



UK Health
Security
Agency

Investigation into acute hepatitis of unknown aetiology in children in England

Technical briefing 4

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Introduction

The UK Health Security Agency (UKHSA) is working with the National Health Service (NHS) and the public health agencies of the 4 nations in the UK to investigate the potential cause of an unusually high number of acute hepatitis cases that was seen in children without any clear underlying conditions, in March 2022 to April 2022. There is no known association with travel, and hepatitis viruses (A to E) have not been detected in these children.

Unless otherwise stated, this technical briefing uses data cut-off of 4 July 2022. More recent case numbers may be cited in other UKHSA public updates but are not included in the analyses presented here. The 4 UK nations are conducting a coordinated investigation and data continues to be reconciled across the UK. For this reason, summary epidemiology data is presented for all 4 nations, whilst some detailed analyses can only be presented for single countries at present.

This technical briefing focuses on epidemiological, virological, and genomic analyses and findings as part of the overall investigation plan outlined in [Table 2](#) to address the working theses.

In collaboration with UKHSA, the Royal College of Paediatrics and Child Health has published [guidance for the early investigation and management of children with acute non-A-E hepatitis, with and without liver failure](#) on 27 May 2022.

Summary

This briefing is produced to share data useful to other public health investigators and academic partners undertaking related work. Although a detailed clinical case review is also taking place, that data is not shared here as, given the small number of cases, there are some risks to confidentiality.

Cases

As of 4 July 2022, there have been 274 cases of acute non-A to E hepatitis with serum transaminases greater than 500 IU/L identified in children aged under 16 years old in the UK, since 1 January 2022. This is the result of an active case finding investigation commencing in April which identified retrospective as well as prospective cases. Fifteen cases have received a liver transplant; no cases resident in the UK have died.

While new cases continue to be identified across the UK, including cases that meet the case definition and reported cases that are pending classification, there is an overall decline in rates of cases, even allowing for reporting lags.

Cases pending classification are usually those in which laboratory testing to rule out known causes of hepatitis is incomplete.

Associated pathogens and proposed hypotheses

Adenovirus remains the most frequently detected potential pathogen in cases. Amongst 274 UK cases, 258 have been tested for adenovirus, of which 170 (65.9%) had adenovirus detected.

In a UK-wide frequency matched case-control study, multivariable regression analyses with 74 cases and 225 controls indicate that cases have statistically significant higher odds of concomitant adenovirus infection compared to controls (adjusted odds ratio [OR] 35.27, 95% CI 15.23 to 81.68). This finding is supported by routine surveillance data, in particular increases in adenovirus detection and positivity in laboratory reports in young children (but not older children and adults) preceding and corresponding to the alert of the clinical phenomenon.

SARS-CoV-2 has been detected by polymerase chain reaction (PCR) testing around the time of admission in 36 out of 237 (15.2%) UK cases with available results, although in English cases only the proportion positive was lower (9.9%). To further explore the potential role of concurrent or preceding SARS-CoV-2 infection in England, analyses comparing positivity in cases to community controls in the same time period were undertaken. A comparison between cases and a random age-matched sample of emergency department admissions in children did not show any significant differences in PCR positivity. Similarly, the weekly swab positivity in cases was consistent with NHS Pillar 1 (testing based on clinical need) and community rates from the Office for National Statistics (ONS) Coronavirus Infection Survey. Furthermore, on comparing

nucleocapsid or spike protein antibody seropositivity to SARS-CoV-2 in cases to NHS age-group matched community controls, no significant differences were found.

While the association between adenovirus infection and cases is helpful in guiding further investigations into the aetiology, the lack of apparent direct toxic effect of the virus on liver tissue and other results suggests this is part of a multiple-step process. Other hypotheses are being investigated, including exposure to environmental toxins (for example, mycotoxins found in food), other viruses, and genetic factors as other 'triggers' for this phenomenon.

As mentioned in the [previous technical briefings](#), analysis of a small number of blood and liver samples with metagenomics showed a strong association with adeno-associated virus 2 (AAV2). Their role in this acute hepatitis syndrome remains unclear and investigations continue. UKHSA and Public Health Scotland have collaborated with academic partners to take forward this part of the investigation.

Research from University College London and Great Ormond Street Hospital

Using genomic, proteomic and immunohistochemical methods, [University College London and Great Ormond Street Hospital \(GOSH\) have reported on an investigation](#) of 28 cases and 136 control subjects. The data shows an association of Adeno-associated virus 2 (AAV2) at high titre in blood or liver tissue, with unexplained hepatitis in children infected in the recent Adenovirus F41 (AdV-F41) outbreak.

In 5 cases who underwent liver transplantation, high levels of AAV2 were detected in the explanted livers. Low levels of Adenovirus (AdV) and Human Herpesvirus 6B (HHV-6B), both of which enable AAV2 lytic replication, were also found in the 5 explanted livers. Four control liver biopsies were tested by PCR for AAV2, AdV and HHV6. AdV was not detected in any of the control liver samples, while AAV2 was positive in one, albeit at very low titres. HHV-6B was detected in 1 out of 4 control livers with similar cycle threshold (Ct) values to the cases.

In non-transplanted cases, AAV2 was also detected at high levels in blood from 10 out of 11 cases. AAV2 was infrequently found and at very low titres in controls, specifically in 6 out of 100 of immunocompetent and 11 out of 32 immunocompromised controls with and without hepatitis. AdV was detected in blood in 15 out of 17 of cases. Whole genomes were not obtained from the blood of any case due to high Ct values. However, GOSH report that partial sequences were identified as AdV-F41 with reads positioned across the entire viral genome and were not suggestive of a recombinant virus.

Analysis of the 5 transplanted cases in the GOSH series carried out under International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) consent, found at least one of these alleles to be present in each of the 5 cases, with HLA DRB1*0401 being present in 4 out of 5.

GOSH also report that assessment by electron microscopy, immunohistochemistry or proteomics could not find AdV or AAV2 viral particles or proteins in explanted livers, suggesting that hepatic pathology is not due to direct lytic infection by either virus.

Research from Medical Research Council UK–University of Glasgow Centre for Virus Research

Investigators at the Medical Research Council - University of Glasgow Centre for Virus Research performed a [case-control investigation](#) of 9 Scottish children hospitalised with acute non-A to E hepatitis that were enrolled in the ISARIC WHO Clinical Characterisation Protocol UK (CCP-UK) study and 58 control children from the [DIAMONDS study](#). Most of the cases had presented with a subacute history of gastrointestinal symptoms up to 11 weeks prior to onset of acute hepatitis. Using metagenomic and target enrichment sequencing and real-time PCR, AAV2 was identified in plasma of 9 out of 9 and liver of 4 out of 4 cases, but in 0 out of 13 of sera/plasma of age-matched healthy controls, 0 out of 12 children with adenovirus infection without hepatitis and normal liver function, and 0 out of 33 children admitted with hepatitis of other aetiology. Near full genomes of AAV2 were detected in all 9 cases.

AAV2 typically needs a co-infecting ‘helper’ virus to replication, most commonly adenovirus or a herpesvirus. Adenovirus (C or F) were found 6 out of 9 case samples, include 3 out of 4 liver biopsies, while human herpesvirus 6B (HHV6B) was detected in 2 out of 9 case samples, including 2 out of 4 liver biopsies. A full genome of adenovirus F41 was retrieved from a faecal sample and was found to be closest to 2 genomes reported from Germany in 2019 and 2022.

SARS-CoV-2 was not detected by PCR and sequencing in any clinical samples, including liver samples, in cases or controls. Six of 9 (67%) of the case patients had SARS-CoV-2 spike (S) or nucleocapsid (N) IgG antibodies, which is comparable to SARS-CoV-2 seroprevalence in children in Scotland during the study period (59 to 67%).

[Analysis of HLA allele positivity in 9 early Scottish cases](#) indicates that 8 out of 9 cases (88.9%) carried the HLA-DRB1*04:01 allele. In comparison, the frequency of HLA-DRB1*04:01 in a control Scottish population (n=974) is 8.9%.

In summary, acute non-A to E paediatric hepatitis in this cluster is associated with the presence of adenovirus infection and both researcher groups also detected AAV2 infection as well as indications of a potential immunological component. AAV2 may be an indicator of a recent adenovirus (or other) infection but given the strong association further investigations are merited.

Planned investigations and findings

As the number of new cases has decreased, the further investigation of these cases will now be undertaken in a research framework. Future findings will be shared through peer-reviewed scientific publications instead of technical briefings. As part of the legacy arrangements from this outbreak, enhanced monitoring of non-A to E hepatitis will occur with NHS clinicians and specialist sites to identify any future similar events.

Part 1. Case definitions and summary data for cases in the UK

1.1 Case definitions

Case definitions in all UK nations have been revised and harmonised to facilitate clinical reporting.

England, Wales, Northern Ireland case definitions

Confirmed

A person presenting since 1 January 2022 with an acute hepatitis which is not due to hepatitis A-E viruses, or an expected presentation of metabolic, inherited, or genetic, congenital, or mechanical cause* with serum transaminase greater than 500 IU/L (Aspartate Transaminase-AST or Alanine Transaminase -ALT), who is 10 years old and under.

Possible

A person presenting with an acute hepatitis since 1 January 2022 with an acute hepatitis which is not due to hepatitis A-E viruses or an expected presentation of metabolic, inherited or genetic, congenital* or mechanical cause** with serum transaminase greater than 500 IU/L (AST or ALT), who is 11 to 15 years old.

Epi-linked†

A person presenting since 1 January 2022 with an acute hepatitis (non-hepatitis A to E) who is a close contact of a confirmed case.

Notes

* Wales case definition also excludes cases of other known critical illness.

** Cases should be reported based on clinical judgement if some hepatitis A-E virus results are awaited, or if there is an acute or chronic hepatic presentation with a metabolic, inherited or genetic, congenital, mechanical, or other underlying cause (in Wales, this also excludes known critical illness). If hepatitis A-E serology results are awaited, but other criteria met, these will be classified as 'pending classification'.

† A person who is epi-linked but also meets the confirmed or possible case definition will be recorded as a confirmed or possible case and their epi-link noted in their record. This prevents double-counting of cases.

Scotland case definition

Confirmed

A person presenting with a serum transaminase greater than 500 IU/L (AST or ALT) without any known cause‡, who is 10 years of age and under or a contact of any age of a confirmed case, since 1 January 2022.

Note

‡ Excluding hepatitis A to E, cytomegalovirus, and Epstein-Barr Virus, metabolic, inherited or genetic, congenital, mechanical, or other underlying cause.

1.2 Summary data on cases in the UK

As of 4 July 2022, there are 274 cases (263 confirmed and 11 possible) cases in the UK. Of these, 195 cases (186 confirmed and 9 possible) are resident in England, 36 (all confirmed) in Scotland, 19 (all confirmed) in Wales and 24 (22 confirmed and 2 possible) in Northern Ireland (see [Figure 1](#)). Between 21 January 2022 and 4 July 2022, 15 children in the UK meeting the case definition have required liver transplantation. For the purposes of this summary, all confirmed and possible cases will be referred to as cases. The public health agencies of the 4 nations continue to work with the NHS to classify reported case-patients who have incomplete laboratory information (referred to as 'pending').

1.3 Outcomes

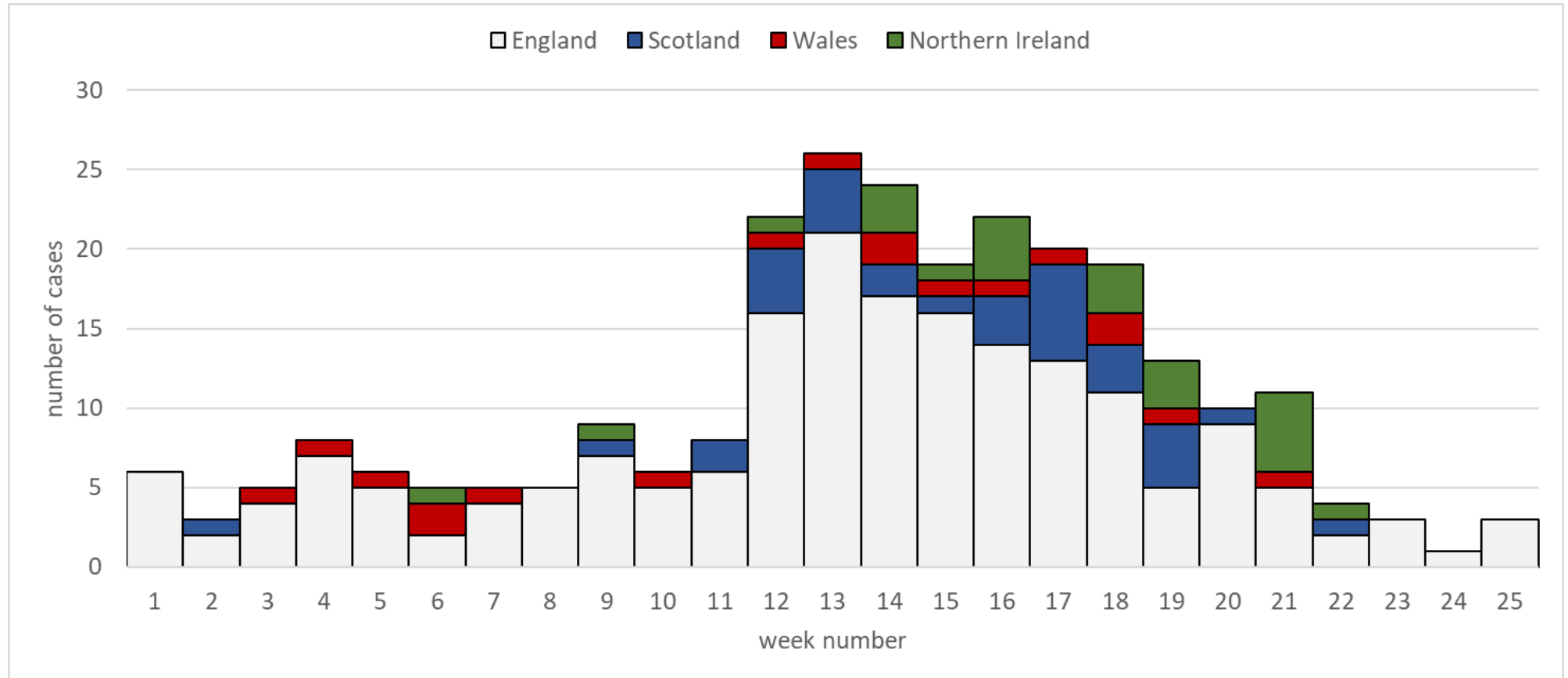
Clinical outcomes for 274 cases (at time of clinical notification or interview with parent or guardian) are shown in Table 1. Where required, cases are being followed up for outcome at 28 days after presentation to health services. No cases have died. Of the 274 cases, 225 reported hospitalisations, of whom 15 have required transplantation. As the case definitions require high transaminases, a milder disease presentation may have not been reported or progressed.

Table 1. Outcome status for UK cases as of 13 June 2022

Outcome	Number	Percentage
Died	0	0.0
Not hospitalised	2	0.7
Hospitalisation reported	225	82.1
Discharged or fully recovered	140	62.2
Where hospitalised, discharge status not yet ascertained:	85	37.8
up to 28 days since presentation	41	
29 or more days since presentation	42	
date of hospitalisation not available	2	
No information	47	17.2
Total cases	274	100

Figure 1. Cases by week of presentation, 1 January to 4 July 2022

Supplementary data is not available for this figure.



Date not available for 6 cases in England, 1 case in Northern Ireland and 1 case in Wales.

Week is based on hospitalisation date where available, then date of arrival at emergency care department where available, then date of presentation to healthcare.

1.4 Possible exposures

Investigations have included interviews of parents conducted by public health specialists to assess a broad range of different exposures (trawling questionnaires), as reported in the [Acute hepatitis: technical briefing 1 and 2](#).

Following the initial exploratory trawling questionnaire, a focused enhanced surveillance questionnaire and structured interview has been carried out with parents and guardians to get more detailed information on course of illness, medical history and preceding household illness, attendance at childcare settings and specific food and diet items. While these are ongoing, there are no new developments or findings to report. A handful of cases have been declassified where further clinical information indicated an underlying clinical condition that was a likely cause of acute hepatitis.

Part 2. Update on planned investigations

The investigations include clinical case investigation in the NHS, public health pathogen investigations, and research investigations under the International ISARIC Clinical Characterisation [Protocol](#) with full appropriate consent. ISARIC is funded by UK Research and Innovation and the National Institute for Health Research.

