recorded in nine children.
- **Respiratory support** was required in 32% of children overall (n=260). The proportion of children requiring respiratory support was highest for those admitted during the Other wave (42%). The majority of children admitted during the Omicron wave (77%) did not require any form of respiratory support.
- **19% of children** required the highest level of invasive ventilation (n=152) for a median of 4 days (IQR: 3–5 days). The highest percentage of children receiving invasive ventilation occurred during the Other wave (n=67, 28%). This almost halved during the Alpha wave, where 15% of children were invasively ventilated.

- 76% of children received vasoactive support (n=619) for a median of 3 days (IQR: 2–4 days). The proportion of children requiring vasoactive support was greatest during the Delta wave (81%).
- Very small numbers of children received renal replacement therapy and extracorporeal membrane oxygenation (ECMO). This was consistent across the waves.
- The median **length of PICU stay** was **2.5 days** (IQR: 1–4 days). Length of stay was highest for children admitted with PIMS-TS during the Other wave (2.9 (IQR: 1.6-5.0)). Median length of stay reduced over the course of the pandemic from 2.9 days (IQR: 1.6-5.0) for children with PIMS-TS in PICU during the Other wave to 2.0 days (IQR: 1.1-3.3) for those admitted during Omicron.
- A diagnostic echocardiogram was performed for 99% of children with clinically diagnosed PIMS-TS (n=809). Evidence of a coronary artery aneurysm(s) was detected in 4% (n=31) of the 722 children admitted before 13th December 2021 where an echocardiogram was performed.
- For children admitted during the Omicron wave with an echocardiogram performed (n=87), 7% (n=6) showed evidence of dilated coronary artery or arteries and/or coronary aneurysm. The echo findings at the time of PICU stay revealed reduced function in either the left or the right side of the heart for 48% (n=42) of these 87 children. Evidence of a pericardial effusion was found in 9% of children (n=8). In 11% of children (n=10), valvar regurgitation was observed.
- **Six children died whilst on PICU (1%)**.

Table 5. Characteristics of children treated in UK PICUs with recorded PIMS-TS, by wave of the pandemic Ω

	Waves (n, %)									
	Other (239, 29.2)		Alpha (242, 29.6)		Delta (241, 29.5)		Omicron (96, 11.7)		**Total (818, 100.0)**	
Median age (years) at admission (IQR)	9.6	(6.1-12.7)	8.9	(5.8-12.2)	10.4	(7.3-12.6)	10.0	(7.9-11.7)	**9.7**	**(5.7)**
Age group at admission (years)										
<1	6	3%	-	-	-	-	0	0%	**12**	**1%**
1-4	35	15%	39	16%	18	7%	5	5%	**97**	**12%**
5-11	122	51%	133	55%	144	60%	69	72%	**468**	**57%**
12-15	76	32%	66	27%	77	32%	22	23%	**241**	**29%**
Sex										
Male	149	62%	138	57%	137	57%	60	63%	**484**	**59%**
Female	90	38%	104	43%	104	43%	36	38%	**334**	**41%**
Ethnic group										
Asian	64	27%	55	23%	36	15%	9	9%	**164**	**20%**
Black	64	27%	38	16%	33	14%	8	8%	**143**	**17%**
Mixed	14	6%	16	7%	-	-	<5	<5%	**42**	**5%**
White	70	29%	100	41%	114	47%	48	50%	**332**	**41%**
Other	6	3%	13	5%	7	3%	-	-	**31**	**4%**
Unknown	21	9%	20	8%	42	17%	23	24%	**106**	**13%**
Primary diagnosis group										
Infection/Respiratory	43	18%	32	13%	20	8%	12	13%	**107**	**13%**
Endocrine/metabolic**	104	44%	137	57%	142	59%	52	54%	**435**	**53%**
Neurological	<5	<2%	-	-	<5	<2%	-	-	**<5**	**<1%**
Cardiovascular	83	35%	65	27%	73	30%	31	32%	**252**	**31%**
Gastrointestinal	<5	<2%	<5	<2%	<5	<2%	0	0%	**7**	**1%**
Other	<5	<2%	6	2%	-	-	-	-	**15**	**2%**
Admission type										
Unplanned	237	99%	239	99%	240	100%	96	100%	**812**	**99%**
PIM3 POD (%)										
Median (IQR)	1.9	(1.4-4.1)	1.7	(1.4-2.5)	1.8	(1.5-2.4)	1.6	1.4-2.2	**1.7**	**(1.4-2.9)**
Co-morbidities††										