2.1 Additional investigations and status

Table 2. Update on planned investigations

	Investigation	Lead	Status
Analytic epidemiology	Case-control study (with residual whole blood samples from hospitalised children for controls) to test association of hepatitis with adenovirus infection	UKHSA	Completed: peer-review publication in progress Protocol published on UKHSA K-Hub.
	Analysis to investigate co-factors associated with hepatitis in cases	UKHSA	Commenced
	Analysis to investigate factors (demographic and clinical features) associated with severe outcome in cases, stratified by adenovirus infection (case-case study)	UKHSA	Commenced
Surveillance for liver syndromes in children	Enhanced surveillance for severe acute hepatitis in children through British Paediatric Surveillance Unit, and referrals to paediatric liver units	UKHSA	Commenced
Mechanism of liver injury	Investigations on liver tissue to include electron microscopy, further histopathology	NHS	Histopathology review complete; additional investigations planned

	Investigation	Lead	Status
	review, T cell subset analysis		
Pathogen investigations	Adenovirus whole-genome sequencing from cases and community samples	UKHSA and GOSH	Underway with first reports available
	Metagenomic sequencing of blood and liver tissue from cases	UKHSA, GOSH, ISARIC4C (CVR Glasgow)	Underway with first reports available
	Viral culture of adenovirus and phenotypic characterisation including assessment of hepatotropism in vitro	UKHSA and academic partners	Viral cultures of clinical materials negative to date
	Adenovirus and SARS-CoV-2 serology of cases	UKHSA	Testing underway
	SARS-CoV-2 sequencing in positive cases	UKHSA	Reported where available
Host characterisation	Harmonised clinical data collation and analysis	ISARIC4C with partners	Recruiting
	Host genetic characterisation	ISARIC4C in partnership with GenOMICC	Recruiting
	Immunological characterisation including T-cell activation studies	ISARIC4C with partners	Recruiting
	Transcriptomics	ISARIC4C with partners	Under consideration

Part 3. Cases in England: descriptive epidemiology and clinical data

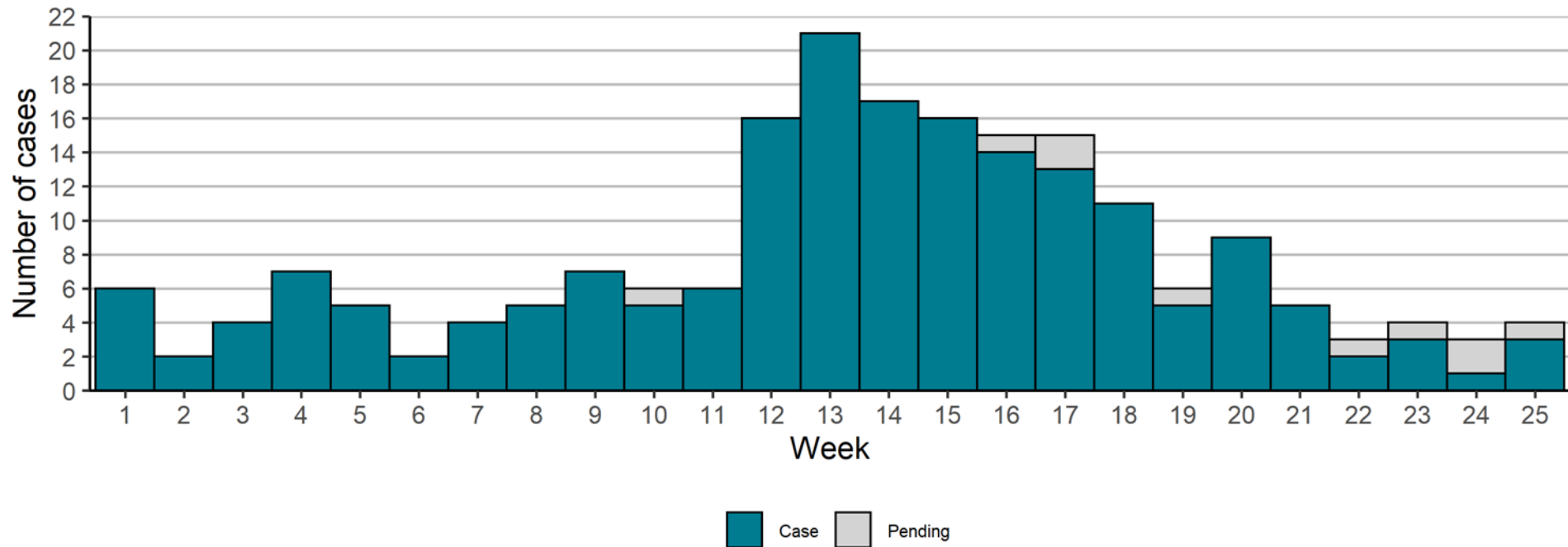
3.1 Cases in England

As of 4 July 2022, there were 195 (186 confirmed and 9 possible) cases in England. Forty-one potential cases in England are awaiting classification with the outcome of investigations (see [Figure 2](#)). Cases are predominantly aged between 3 and 5 years old (106; 54.4%), median age 3 (interquartile range: 2 to 5 years) and 50.3% are female. The majority are of White ethnicity (163 out of 195; 83.6%) where information was available. Eleven cases who were resident of England required a liver transplant.

In England, 74.3% (124 out of 167) of all notifications that were initially classified as pending were later classified as a case (n=96) or assessed as not meeting the incident case definition (n=28) when more information became available. A handful of cases initially classified as confirmed or possible cases were assessed as not meeting the incident case definition.

Figure 2. Notifications by week of presentation to care and investigation status (case and pending classification) in England, 1 January to 4 July 2022

Supplementary data is not available for this figure.



37 cases excluded due to date not being reported.

Week is based on hospitalisation date where available, then date of arrival at emergency care department where available, then date of presentation to healthcare. A total of 37 notifications (6 cases and 31 pending classification) are excluded due to date not being reported. Pending cases are those which have been notified to UKHSA but whose hepatitis A-E serological results are awaited.

3.2 Clinical features

The most common presentation reported in cases remains jaundice (135 out of 195; 69.2%) followed by vomiting (113 out of 195; 57.9%). Pale stools were also frequently reported (40.5%). Gastro-intestinal symptoms were commonly reported at presentation including diarrhoea (41.5%), abdominal pain (38.5%) and nausea (26.2%). Additionally, lethargy (47.7%), fever (23.1%) and less frequently, respiratory symptoms (17.9%) were reported. Note that the denominator includes those who have reported the symptom, absence of symptom and unknown (missing information).

Part 4. Cases: pathogen investigations

4.1 Potential pathogens detected through routine clinical testing: all UK cases

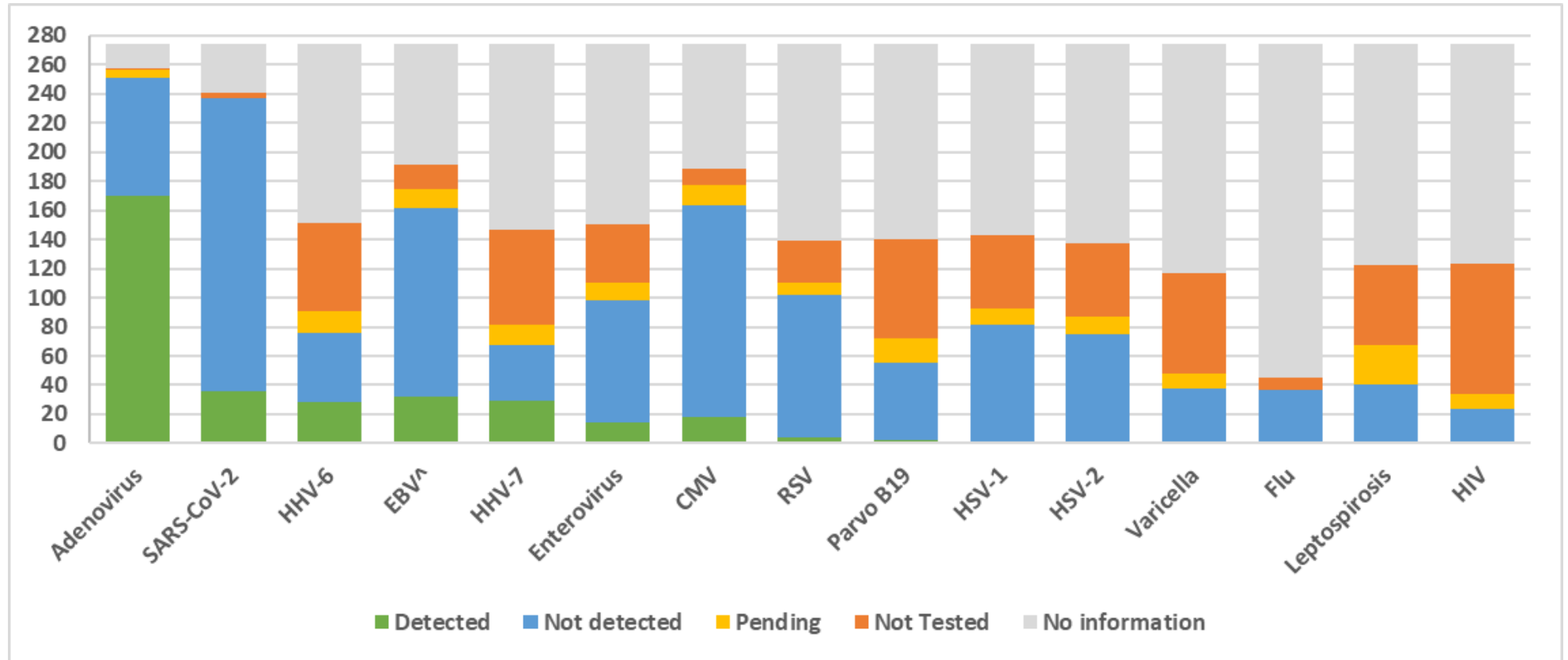
Cases have been tested for pathogens at or around the time of admission. Test choice is a local clinical decision and not all cases have been tested for the same pathogens (from [8 April 2022](#), UKHSA recommended a panel of tests to perform on all cases). All hospital admissions were recommended to have SARS-CoV-2 PCR tests. Testing information is gathered from a variety of sources, including direct reports from clinicians, direct reports from laboratories, information from UKHSA reference laboratories and from linkage to data sources including Second Generation Surveillance System (SGSS) and the COVID-19 Unified Sample Dataset.

Adenovirus remains the most common pathogen detected around the time of admission or presentation ([Figure 3](#)). Of 274 UK cases, 251 were tested for adenovirus. Adenovirus was detected in 170 (67.7%), and not detected in 81 (32.3%) cases. Six cases have results pending, one was not tested, and no information is available for 16 cases. On a review of cases who were negative for adenovirus, just under a quarter did not have a blood sample tested (the preferred sample type).

A more detailed breakdown of pathogen results for cases, where available to UKHSA, is provided in [Figure 3](#).

Figure 3. Pathogens tested for and results in cases in UK

Supplementary data is not available for this figure.



SARS-CoV-2 testing presented here is based on testing around hospital admission or attendance.

[^] including one past positive.

4.2 Adenovirus

In England, 183 of 195 cases were tested for adenovirus, and adenovirus was detected in 122 (69%) cases, where results are available (Table 3). Further details on adenovirus testing can be found in [technical briefing 2](#).

For cases in England, adenovirus was detected more commonly in blood or serum samples from cases (106 out of 149; 71.1%), than in stool (30.0%) or respiratory (22.4%) samples. However, a consistent sample set has not been tested for most cases (see Table 3).

Of the 55 cases where adenovirus was not detected, 18 had no testing on blood reported (7 with no sample type reported). In the previous technical briefing, we reported that whole blood (whole blood/serum/plasma combined) is the most relevant sample type for the syndrome, and there are performance differences between assays in clinical use. Therefore, the presence of adenovirus cannot be definitively excluded in sample types other than blood when it is not detected.

Fifty-two of the 106 cases with adenovirus in blood have been successfully subtyped, of which 48 (92.3%) are type 41F. Other subtypes included adenovirus type 1, 2 and 5.

Of the 11 England-resident patients who required a liver transplant, 9 out of 10 who were tested for adenovirus in blood samples had the virus detected. The case where adenovirus was not detected had a serum/plasma sample tested rather than whole blood. Samples from 6 cases who had a liver transplant were successfully subtyped, as 41F.

Table 3. Adenovirus testing* results of cases resident in England

Adenovirus testing	Number of cases	Number of cases with each sample type (there may be multiple samples per case)			
		Blood	Stool	Respiratory	Other or unknown
Positive (% positivity, excluding pending)	122 (68.9%)	106 (71.1%)	24 (30.0%)	15 (22.4%)	21 (46.7%)
Negative	55	43	56	52	24
Pending	6	5	11	8	14
Total tested	183	154	91	75	59

* Testing locations: any diagnostic laboratory.

Adenovirus sample analysis

The summary of findings as of 12 July 2022 in different sample types is based on samples submitted (real world data). There is considerable variation in samples that have been

submitted for each case, with the majority of samples being blood. Complete sets of blood respiratory and faecal samples are available for only a small proportion of cases. Samples submitted early during the investigation were tested using 2 different PCR targets, Hexon gene PCR and Fibre gene PCR. Hexon gene PCR target is a pan adenovirus detection assay whereas the Fibre gene PCR detects enteric adenoviruses 40 and 41. PCR detection tests are based on published studies ([Heim and others, 2003](#) and [Tiemessen and Nel, 1996](#)).

Using the dual PCR target approach, there is good concordance for detection of adenovirus in blood using both targets, showing a similar distribution of Ct values for detection. As the investigation has developed, testing of cases has been streamlined to a single Hexon gene PCR target followed by sequence analysis. Figure 4 shows the detection of adenovirus in different sample types submitted from cases from all over UK. A total of 125 out of 214 samples (58.4%) in blood, 11 out of 39 (28%) in faecal samples, 9 out of 321 (29 %) in respiratory samples and 4 out of 4 (100%) liver tissue samples. This pattern of detection has been reported in previous technical briefings and encompasses the data provided for England above. Characterisation of detected adenovirus by Hexon gene sequence analysis ([Figure 5](#)) demonstrates that adenovirus subtypes detected in blood of cases are majority Adenovirus 41 (96%), although type 2 and 7 subtypes have occasionally been detected in blood (less than 5%). In contrast, the Adenovirus subtypes detected in respiratory or faecal samples taken from cases of hepatitis reflects a diversity of subtypes but is rarely (less than 5%) an enteric Adenovirus subtype (even when Adenovirus 41 has been detected in blood. This suggests coinfection with different Adenoviral subtypes in a proportion of cases. Detailed comparison of clinical history of cases demonstrating co-infections has not been undertaken. Analysis of explanted livers from 4 transplanted cases by PCR demonstrated detection of adenovirus 41 in all cases, with Ct values of 30 to 36. Taken together, these results suggest that the syndrome is closely associated with the presence of enteric adenovirus 41 in blood.

Figure 4. Hexon gene detection from case (N=125) samples

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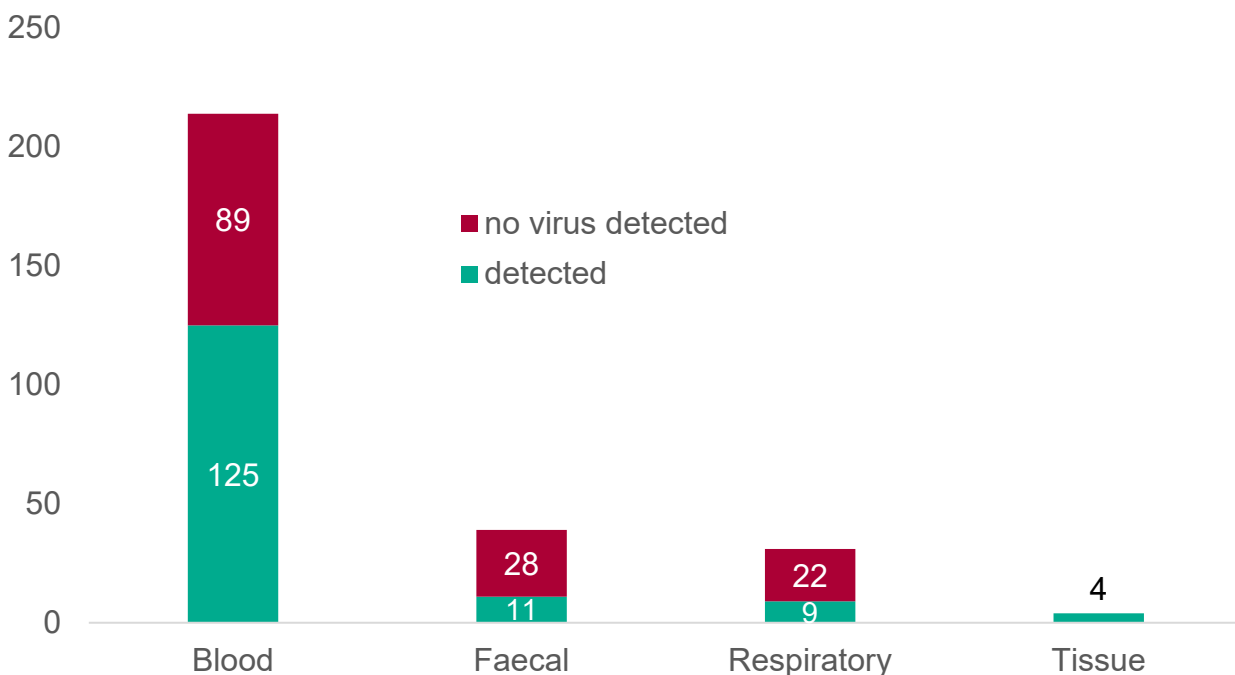
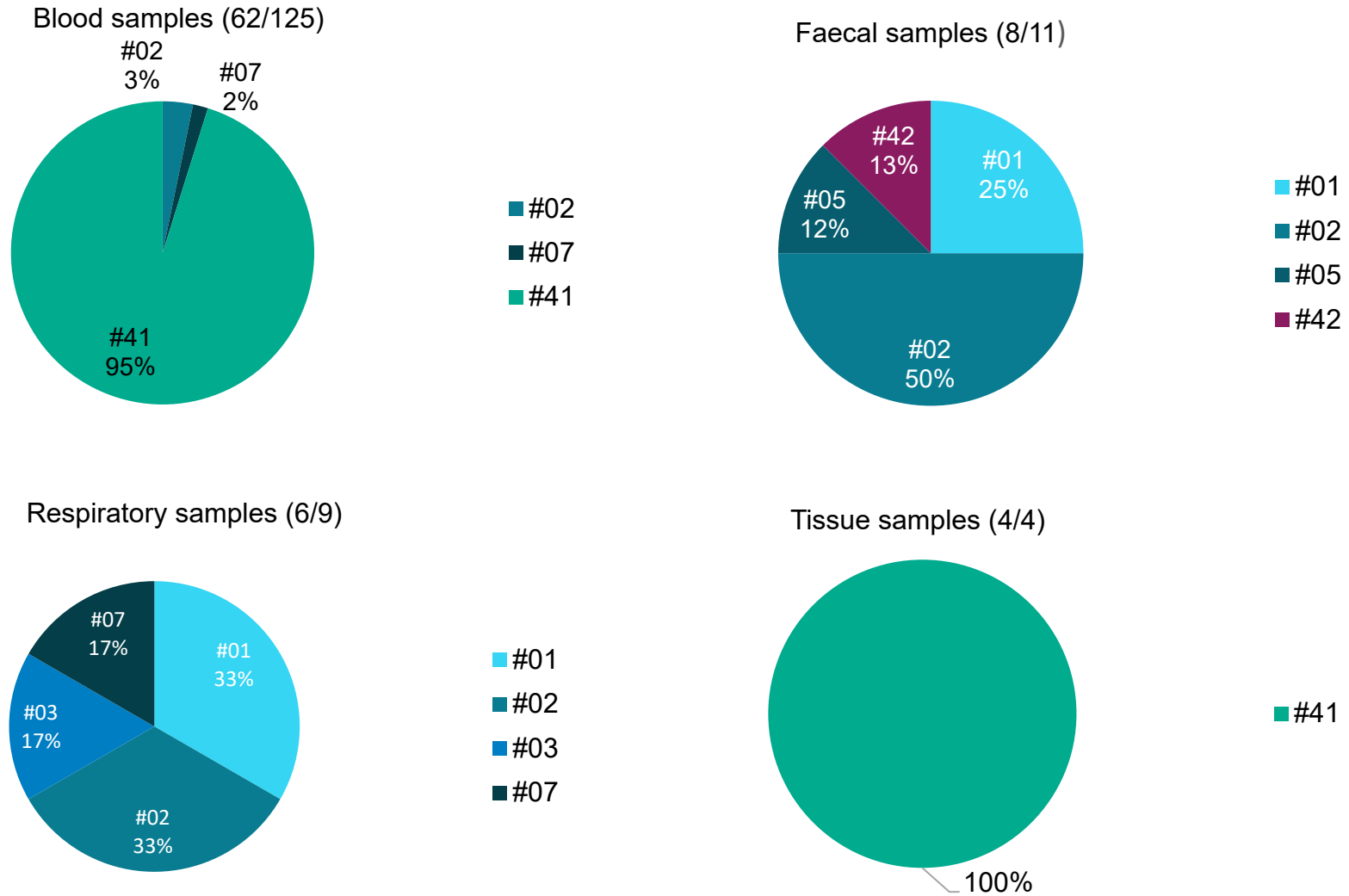


Figure 5. Diversity of adenovirus subtype in case samples. Hexon sequencing result following detection by PCR

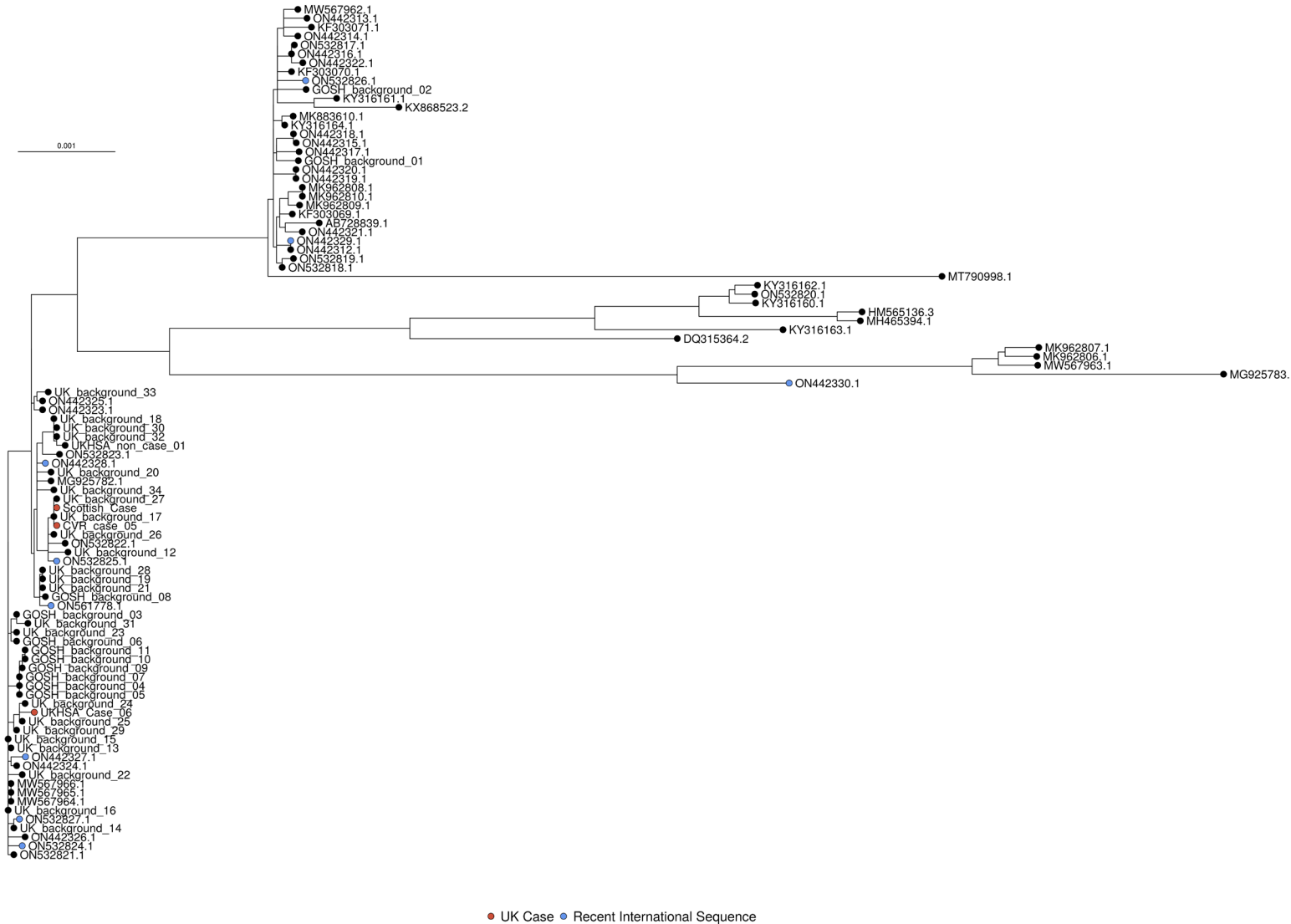
Supplementary data is not available for these figures.



4.3 Metagenomics and whole-genome sequencing of adenovirus

Whole-genome sequencing (WGS) of adenovirus is ongoing. Two additional sequences from cases typed as adenovirus 41F have been produced since the last WGS update, meaning 3 are now available in total. These have been added to the phylogenetic tree ([Figure 6](#)). This tree contains background adenovirus 41F whole genome sequences gathered; from Genbank, from UK from patients who do not meet the hepatitis case definition (currently unpublished), as well as (unpublished) genomes provided by GOSH. The 3 UK sequences are highlighted in red. Sequences highlighted in blue represent international sequences gathered from Genbank with an annotated sample date in 2022.

Figure 6. Phylogenetic tree containing background whole genome sequences of ADV 41F gathered from Genbank (black) as well as UK currently unpublished sequences (black). Three UK case sequences (red) and recent (2022) international sequences (blue). Tree is rooted on ADV C (not included in figure)



There are limited whole genome sequences from cases available, however, the 3 available sequences sit amongst background cases from the UK and internationally. It is currently unknown if the background international cases meet the hepatitis case definition, especially those highlighted in blue in [Figure 6](#).

Single nucleotide polymorphism (SNP) analysis has been performed on the whole genome sequences of the 3 UK case sequences. The 3 sequences do not share any detected SNPs that are not also present in non-case background 41F sequences.

Metagenomics

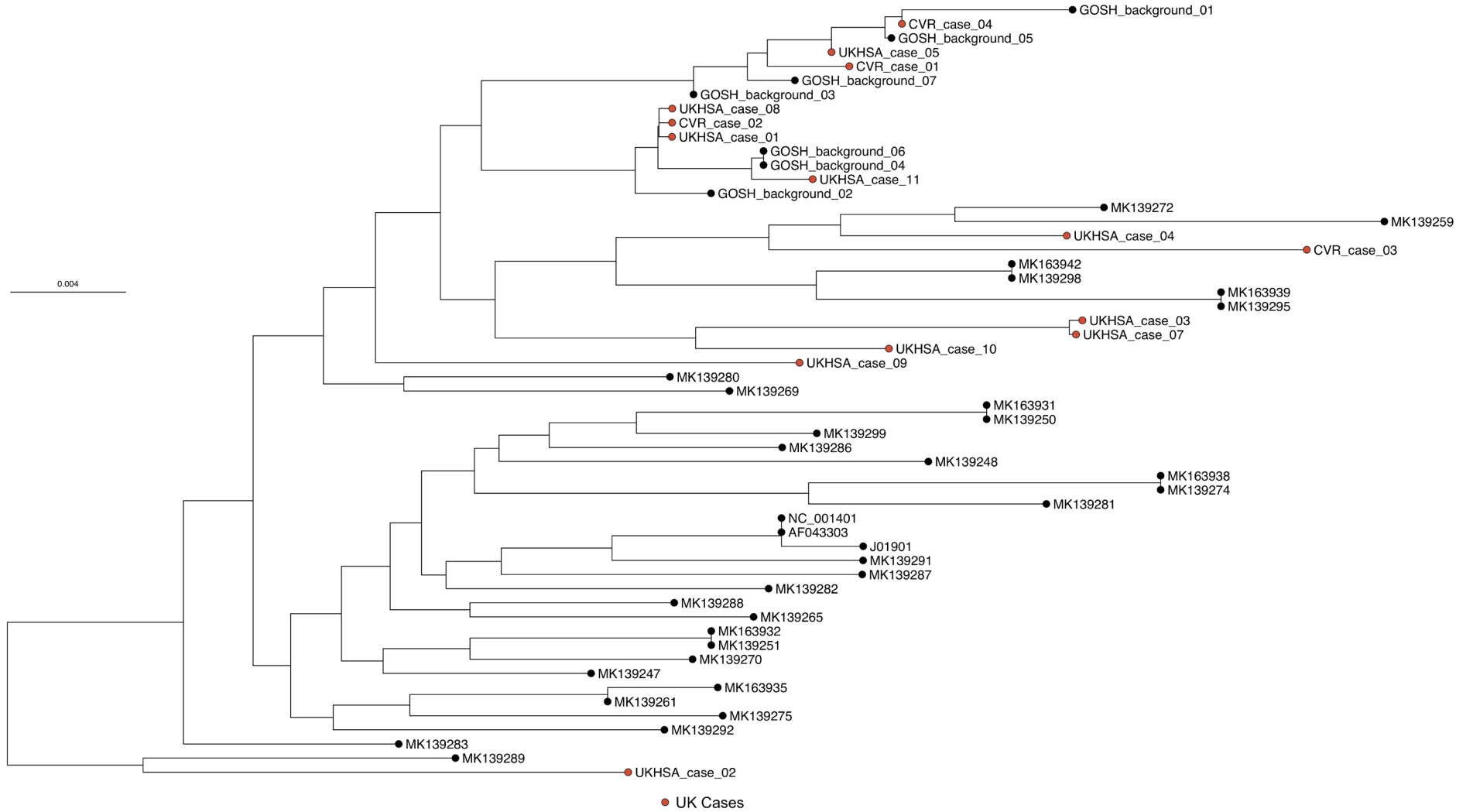
Metagenomics was performed on a limited number of English case samples at GOSH. Metagenomics results were gathered from 11 samples, representing 10 cases (1 serum, 4 blood, 5 liver). One sample's results are still pending analysis, and another failed to detect any pathogens in DNA sample (RNA analysis failed). In the remaining 9 samples more than 60 reads of AAV-2 were detected in all 9 samples (representing 8 cases, 1 serum, 4 liver, 3 blood). HHV-6 was detected in 3 samples (3 cases), 2 with low numbers of reads and 1 with greater than 200 reads. HHV-6 was PCR confirmed in all 3 samples. Out of 10 cases, HHV-6 was confirmed by PCR in 8, there was no material remaining for sampling in one, and HHV-6 was not detected in one. Two samples with metagenomics analysis performed also contained low read numbers of Torque teno virus, and one of these 2 also identified reads of Astrovirus.

After detection of AAV2 and HHV-6 through metagenomics, targeted WGS was performed on these samples, and additional samples not tested through metagenomics by GOSH. The following sections detail the WGS available for these viruses.

Adeno-associated virus 2 (AAV2)

AAV2 coverage was of high in all but 2 samples, with over 85% coverage of the AAV2 genome from 30 read depth consensus sequences. GOSH_background_07 and CVR_case_04, are poorer quality, with less than 50 percent of the genome covered. Phylogenetic analysis of these sequences alongside non-case background sequences from GOSH and international sequences from Genbank, does not show clustering of the UKHSA or CVR cases together (red in [Figure 7](#)). Additionally, most of the cases are dispersed around the background UK sequences obtained from recent non-case samples.