Neurological‡	11	5%	-	-	5	2%	<5	<5%	**23**	**3%**
Cardiac	10	4%	5	2%	14	6%	6	6%	**35**	**4%**
Preterm	0	0%	0	0%	-	-	-	-	**<5**	**<1%**
Genetic	<5	<1%	0	0%	0	0%	0	0%	**<5**	**<1%**
Malignancy†	<5	<1%	0	0%	0	0%	0	0%	**<5**	**<1%**
Metabolic**	0	0%	<5	<2%	<5	<2%	0	0%	**4**	**<1%**
Other β	<5	<2%	<5	<2%	<5	<2%	<5	<5%	**8**	**1%**
No recorded co-morbidities	185	77%	192	79%	139	58%	43	45%	**559**	**68%**
No symptoms recorded	6	3%	<5	<2%	<5	<2%	0	0%	**9**	**1%**
Maximum respiratory support										
None	138	58%	182	75%	164	68%	74	77%	**558**	**68%**
High flow nasal cannula therapy	25	10%	16	7%	34	14%	9	9%	**84**	**10%**
Non-invasive ventilation	9	4%	-	-	<5	<2%	0	0%	**20**	**2%**
Invasive mechanical ventilation	64	27%	34	14%	41	17%	13	14%	**152**	**19%**
High frequency oscillatory or jet ventilation	-	-	-	-	0	0%	0	0%	**4**	**<1%**
Renal support										
No	234	98%	239	99%	238	99%	96	100%	**807**	**99%**
Vasoactive support										
No	74	31%	59	24%	46	19%	20	21%	**199**	**24%**
Yes	165	69%	183	76%	195	81%	76	79%	**619**	**76%**
Days of vasoactive support (median (IQR))	3.0	(2.0-5.0)	2.0	(2.0-4.0)	2.0	(2.0-4.0)	2.0	(2.0-3.0)	**3.0**	**(2.0-4.0)**
ECMO										
No	235	98%	242	100%	241	100%	96	100%	**814**	**100%**
Discharge status φ										

Alive	235	98%	242	100%	239	99%	96	100%	**812**	**99%**
Dead	<5	<2%	-	-	<5	<2%	0	0%	**6**	**1%**
Days of invasive ventilation										
n (%)	67	28%	35	15%	41	17%	13	14%	**156**	**19%**
Median (IQR)	4.0	(3.0-7.0)	4.0	(3.0-5.0)	4.0	(2.0-5.0)	2.0	(1.0-4.0)	**4.0**	**(3.0-5.0)**
Length of stay (days) ¶										
Median (IQR)	2.9	(1.6-5.0)	2.3	(1.2-3.7)	2.2	(1.4-3.8)	2.0	(1.1-3.3)	**2.5**	**(1.4-4.1)**

Abbreviations; IQR = interquartile range; PIM3 POD = Paediatric Index of Mortality 3 predicted probability of death; ECMO = extracorporeal membrane oxygenation

Ω Waves of the COVID-19 pandemic are defined as follows: Other: 14th March–31st December 2020; Alpha: 1st January 2021 –16th May 2021; Delta: 17th May 2021 – 12th December 2021; Omicron: 13th December 2021 – 31st January 2022. Children were assigned to one of four waves based on the date of admission to PICU.

†† comorbidities not mutually exclusive;

‡ neurological/developmental including epilepsy, cerebral palsy;

**metabolic/endocrine including diabetes;
† malignancy including leukaemia, lymphoma, solid tumours;
β other including autism and attention deficit hyperactive disorder (ADHD)
¶ where a child had multiple admission events the number of days is summed across all events;
φ where a child had multiple admission events, the status from the last recorded admission is presented
-statistical disclosure control applied

Table 6. Treatment for 818 children with clinically diagnosed PIMS-TS, by wave of the COVID-19 pandemic.