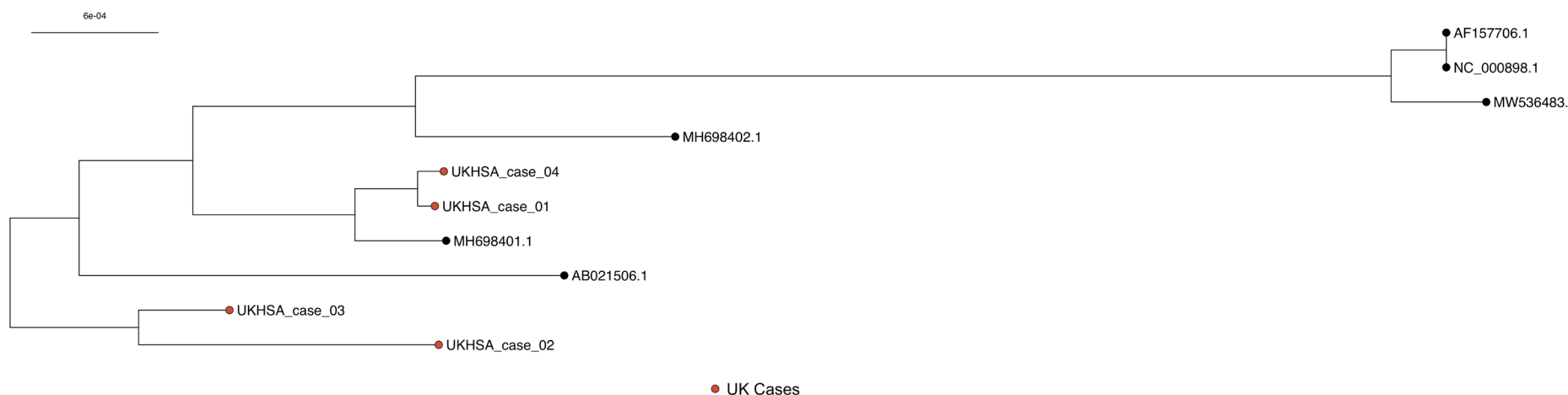
Figure 7. Phylogenetic tree containing background whole genome sequences of AAV2 gathered from Genbank as well as UK currently unpublished sequences (black). Ten UKHSA cases and 4 CVR cases (red). The tree is rooted on AAV1 (not included in figure)



Human HHV6

HHV6 consensus sequences varied in sequence quality and consensus coverage of the HHV6B genome. Two sequences have high genome coverage at over 80 percent (UKHSA_case_01 and UKHSA_case_04). One sequence had moderate genome coverage of 65% (UKHSA_case_02). UKHSA_case_03 sequencing coverage was low at less than 50% of the genome. Phylogenetic analysis indicates that the cases (red in Figure 8), do not cluster in the tree. There is limited non-case background samples of circulating virus for this investigation.

Figure 8. Phylogenetic tree containing background whole genome sequences of HHV6B gathered from Genbank (black) and 4 CVR cases (red). The tree is rooted on HHV6A (not included in figure)



UK Genomes from all viruses related to cases (from metagenomics and WGS) are being processed for upload to Genbank. These sequences will be uploaded with metadata (where available) as outlined on [GitHub](#). [Further information on the proposal](#) can be found on the UKHSA Genomics GitHub page.

Preliminary findings from a UK case-control study to investigate association of adenovirus with acute hepatitis (non-A to E)

As adenovirus has been identified in cases, including those with severe outcome of transplantation, a UK-wide case control study was designed to test the hypothesis that adenovirus is associated with acute hepatitis (non-A to E) in young children. The protocol has been published on UKHSA K-Hub. A frequency-matched case-control study was rapidly implemented in response to the incident in May 2022. Cases were included if they met the incident case definition, had adenovirus testing done on a blood/serum sample, and were aged 1 to 10 years. Controls were identified through UK laboratories where a residual sample of blood or serum had been taken on a child aged 1 to 10 years at the time of hospital presentation for an acute illness, which was not hepatitis. Controls were frequency matched by age, month of sample and region with up to 4 controls to case to allow for attrition due to insufficient samples. Control samples were tested for adenovirus infection. SARS-CoV-2 test results and demographics were also obtained for cases and controls by data linkage.

Preliminary findings from multivariable regression analyses with 74 cases and 225 controls indicate that cases have statistically significant higher odds of concomitant adenovirus infection compared to controls (adjusted odds ratio [OR] 35.27, 95% CI 15.23-81.68). In addition, cases did not have a higher likelihood of concomitant or recent infection with SARS-CoV-2 compared to controls. Full findings will be published in due course.

4.4 SARS-CoV-2

For cases resident in England, 16 cases tested positive for SARS-CoV-2 on admission (PCR or lateral flow device), of 162 cases with available test data (9.7%). An additional 3 cases tested positive in the 8 weeks prior to admission and were negative on admission giving a total period prevalence of 19 out of 164 (11.6%). Eight cases were co-infected with adenovirus and SARS-CoV-2.

Six cases have WGS for SARS-CoV-2 from a sample within 8 days of hepatitis case presentation. One case has had 2 genomes sequenced and assigned as VOC-21NOV-01 (lineage BA.1.17). The remaining 5 cases have been assigned as VOC-22JAN-01 (2 lineage BA.2, 3 lineage BA.2.3).

SARS-CoV-2 positivity in cases compared to a random sample of emergency admissions

Of the cases that attended an emergency department and were tested for SARS-CoV-2, 8.2% (CI: 3.3 to 13.1) tested positive on admission (2 days prior to admission, up to 2 days post admission). This is different to the positivity above which uses wider criteria for testing and is therefore also in a wider number of cases. For comparison, a random sample of all emergency department admissions in children aged 0 to 15 years during the same time period was selected with their age distribution weighted to match the age distribution of the cases.

From the 1 January to 1 June 2022 there were 122 hepatitis cases linked to a SARS-CoV-2 test result. The total number of children (based on unique NHS numbers) aged 0 to 18 admitted to hospital during this time was 193,011. From this, 54,037 patients were selected using matching weights for the age. Positive SARS-CoV-2 tests were identified through linkage of the patient NHS number to the Second-Generation Surveillance System (SGSS) and negative tests through linkage to the Unified Sample Dataset (USD).

There were similar testing rates in both the cases admitted to hospital through an emergency department (53.7%) and the random age-weighted sample (48.5%). Positivity when tested on admission in the random sample was broadly consistent at 7.2% (CI: 6.9 to 7.5) supporting earlier analysis that cases are no more likely to test positive for SARS-CoV-2 than other children presenting to emergency departments.

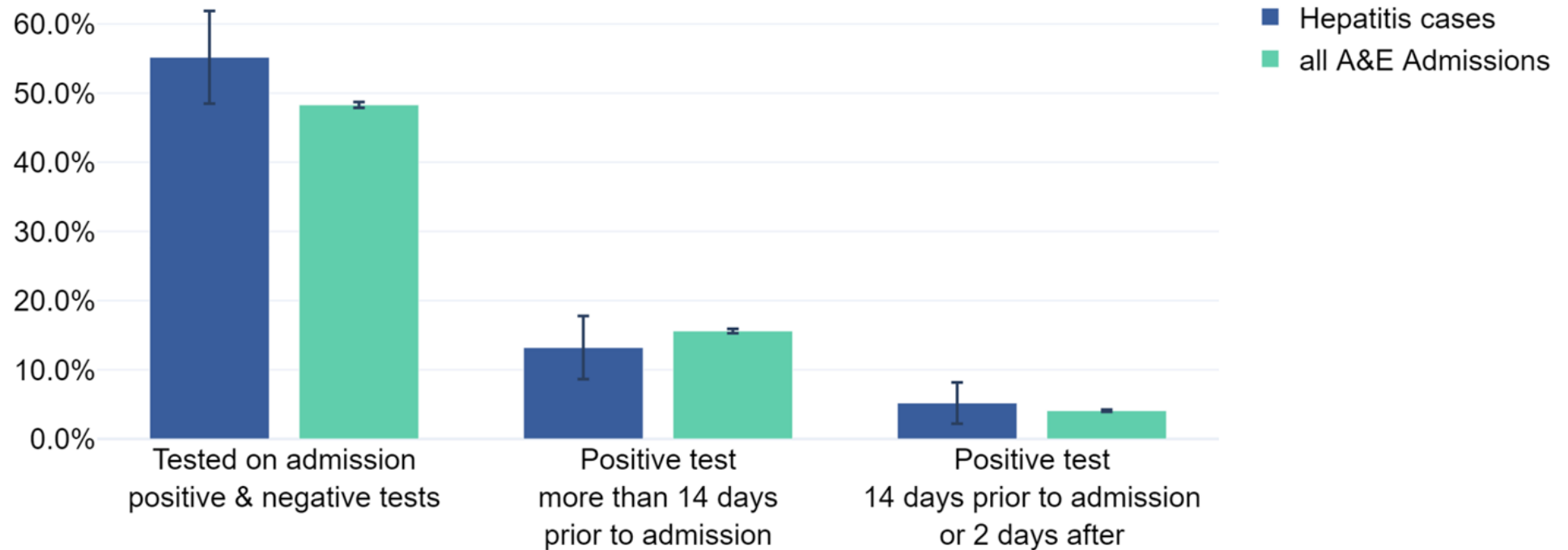
For cases, 11.9% tested positive prior to admission (any positive test more than 14 days before admission) compared to 15.6% in the random age-weighted sample. There was no statistical significance between these groups indicating that cases are no more likely to have previously tested positive for SARS-CoV-2 than other children presenting to emergency departments.

Table 4. SARS-CoV-2 testing rates and proportion of patients testing positive for acute hepatitis cases, 1 January to 1 June 2022

Category	Hepatitis cases (%)	All A&E admissions (%)
Tested on admission	53.7% (CI: 47.3 to 60.2)	48.5% (CI: 48.1 to 48.9)
Positive test 14 days prior to admission or 2 days after	4.4% (CI: 1.7 to 7.1)	4.0% (CI: 3.8 to 4.2)
Positive test more than 14 days prior to admission	11.9% (CI: 7.7 to 16.1)	15.6% (CI: 15.3 to 15.9)

Figure 9. SARS-CoV-2 testing rates and proportion of patients testing positive for acute hepatitis cases, 1 January to 1 June 2022

Supplementary data is not available for this figure.



Error bars represent 95% confidence intervals of the standard error of proportion.

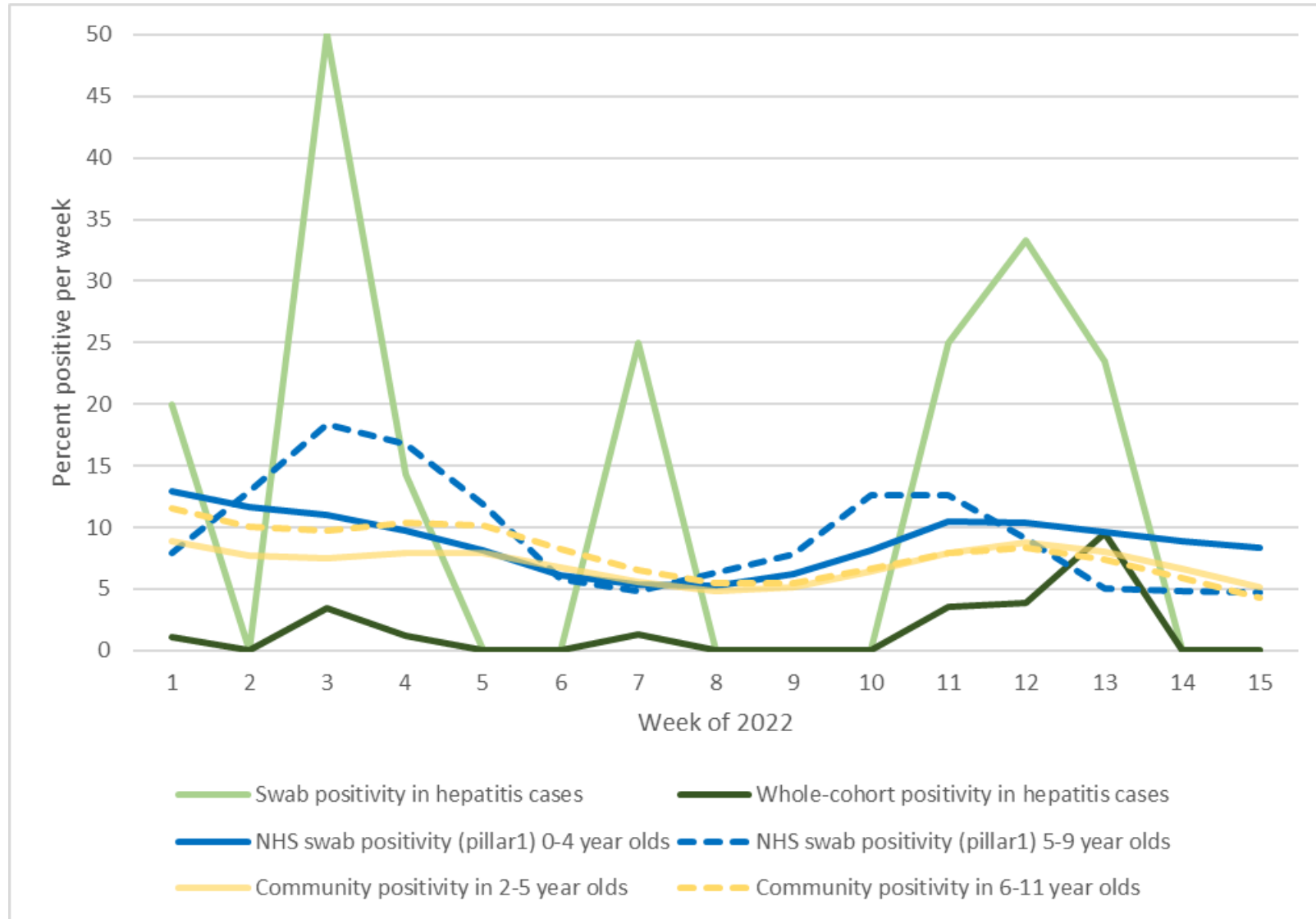
Positivity: proportion of cases with a positive test result.

Weekly SARS-CoV-2 PCR positivity in cases compared to community and healthcare controls

Weekly SARS-CoV-2 positivity in respiratory swabs was compared between hepatitis cases and 2 different control groups. The weekly number of coronavirus (COVID-19) positive results for hepatitis cases was converted into a percent of the number of swabs known to have been taken that week (swab positivity), and as a percent of the total number of children who would become hepatitis cases, not yet in hospital at the start of that week, (whole cohort), based on known cases as of week 16, 2022. These were plotted ([Figure 10](#)) against relevant age groups' weekly swab positivity in NHS pillar 1 (testing based on clinical need) and modelled weekly positivity in the community (prepared by the University of Oxford from ONS COVID-19 Infection Survey data).

The weekly percentage and variability in SARS-CoV-2 positivity in hepatitis cases is considered consistent with NHS and community positivity rates.

Figure 10. SARS-CoV-2 positivity in hepatitis cases in England (as positivity per swab and positivity in the whole cohort of cases), in NHS pillar 1 testing and in the community (using ONS COVID-19 Infection Survey data) weeks 1 to 15, 2022

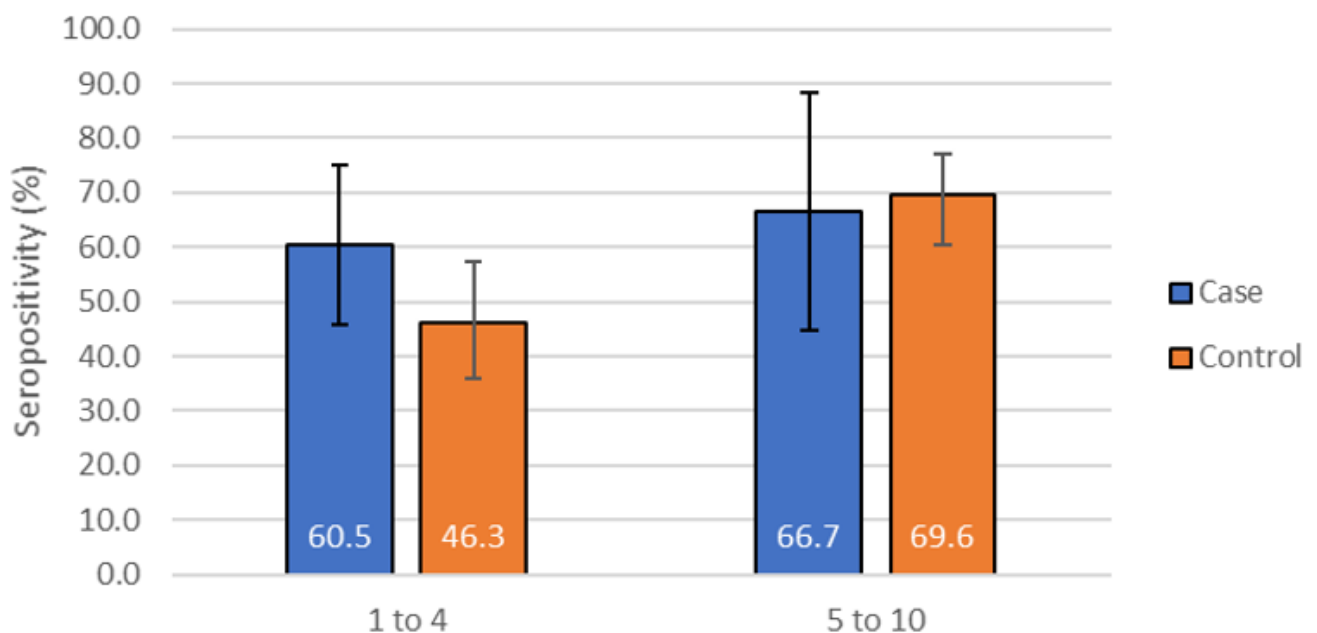


SARS-CoV-2 antibody (sero)prevalence in cases compared to a random sample of community controls

Serum from 61 cases and 627 residual serum samples from unlinked, anonymous, age-matched NHS patients (controls) was tested at UKHSA laboratories for SARS-CoV-2 nucleocapsid or spike protein antibody. Figure 11 below shows that there is no statistical difference in antibody positivity between hepatitis cases and NHS patient controls in either 1 to 4 year olds or 5 to 10 year olds.

Figure 11. SARS-CoV-2 nucleocapsid serum antibody positivity in hepatitis cases and NHS patient controls by age-band

Supplementary data is not available for this figure.



Part 5. Cases: toxicology investigations

As of 5 July 2022, a total of 307 samples have been received, with 230 samples from 57 confirmed cases. The rest (77) are age-matched control samples from the biobank. Of these, 148 out of 223 plasma or serum samples are from 52 confirmed cases, whilst 43 whole blood samples are from 21 confirmed cases and 39 out of 41 urine samples are from 35 confirmed cases.

Of these samples, 69 were taken within 5 days of presentation, 27 between 5 and 10 days from presentation and 26 were taken more than 10 days from presentation. The timing of the remainder is unknown. Additionally, 4 liver samples have been received from transplant cases.

Paracetamol and fluconazole have been investigated in more detail because of their known relationship with liver injury dependent on dose and individual susceptibility but current evidence indicates they are likely to have been therapeutically used and not causative.

Some elevated levels in metals were observed compared with published data from national surveys in the USA and Canada. We have compared these results to samples obtained for UK biomonitoring studies and concluded that the levels of metals detected in the whole blood and urine analyses are not likely to be causative.

Mycotoxins are known to cause liver injury with a pathology similar to that seen in cases. We are currently investigating mycotoxins which can be found in food, and are known to cause hepatic disease, by developing targeted quantitative methods for a range of mycotoxins previously associated with hepatotoxicity using control serum and urine ready to apply to case samples. It is extremely likely that mycotoxins will have already been metabolised and excreted before samples were collected on admission, therefore UKHSA is also developing assays for the longer-lived protein adducts.

Part 6. Relevant surveillance data

6.1 Increases in laboratory reports of new diagnoses and exceedances in potentially relevant pathogens

Laboratory data on pathogens reported by the NHS and public health laboratories through SGSS are routinely monitored for changes in trends and statistical exceedances. Increases in new laboratory diagnoses and statistical exceedances have been observed in adenovirus, enterovirus, human metapneumovirus, rhinovirus and norovirus in under 10 year olds since the end of 2021. There has been a marked exceedance of adenovirus, which appears to be driven by adenovirus in faecal samples and in the 1 to 4 year old age group, although the number of laboratory diagnoses is decreasing now.

Adenovirus positive test reports from diagnostic laboratories

Adenovirus positive tests from routine clinical testing are recorded in SGSS and can be analysed by UKHSA. The testing patterns for adenovirus are likely to be variable, influenced by clinical presentation, and as it is not a notifiable disease there is also likely to be under-reporting.

Reports in England of positive adenovirus tests from any site in 1 to 4 year olds are higher compared to the previous 5 years (see [Figure 12](#)). Between November 2021 and April 2022, approximately 200 to 300 specimens of adenovirus were reported into SGSS per week compared to 50 to 150 per week in the pre-pandemic period and less than 50 per week between March 2020 and May 2021. The increase in younger age groups begins in November 2021. This pattern is also seen specifically in enteric samples in the same age group (see [Figure 13](#)). Since the peak in April 2022, there is now a clear trend of declining enteric adenovirus detections, with a less pronounced plateauing for all specimen types, although very recent data may reflect incomplete reporting. When these numbers are converted to rates (per 100,000 people) of adenovirus detection in faecal samples, the same trend of decreasing rates are observed in 1 to 4 year olds.

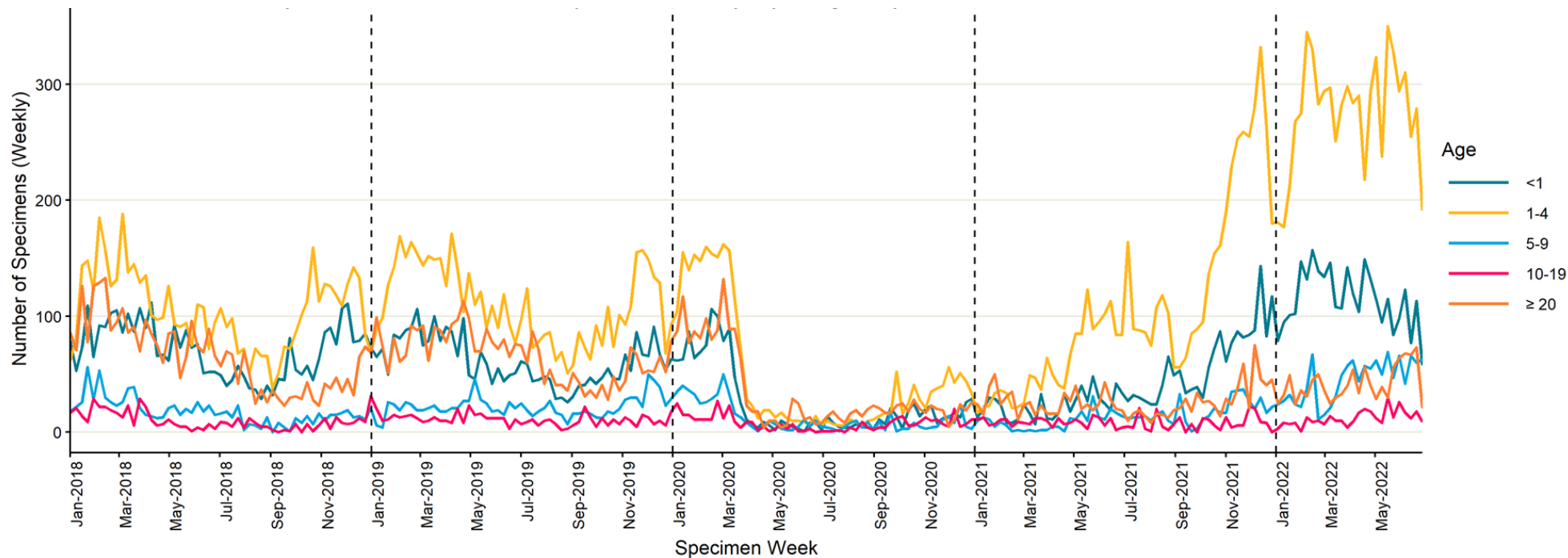
Adenovirus positivity from diagnostic laboratories

Negative results are not recorded in SGSS, but a different system (Respiratory Datamart) does take positive and negative test data derived from respiratory samples from a sentinel laboratory network; no significant changes in adenovirus positivity were observed in Respiratory DataMart. Other laboratories in England were asked to provide data on positive and negative faecal and blood samples to understand background adenovirus positivity levels in 2022 and historically. Adenovirus positivity data during 2017 to 2022 from Manchester Foundation Trust/UKHSA did not show any clear trend for blood, faecal or respiratory samples, although there was a slight

increase in positivity in faecal samples in 1 to 4 year olds since late 2021 but at similar levels seen in previous (pre-COVID) years. Positivity data from Micropathology Limited that provides adenovirus testing for several NHS trusts across England was obtained for December 2021 to June 2022. The number of faecal and respiratory samples was too small to discern any age-specific trends. However, an increase in adenovirus positivity was seen in children 10 years and younger from December 2021 to May 2022, with evidence of a decline in June 2022, whereas no increase in positivity was seen in 11 to 15 year olds or adults. These trends are interpreted with caution due to small numbers in the paediatric age groups compared to adults.

In Wales, adenovirus laboratory surveillance includes all tests, whether positive or negative. Compared to the same period in 2017 to 2019, the positivity for adenovirus tests on respiratory samples in under 5s was significantly higher in January 2022 to May 2022. Positivity in under 5s is now decreasing from the peak in early 2022, in common with other UK nations. In Northern Ireland, a similar trend was observed from end of 2021 to early 2022: positivity of adenovirus from all specimen types increased at the end of 2021, peaking in early 2022. This was driven by increases in under 5s, and by faecal positive samples. More recent data appears to indicate a downward trend.

Figure 12. Adenovirus positive specimens (any type) by age and week of specimen, England 1 January 2018 to 3 July 2022*
Supplementary data is not available for this figure.

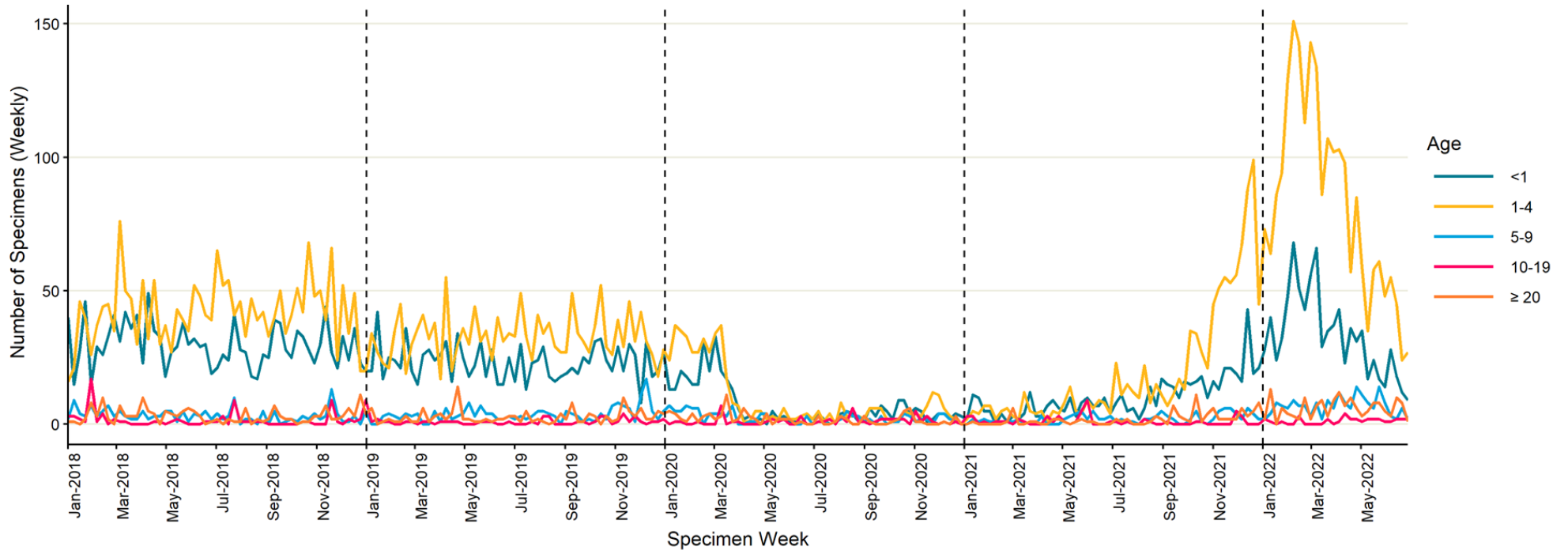


Data source: SGSS

* Dotted lines indicate year start, most recent point affected by reporting delay. The presented figures are based on laboratory reports through SGSS. Testing and reporting procedures vary by virus, UKHSA centre and over time, including short-term trends in testing. Therefore, comparisons should be done with caution.

Figure 13. Adenovirus positive faecal/gastro-intestinal specimens by age and week of specimen, England 1 January 2018 to 3 July 2022*

Supplementary data is not available for this figure.



Data source: SGSS

*Dotted lines indicate year start, most recent point affected by reporting delay. The presented figures are based on laboratory reports through SGSS. Testing and reporting procedures vary by virus, UKHSA centre and over time, including short-term trends in testing. Therefore, comparisons should be done with caution.

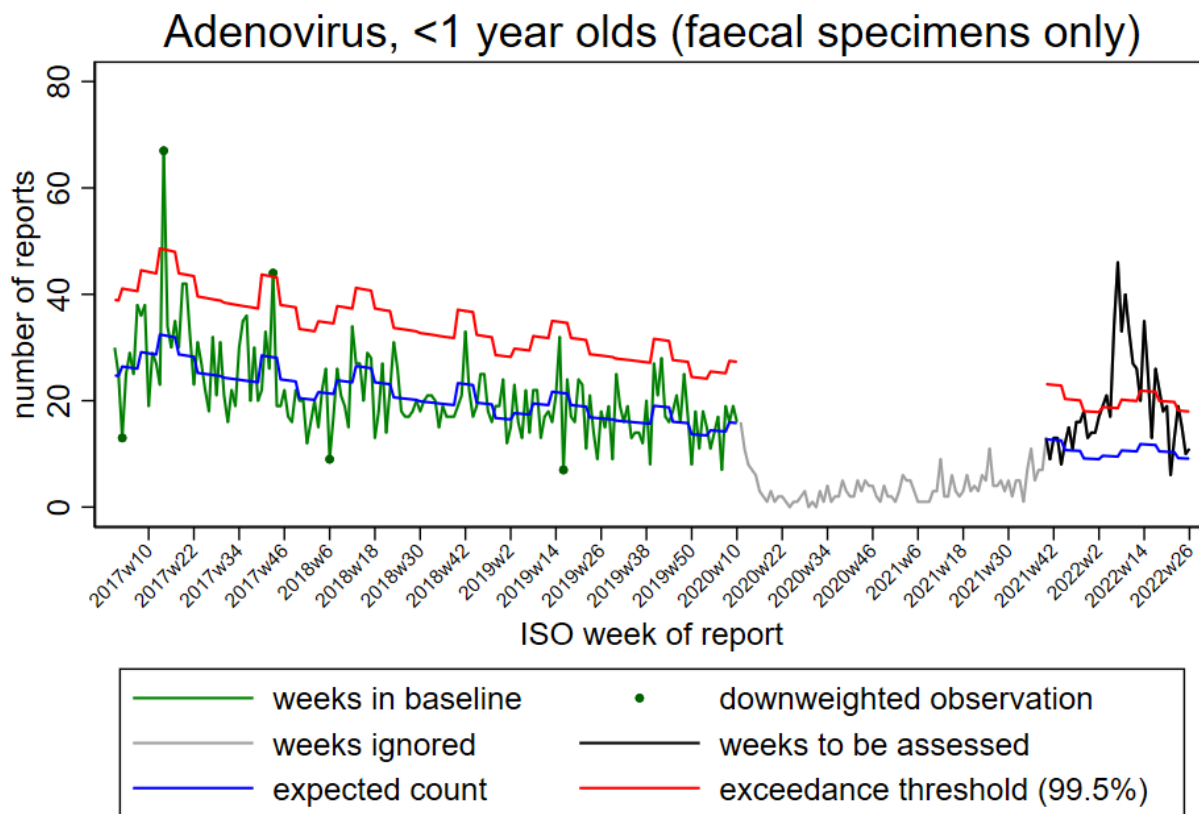
Exceedance monitoring

There has been an exceedance from end of 2021 in adenovirus from all sites – faecal and respiratory – in younger children but not among older children or adults. Methodology for exceedance monitoring can be found in the [Sources and acknowledgements](#) section.

The plots in Figure 14 show trends in adenovirus reports in children from faecal samples. The graphs compare recent data to the trends seen in previous years. Values above the red line indicate periods where the figures are higher than would be expected within the normal range.