	Waves (n, %)									
	Other (239, 29.2)		Alpha (242, 29.6)		Delta (241, 29.5)		Omicron (96, 11.7)		**Total (818, 100.0)**	
No treatment recorded	8	3%	12	5%	-	-	-	-	**28**	**3%**
Steroids*	82	35%	114	47%	147	61%	82	85%	**425**	**52%**
Immune modulators†	134	57%	119	49%	87	36%	33	34%	**373**	**46%**
IVIG	126	54%	110	45%	74	31%	30	31%	**340**	**42%**
Anakinra	10	4%	8	3%	-	-	<5	<5%	**29**	**4%**
Tocilizumab	9	4%	11	5%	-	-	-	-	**25**	**3%**

* Steroids include oral, IM, and IV Corticosteroids such as Methylprednisolone, Prednisolone, Dexamethasone (excluding administration for extubation).
† Immune modulators include Anakinra, Dexamethasone (excluding administration for extubation), Hydroxychlorquine, Intravenous immunoglobulin (IVIG), Tocilizumab.
- statistical disclosure control applied

3.4.1 Treatment of PIMS-TS

Table 6 presents information on the treatment(s) used for children with clinically diagnosed PIMS-TS.

- **Medication was used to treat 97% (n=790) of PIMS-TS patients.** 3% of children (n=28) **did not receive any of the treatments** listed or specified in the PICANet COVID-19 customised data collection, and had no other antiviral or immune modulator medications recorded. The proportion of children receiving medication as a form of treatment for PIMS-TS was broadly similar across the four waves of the COVID-19 pandemic.
- The use of steroids to treat children with PIMS-TS in PICU increased across the four waves. 35% (n=82) of children admitted to PICU with PIMS-TS during the first (Other) wave were treated with steroids. The proportion of children receiving steroids increased to 47% (n=114) during the Alpha wave, 61% (n=147) during the Delta wave and 81% (n=82) for children in PICU during the Omicron wave.
- Immune modulator medication usage reduced across the four waves. 57% of children (n=134) were treated with immune modulator medication when admitted during the Other wave. This proportion decreased to 49% of children during the Alpha wave (n=119), 36% in the Delta wave (n=87) and 34% of children in PICU during the Omicron wave (n=33).

4. Discussion

The report summarises over 22 months of data related to COVID-19 and PIMS-TS, in critically ill children admitted to a PICU in the UK and ROI. The report includes summary clinical details of over 1500 children using information obtained from the COVID-19 custom audit and the PICANet admission dataset, spanning original version and the three main variants of SARS-CoV-2.

4.1 Key findings

- COVID-19 and PIMS-TS related PICU admissions accounted for 7% of all PICU admissions during this time period. Highest numbers of admissions with COVID-19 were recorded in the final month of this report -January 2022.
- Requirement for invasive mechanical ventilation (62% of children with COVID-19), inotropic support (76% of children with PIMS-TS) confirmed that the disease was severe in the majority of children requiring PICU admission.
- The children admitted to PICU with either COVID-19 or PIMS-TS were older (52% of children [COVID-19], 86% of children [PIMS-TS] in the 5-15 years age group), compared with 29% of children in the 5-15 year age group other PICU admissions. 41% of children admitted with COVID-19 during the Omicron variant, however, were less than 1 year of age.
- Disproportionately higher proportion of children were of Asian, black or mixed ethnicities (42% for PIMS-TS, 29% for COVID-19) compared with the other PICU population (18%)
- Among those reported to have a positive SARS-CoV-2 PCR during the PICU stay, ~30% of children were asymptomatic—the so-called admissions **with** COVID-19 (or incidental) rather than **for** COVID-19. In addition, a small proportion of children who did develop symptoms may not have required PICU because of COVID-19, but were admitted for other reasons.
- Majority of affected children did not have any underlying co-morbidity reported (61% and 68% with no co-morbidities in the COVID-19 and PIMSTS cohort respectively). Among those

with underlying co-morbidities, neurological and cardiac co-morbidities were the most common. This is in keeping with the pattern observed in the other PICU population.