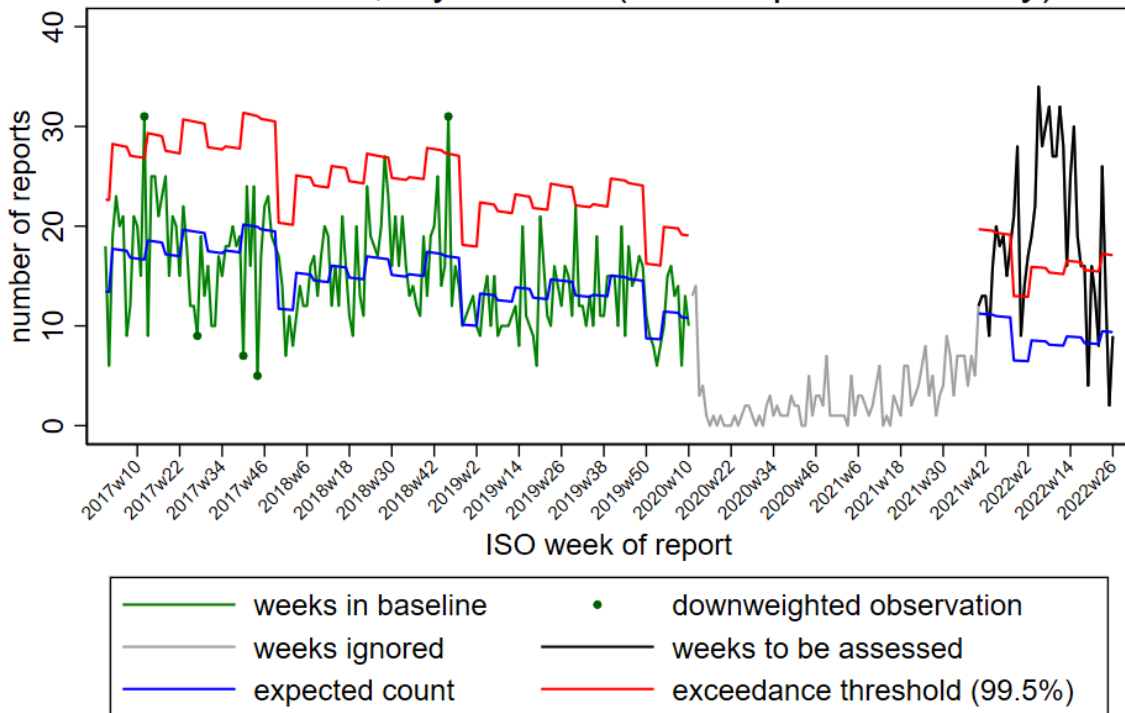
Exceedance for faecal specimen adenovirus was seen in all younger children under 1 year to 9 years old since 2022. Laboratory adenovirus reports have declined in recent weeks and the number for children aged 1 to 5 years is below the exceedance threshold. By contrast, respiratory sample exceedance continues for 3 to 5 year olds. Exceedance for faecal specimen adenovirus was not observed in older children or adults.

Figure 14. Exceedance for faecal specimen adenovirus as seen in under 1 to 9 years old
Supplementary data is not available for these figures.



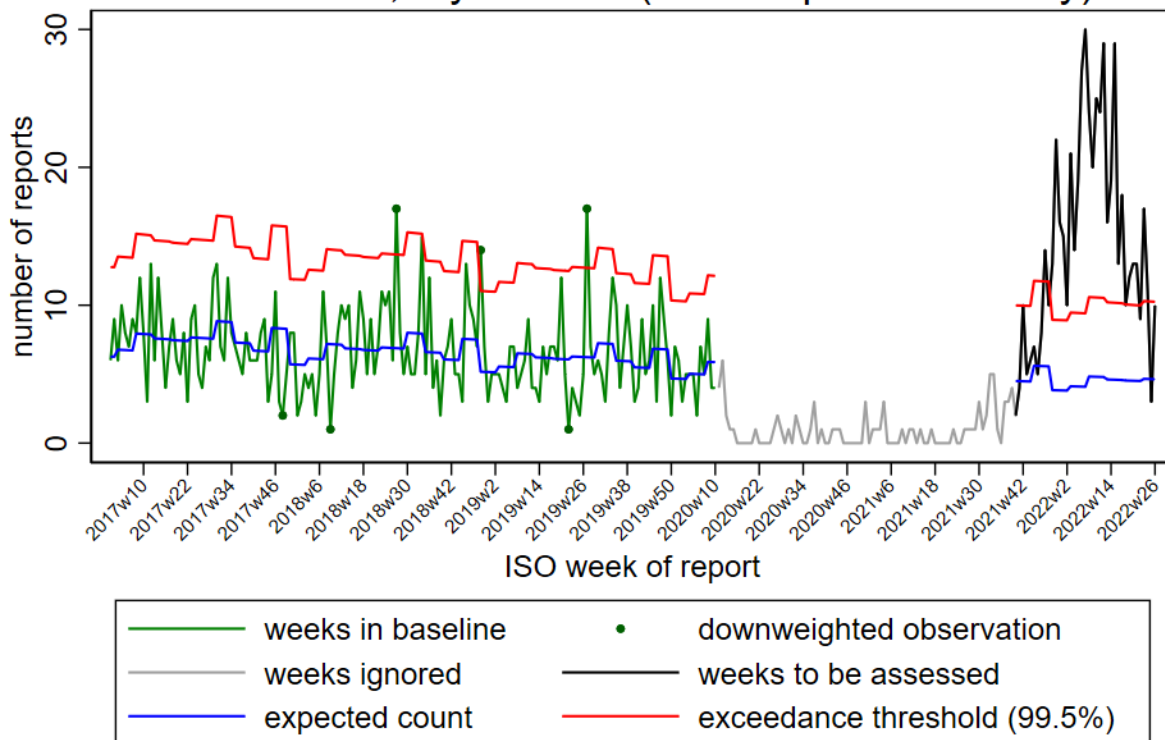
Data source : SGSS vw_Weekly_Exceedance table, latest week of reporting 26, 2022

Adenovirus, 1 year olds (faecal specimens only)



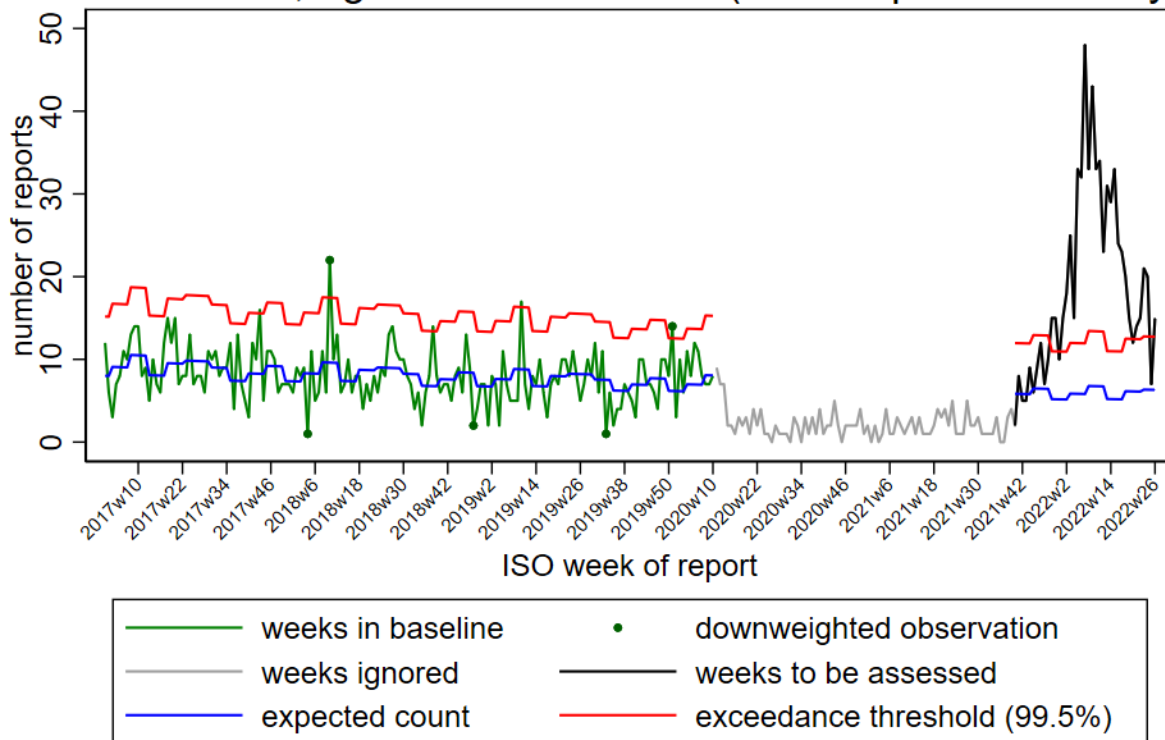
Data source : SGSS vw_Weekly_Exceedance table, latest week of reporting 26, 2022

Adenovirus, 2 year olds (faecal specimens only)



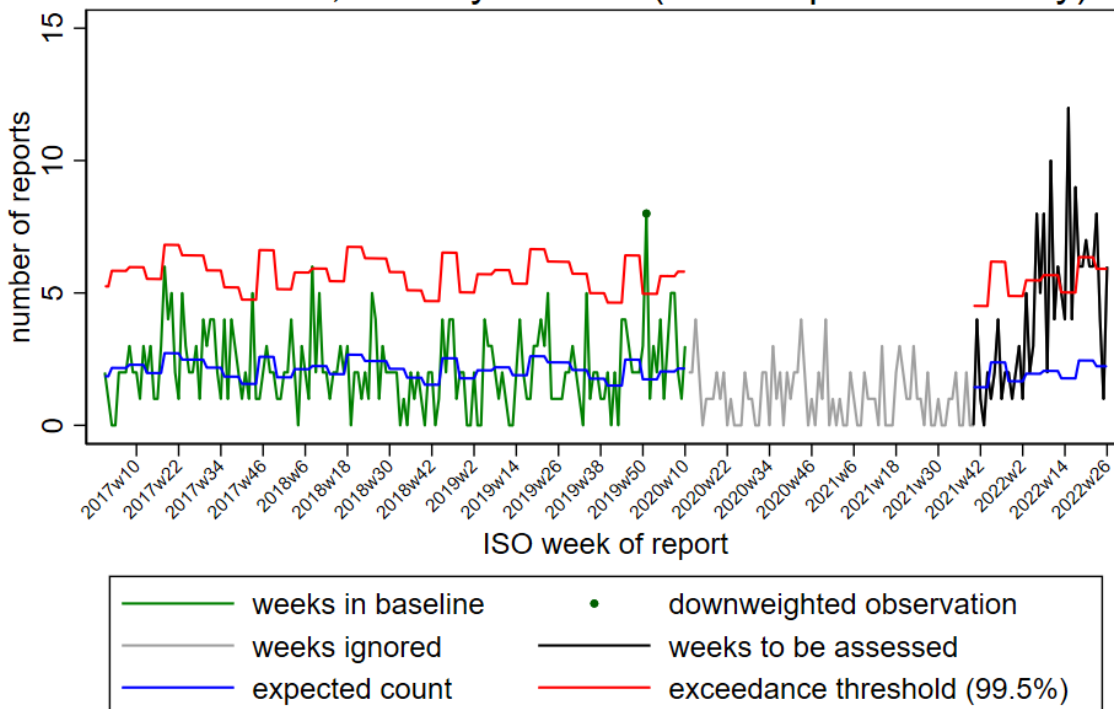
Data source : SGSS vw_Weekly_Exceedance table, latest week of reporting 26, 2022

Adenovirus, aged 3 to 5 inclusive (faecal specimens only)



Data source : SGSS vw_Weekly_Exceedance table, latest week of reporting 26, 2022

Adenovirus, 5 to 9 year olds (faecal specimens only)



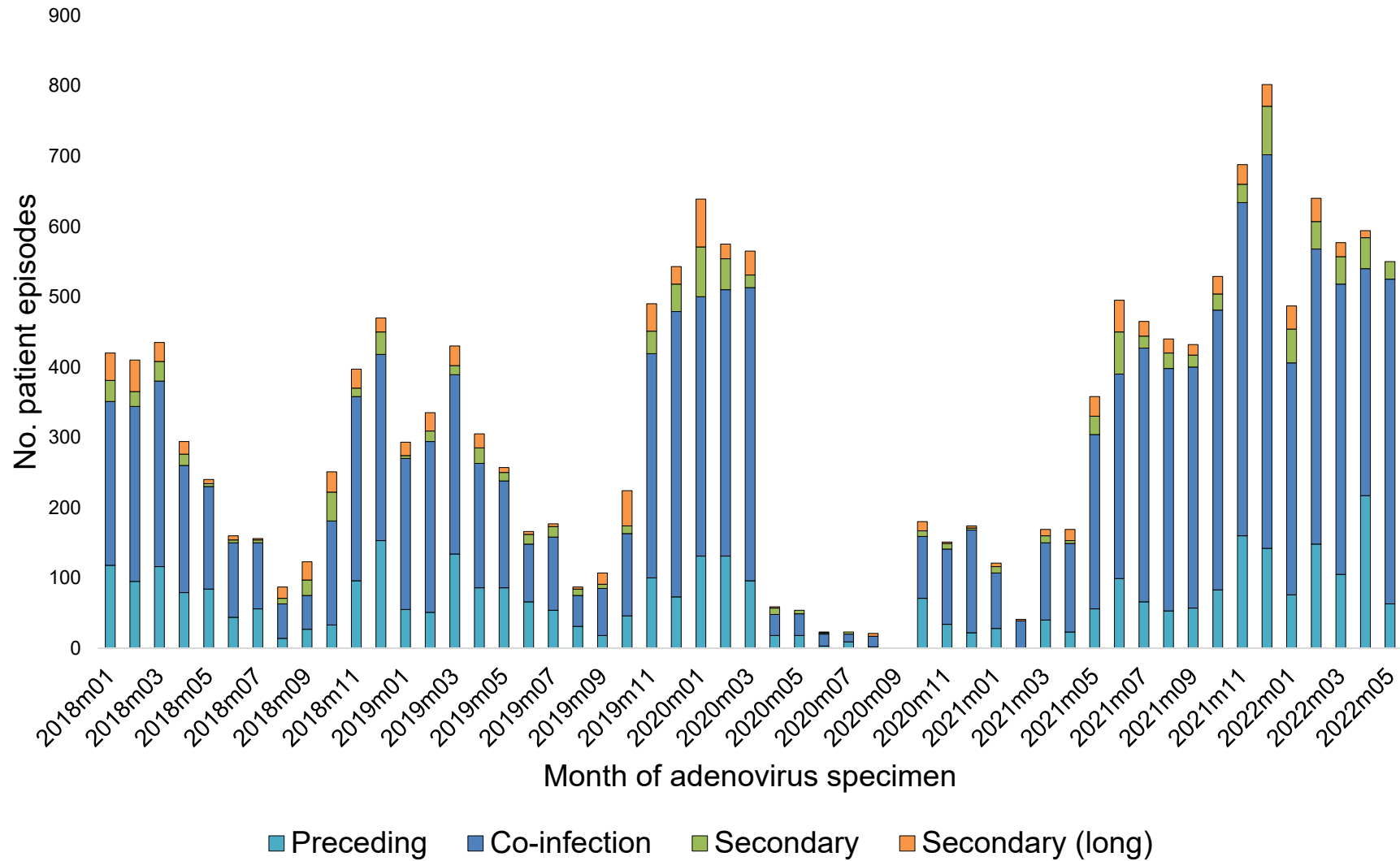
Data source : SGSS vw_Weekly_Exceedance table, latest week of reporting 26, 2022

Interaction between adenovirus and other infections

Adenovirus data and microbiological data for other organisms from SGSS were linked using various demographic variables. Interactions were explored in statistical models to understand whether infection with other organisms in the general paediatric population preceded, coinfecting or was a secondary infection within 27 days, or more delayed secondary infection to 59 days after an adenovirus episode. This analysis is limited by ability to link across demographic variables but gives a sense of whether there has been a more recent increase in infection with adenovirus and other organisms. The data show that between October 2020 and March 2022, there has been a rise in mainly co-infections among children under 10, and this rise is greater than the seasonal variations observed pre-COVID-19. The organisms most frequently encountered as a co-infection were rhinovirus, enterovirus/rhinovirus, and respiratory syncytial virus (RSV) in 2022 and 2021, but mainly rhinovirus alone in 2020.

Figure 15. All adenovirus patient-episodes in under 10 year olds in England, 1 January 2018 to 30 May 2022, by pre-/co-/secondary infection status

Supplementary data is not available for this figure.



6.2 Trends in hepatitis or associated clinical syndromes

Using hospital activity data which monitor emergency department attendances and hospital admissions combined with liver condition codes and diagnoses that roughly align with the clinical syndrome seen in cases, trends can be monitored in different age groups.

Syndromic surveillance of emergency department attendances with liver conditions

Clinical codes related to 'liver conditions'* diagnoses that are routinely used and captured in emergency departments (EDs) have also been grouped together and reviewed across 104 EDs in England which have contributed syndromic surveillance data on attendances between 1 April 2018 and 3 July 2022**. In children aged 1 to 4 years (see [Figure 16A](#)), there have been decreases in the numbers of daily emergency department attendances for liver conditions, compared with previous months. These are small numbers in absolute terms. There has also been a decrease in the numbers of daily attendances in children aged 5 to 14 years (see [Figure 16B](#)). A caveat in interpreting this data is that the codes used will also capture hepatitis with known causes.

Notes

* 'Liver conditions' primary diagnoses includes inflammatory disease of the liver (46%), hepatic failure (32%), injury of liver (16%), acute infectious hepatitis (3%), viral hepatitis A (1%), viral hepatitis B (1%), Acute hepatitis caused by infection (<1%).

** ED attendances as identified by syndromic surveillance, including 104 EDs:

- type 01 ED attendances only
- limited to EDs which started reporting through this route during 2018
- ED syndromic surveillance reporting through the route reported here commenced April 2018
- limited to EDs which reported quickly and frequently in the most recent week (received data for 7 out of 7 of the days 27 June to 3 July 2022, and the data arrived with the UKHSA Real-time Syndromic Surveillance Team within 2 calendar days of the patient attendance)
- EDs are excluded where historical issues with diagnosis coding have been identified

These notes also apply to the following two graphs, Figure 16A and Figure 16B.

Figure 16A. Cumulative daily number of ED attendances for children aged 1 to 4 years, with a 'liver condition'* primary diagnosis, 1 April 2018 to 3 July 2022 (see notes on page 43)**

Supplementary data is not available for this figure.

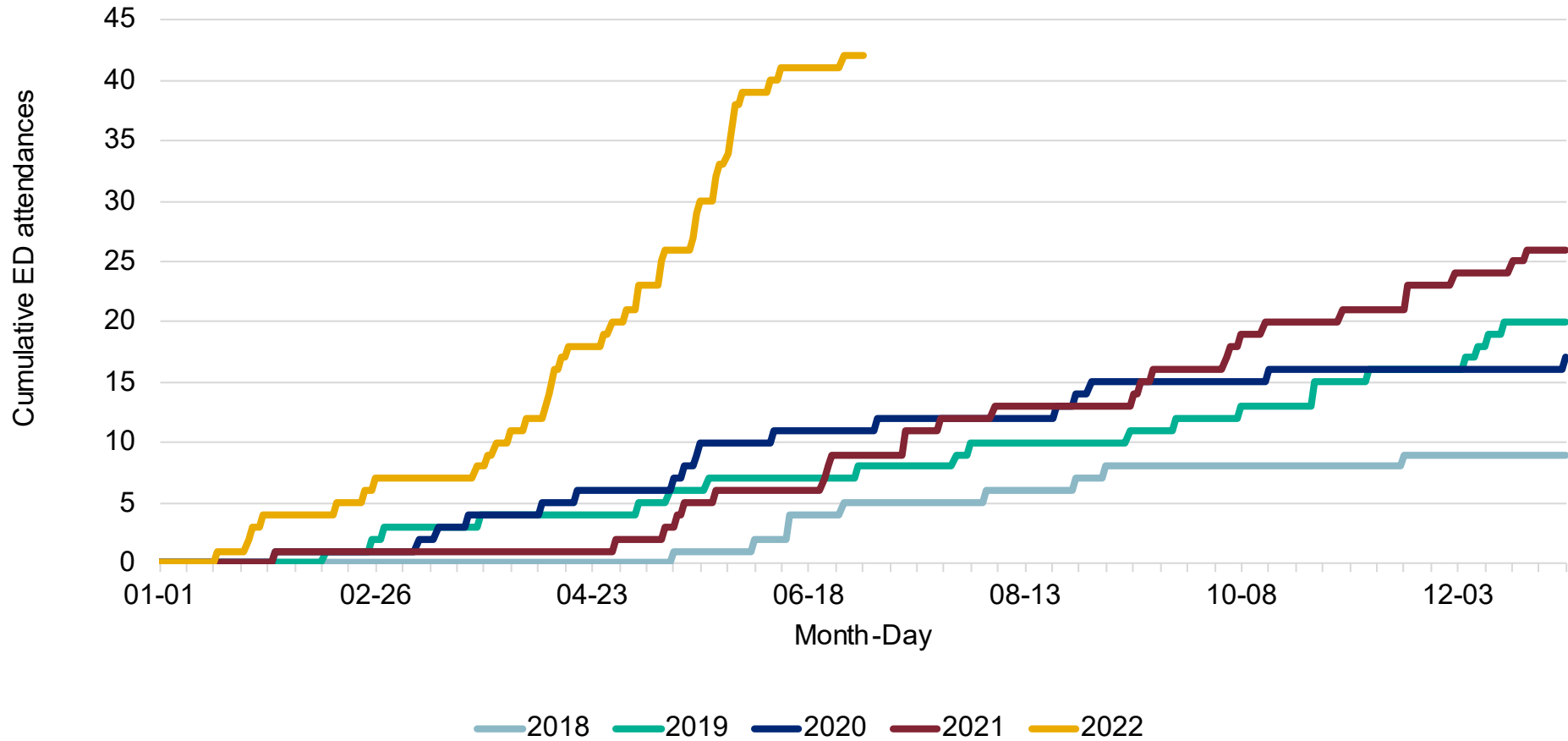
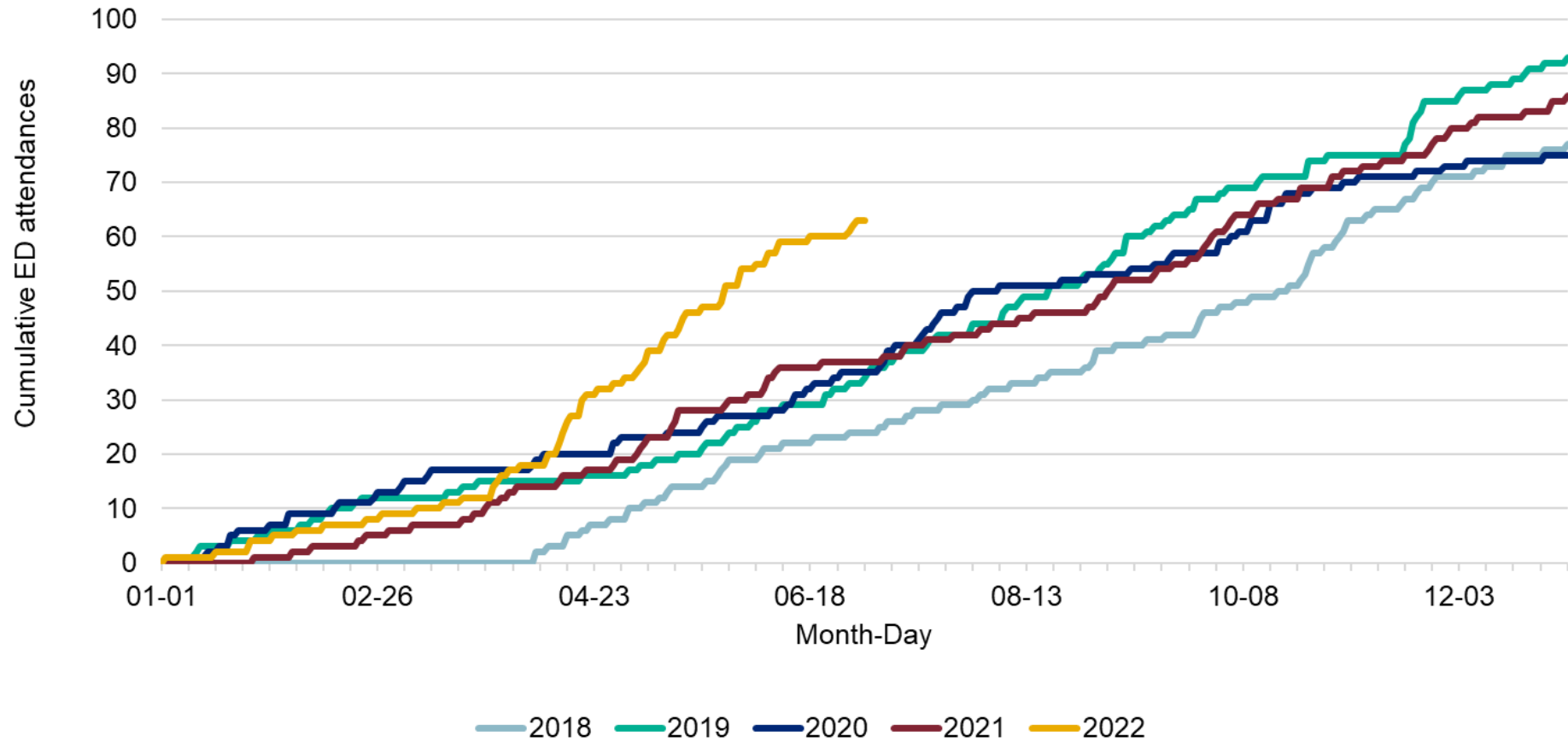


Figure 16B. Cumulative daily number of ED attendances for children aged 5 to 14 years, with a 'liver condition'* primary diagnosis, 1 April 2018 to 3 July 2022 (see notes on page 43)**

Supplementary data is not available for this figure.



Emergency department presentations with jaundice

Data from the Emergency Care Data Set (ECDS), the national data set for urgent and emergency care, shows that the cumulative number of 1 to 4 year olds attending emergency care presenting with jaundice so far in 2022 remains much higher than in 2021, although this appears to have peaked in April.

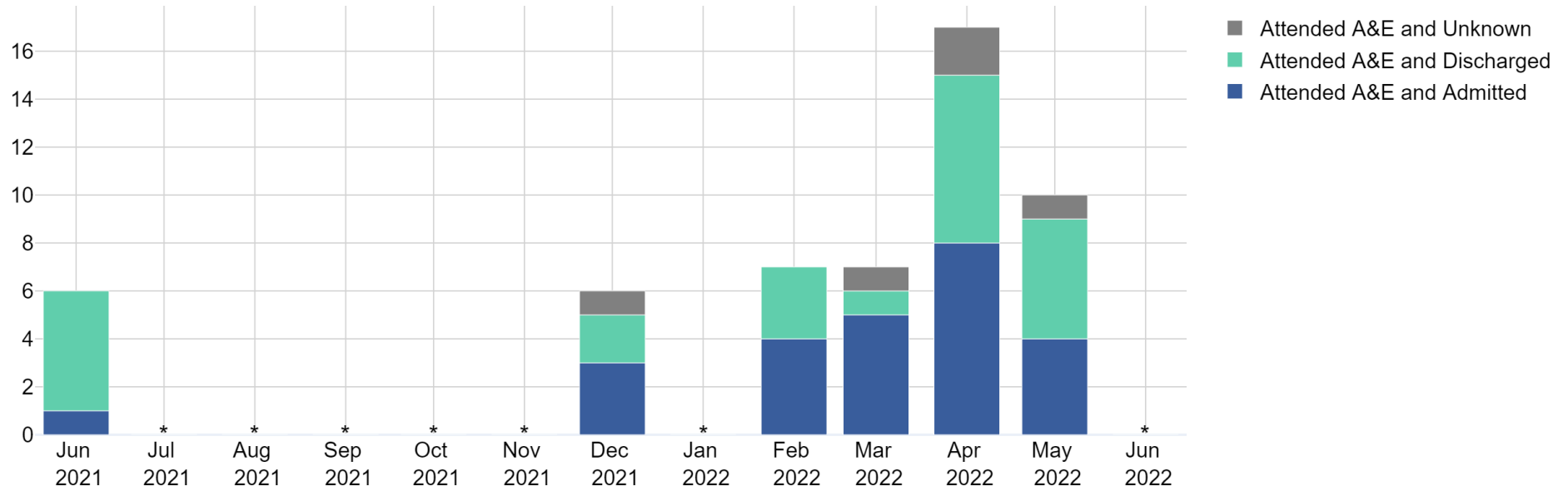
The cumulative number of 1 to 4 year olds in 2022 attending emergency care with jaundice, and who are then subsequently admitted, remains higher than for 2021.

There still is currently no similar trend shown in the 5 to 9, 10 to 19 or over 17 years age groups ([Figure 17](#)). The monthly attendance to emergency care in infants (0 to 1 year) has remained stable at a much higher level than that seen in other age groups, likely largely reflecting newborn jaundice cases ([Figure 18](#)).

Cumulative numbers are small. Data may be an underestimate as the data uses the chief complaint as assessed by the care professional, which is not recorded in 18% of patients, and some cases will be admitted to hospital without first presenting to emergency care.

Figure 17. Monthly attendances to emergency departments with a chief complaint of 'jaundice', age 1 to 4 years

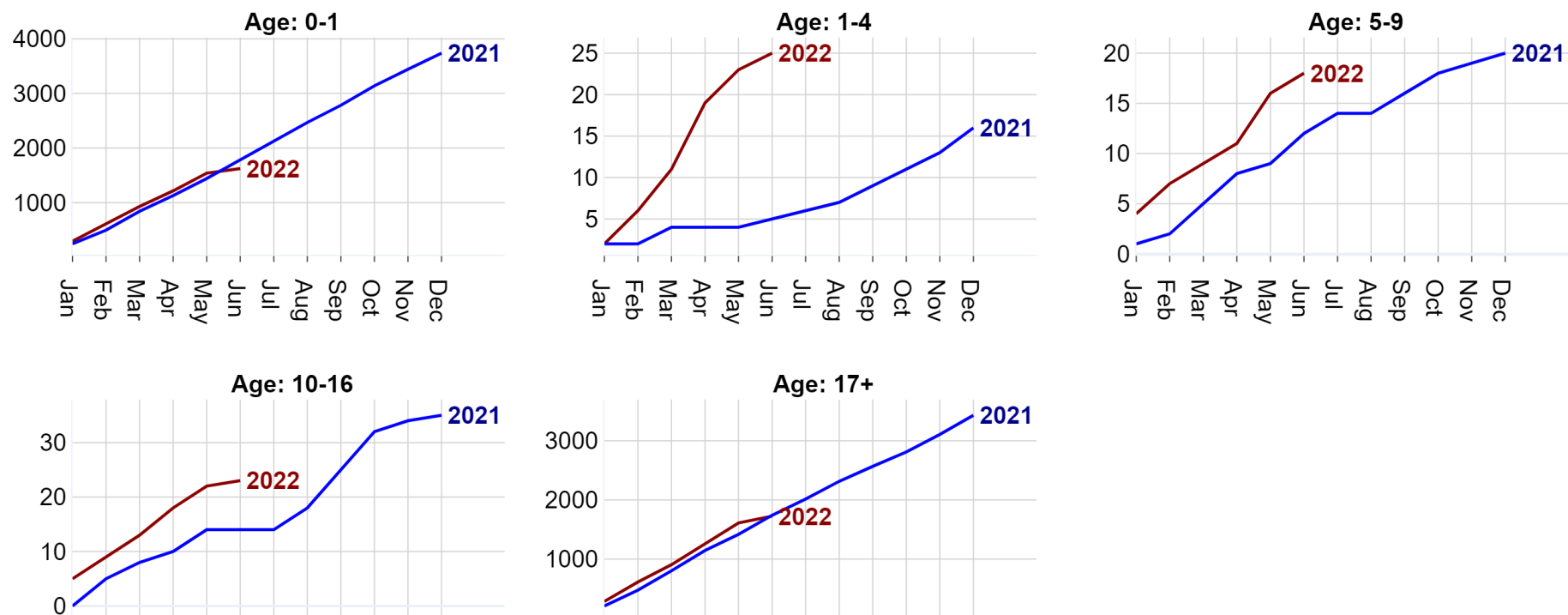
Supplementary data is not available for this figure.