- Co-infections were reported in 16% of children admitted with COVID-19. Two-thirds of the co-infections were with another viral pathogen.
- In the PIMS-TS cohort of children, at least 37 children were reported as having either dilated coronary arteries or meeting criteria for coronary aneurysm.
- Remdesivir and dexamethasone appeared to be the most common specific treatment provided for COVID-19. Whereas for PIMS-TS, a clear evolution of treatment trends with an increase in proportion of patients receiving steroids with time, along with a reduction in patients receiving IV immunoglobulin and other immunomodulators can be observed.
- No children have been recorded to have potential vaccine-related complications requiring PICU admission (e.g. myocarditis/pericarditis).

4.2 Potential clinical implications

- Severe illness related to SARS-CoV-2 virus infection continued to be a significant problem at the time of cut-off date for inclusion in this report.
- Children with and without co-morbidities were both significantly affected by both COVID-19 and PIMS-TS. Children of minority ethnic origin appeared to be disproportionately affected. These data may inform public health strategies including booster campaigns for vaccination.
- Proportion of patients with incidental COVID-19 (30%) remained consistent with other similar reports published earlier.
- Clear patterns in treatment of PIMS-TS were visible, with fewer patients requiring mechanical ventilation, and intravenous immunoglobulin during the later stages of the pandemic. A higher proportion of patients received steroids during the later stages of the pandemic. These treatment patterns were detected despite concurrent recruitment to RECOVERY trial.

- Co-infection remains a concern. 10% of patients with COVID-19 were reported to also be co-infected with another virus, which is remarkable given other respiratory infections were less common. These patterns will need to be monitored carefully going into the winter season without significant social mobility, or non-pharmacological restrictions.
- Detection of coronary abnormalities in at least 37 children with PIMS-TS suggests that practice of involving cardiology as part of the multi-disciplinary team managing severe PIMS-TS.

5. References

1. Birrell, P., Blake, J., van Leeuwen, E., Gent, N., & de Angelis, D. (2021). Real-time nowcasting and forecasting of COVID-19 dynamics in England: The first wave. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *376*(1829). https://doi.org/10.1098/rstb.2020.0279

2. Birrell, P., Blake J,. van Leeuwen. E., MRC Biostatistics Unit COVID-19 Working Group., De Angelis D. (2022) COVID-19: nowcast and forecast. MRC Biostatistics Unit, University of Cambridge, Cambridge. http://www.mrc-bsu.cam.ac.uk/now-casting/ (25 October 2022, date last accessed).

6. Appendix

Methods

PICANet COVID-19 Customised Data Collection

A PICANet customised audit was established at the start of the COVID-19 pandemic following a request by NHS England to facilitate the collection of additional information concerning:

1. All children who tested positive for SARS-CoV-2 infection either prior to or during their PICU admission, and;
2. Children who remained COVID-19 suspected or probable after repeated COVID-19 negative laboratory test results and in the presence of no other positive virology and bacteriology results. This included children admitted with PIMS-TS exclusive of other anti-microbial causes[1].

As with all data collection, there is a lag in terms of reporting and therefore information presented here is **provisional and may be subject to change**.

Admission episode

If a child was transferred between PICUs or was readmitted to PICU less than 48 hours post PICU discharge then the child's care is classed as a continuous care episode. For children readmitted to PICU more than 48 hours post PICU discharge the re-admission is considered separately as a new episode of PICU care. Analysis based on PICU care episodes uses the first available patient characteristics and admission details and the last available discharge information. Treatment provided in a care episode is an aggregate of all information available. Length of stay is calculated based on PICU care episode as the difference in days between the admission date for the care episode and the discharge date from the episode; in cases where the child was re-admitted to PICU within 48 hours of PICU discharge or transferred, the calculation of length of stay includes the period where the child was not being treated within a PICU.

Length of stay in days was calculated as the difference in days between the admission date and discharge date. Days of invasive ventilation includes any day where invasive ventilation was given at any point.

Co-morbidities

Co-morbidities were reviewed for all children and grouped into major diagnostic categories:

- Inherited genetic / Chromosomal abnormalities
- Chronic Pulmonary Disease
- Congenital Heart / Cardiac Disease
- Malignancy including leukaemia, lymphoma, solid tumours
- Neurological/Developmental incl. autism, epilepsy, cerebral palsy
- Metabolic/Endocrine incl. diabetes
- Preterm

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