Data source: Secondary Uses Service (SUS) Emergency Care Data Set (ECDS); Counts below 5 have been suppressed to avoid deductive disclosure.

Figure 18. Monthly cumulative admissions presented to Emergency Care with jaundice, by age group

Supplementary data is not available for this figure.



Source: Emergency Care Dataset (ECDS) / NHS-Digital, produced by UKHSA. Data extracted on 4 July 2022 with data from 1 January 2021 to 10 June 2022. This data only shows whether a case has attended emergency care at an NHS hospital and was subsequently admitted as an inpatient. The data does not include cases who were directly admitted without first presenting to emergency care. Jaundice chief complaint recorded on ECDS-Snomed-CT: 18165001. Data is subject to change in the most recent weeks due to reporting delays.

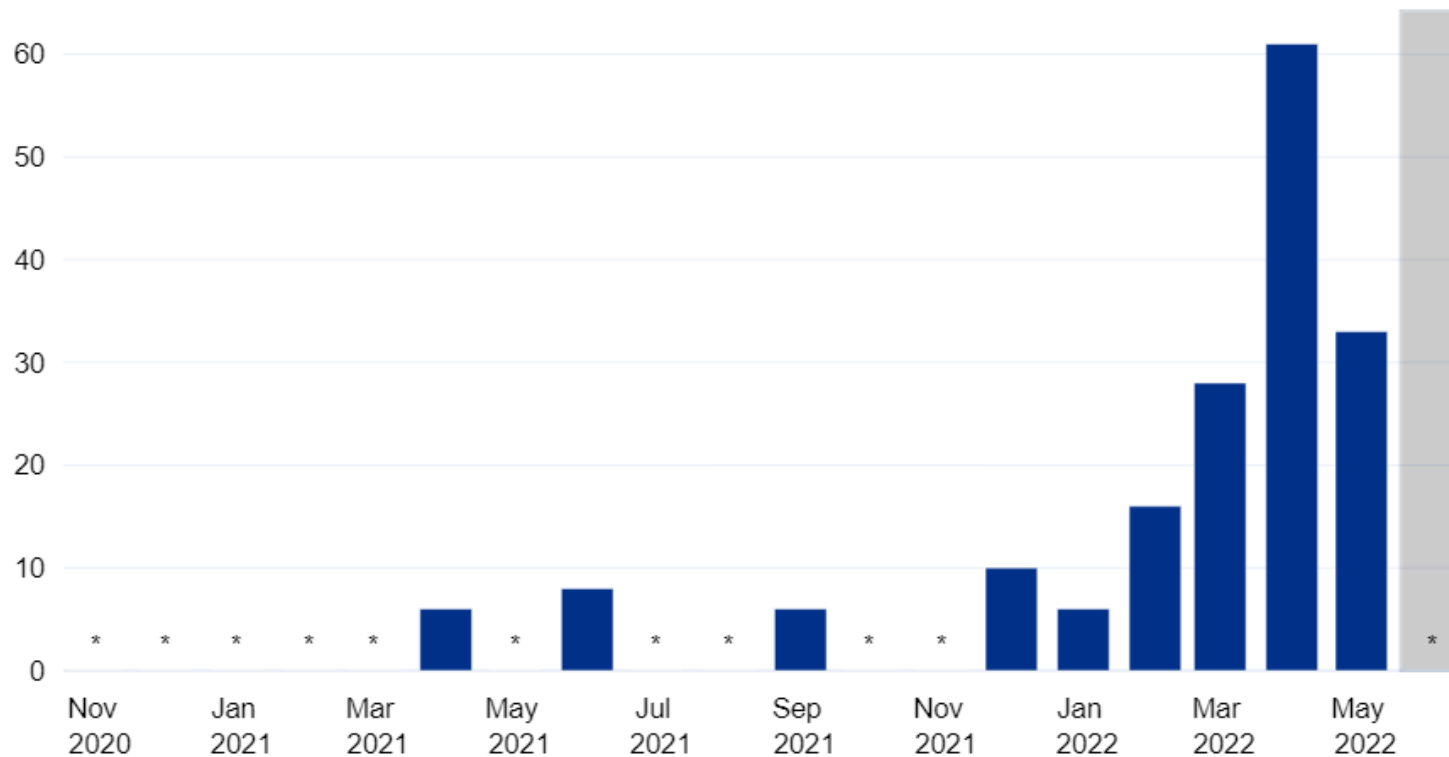
Emergency admissions of children with liver-related illnesses (non A-E hepatitis)

Admitted patient care data shows that between January 2022 and April 2022, there was a large increase in the number of diagnoses in children aged 1 to 4 years with codes which may represent non-A-E hepatitis (see [Figure 19](#)). There is no signal in the other paediatric age groups or in adults. This data uses the primary or secondary diagnosis codes from the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) completed by a care professional when a patient is discharged, and therefore is subject to a significant time lag. For this reason, although numbers in May 2022 suggest a decline, data from June 2022 is incomplete and recent trends are therefore unclear.

This data should be interpreted cautiously, particularly in the absence of data from before the COVID-19 pandemic and due to potential lower than usual health-seeking behaviour and lower admissions related to infectious causes due to reduced social mixing during the pandemic.

Figure 19. Monthly hepatitis admissions for ages 1 to 4 year olds

Supplementary data is not available for this figure.



Source: APC data, produced by UKHSA

Data extracted on 04 July 2022 with data from 01 November 2020 to 25 June 2022

Bars with counts of 5 or below have been redacted and are indicated by a star (*)

The following primary or secondary diagnosis codes were used to link hepatitis:

B178, B179, B190, B199, K716, K720, K752, K759

Data source: the Secondary Uses Service (SUS) Admitted Patient Care (APC), a national data set for in patients. Counts below 5 have been suppressed to avoid disclosure.

Appendix 1. Additional data

Relevant surveillance data

Figure a) Seven-day moving average of ED attendances with a 'liver condition'* primary diagnosis by age 1 to 4 years**

Supplementary data is not available for these figures. See notes on page 53.

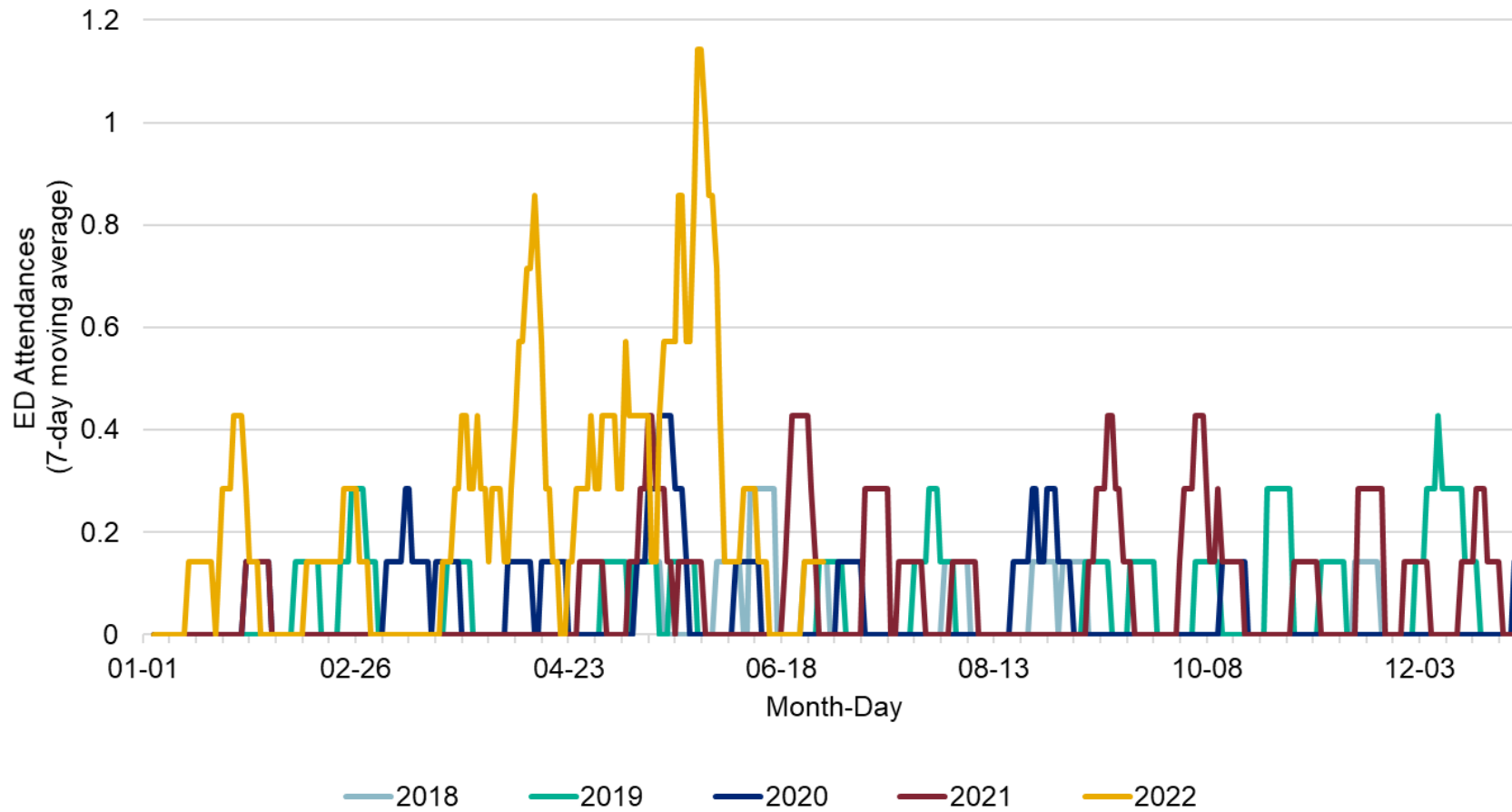
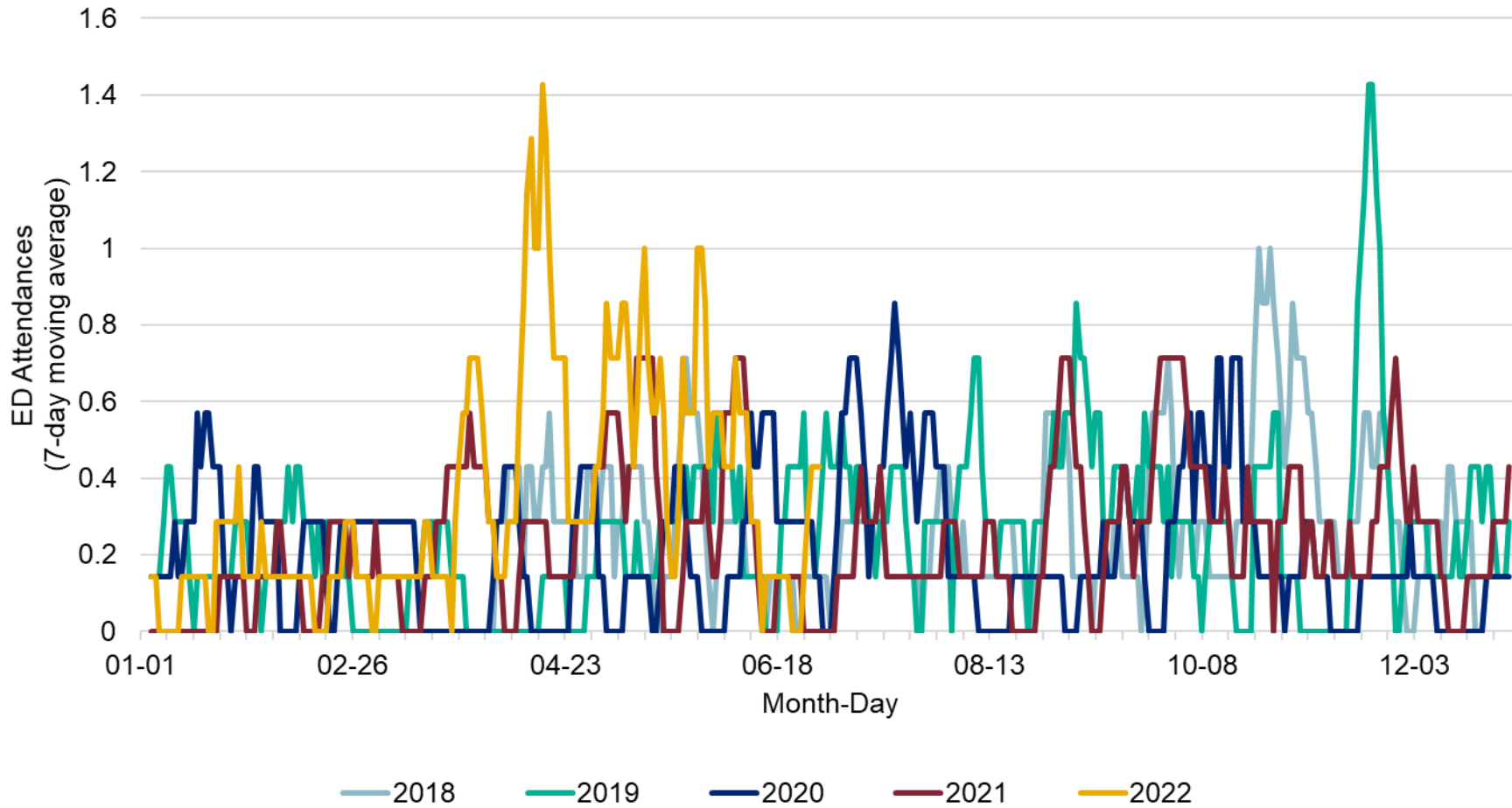


Figure b) Seven-day moving average of ED attendances with a 'liver condition'* primary diagnosis by age 5 to 14 years**



Notes to figures a) and b)

* 'Liver conditions' primary diagnoses includes inflammatory disease of the liver (46%), hepatic failure (32%), injury of liver (16%), acute infectious hepatitis (3%), viral hepatitis A (1%), viral hepatitis B (1%), acute hepatitis caused by infection (<1%)

** ED attendances as identified by syndromic surveillance, including 104 EDs:

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- ED syndromic surveillance reporting through the route reported here commenced April 2018
- limited to EDs which reported quickly and frequently in the most recent week (received data for 7 out of 7 of the days 27 June to 3 July 2022, and the data arrived with the UKHSA Real-time Syndromic Surveillance Team within 2 calendar days of the patient attendance)
- EDs are excluded where historical issues with diagnosis coding have been identified

Sources and acknowledgments

Data sources and methodologies

Exceedance monitoring

UKHSA monitors trends in pathogens through routine and ad hoc surveillance of laboratory notifications of positive test results undertaken as part of clinical care reported through SGSS. Exceedance monitoring is also used as part of assessing whether disease activity is above that expected. This uses a statistical threshold based on a moving average and secular trends in detection of a pathogen (thus addressing both changes in laboratory testing practices over time, and seasonal variation in disease activity). Further details of the statistical methods are described by [Noufaily and colleagues](#).

Data sources

Data used in this investigation is derived from:

- Second Generation Surveillance System (UKHSA)
- Secondary Uses Service (NHS Digital)
- Emergency Care Data Set (NHS Digital)
- Admitted Patient Care (NHS Digital)
- Respiratory Datamart (UKHSA)
- Syndromic surveillance (UKHSA)
- NHS Blood and Transplant
- COVID Unified Data Set (UKHSA)
- NOIDs (UKHSA)
- HPZone (UKHSA)
- International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) UK
- ONS Coronavirus Infection Survey
- All Wales Laboratory Information System and Datastore
- Health Protection Case and Incident Management System Wales
- MRC-University of Glasgow CVR
- Micropathology Limited

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UKHSA Clinical Cell

UKHSA Epicell

UKHSA Genomics Public Health Analysis

UKHSA Toxicology Cell

UKHSA Virology Cell

UKHSA Virus Reference Department

International Severe Acute Respiratory and emerging Infection Consortium (ISARIC)

Glasgow Centre for Virus Research

Great Ormond Street Hospital with University College London

Public Health Scotland

Public Health Wales

Public Health Agency Northern Ireland

Micropathology Limited

Hepatitis Technical Group

The Hepatitis Technical Group includes members with expertise in clinical infectious diseases, clinical research, epidemiology, genomics and virology.

For any queries relating to the technical briefing on acute hepatitis of unknown aetiology please contact genomics.reports@ukhsa.gov.uk

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological, and nuclear incidents, and other health threats. We provide intellectual, scientific, and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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