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Trends in Pediatric Hospital Admissions Caused or Contributed by SARS-CoV-2 Infection in England

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Objective To investigate the changing characteristics of SARS-CoV-2 related pediatric hospital admissions over time.

Study design A national, observational cohort study from 1, July 2020, to August 31, 2023, using English population-linked electronic health records. We identified 45,203 children under 18 years old in whom SARS-CoV-2 either caused or contributed to hospitalization, excluding those admitted with "incidental" infection. Studied outcomes were types of hospitalization and severe hospitalizations involving either critical care or PIMS-TS.

Results There were 45,920 SARS-CoV-2 related hospitalizations in children: 34,870 (75.9%) due to COVID-19; 1,845 (4.0%) due to pediatric inflammatory multisystem syndrome – temporally associated with SARS-CoV-2 (PIMS-TS); 8,330 (18.1%) with SARS-CoV-2 as contributor to admission; and 875 (1.9%) acquired nosocomial SARS-CoV-2 infection. The most notable changes between the first three waves (March 2020 through November 2021) and the omicron era (December 2021 onwards) were: a fall in PIMS-TS from 1,575 of 14,020 (11.2%) to 270 of 31,905 (0.8%); a reduction in critical care use from 1,175 of 14,020 (8.4%) to 1,390 of 31,905 (4.4%); a fall in mortality rate among those hospitalized from 521 per 100,000 to 249 per 100,000; and a drop in the median age of hospitalized children from 4.7 (IQR 0.6,12.3) to 1.1 (IQR 0.3,6.4) years. Of children hospitalized, infants, 10.2% of whom had a recorded underlying health condition, comprised 4,225 of 14,020 (30.1%) admissions 2020 through 2021 and 15,555 of 31,900 (48.8%) since 2022. ($p<0.001$ for all comparisons).

Conclusions Infants are now the most affected age group by SARS-CoV2, at least partially related to having the least immunity to the virus, and are most vulnerable to respiratory illnesses.

Among 11.9 million children and adolescents resident in England,[1] we previously studied hospital admissions related to SARS-CoV-2 infection, between July 2020 when the testing program had been set up and February 2022;[2] finding that this infection was causal or a contributory factor in the hospitalization of 21,000 individuals.[2] Since February 2022, children's SARS-CoV-2 exposure histories,[3] relevant SARS-CoV-2 testing and health protection policies,[4] and variant dominance[5] have evolved. In England, over 90% of school age children had detectable SARS-CoV-2 antibodies in March 2022.[6] This was largely due to infection, especially in younger children; by October 2023, at least one dose of COVID-19 vaccine had been received in only 9% of 5-11 year-olds; 42% of 12-15 year-olds and 61% of 16 to 17 year-olds.[7] For children in England under 5 years old, only those with significant underlying health conditions have ever been eligible for COVID-19 vaccination. Since 2023, only children with significant underlying health conditions are eligible for any SARS-CoV-2 vaccines across all age groups.[8] Increased SARS-CoV-2 immunity from previous infection or vaccination may be responsible for the noted drop in incidence of pediatric inflammatory multisystem syndrome in children temporally associated with COVID-19(PIMS-TS) (also known as multisystem inflammatory syndrome in children in some countries, MIS-C) ,[9] however, the wider impacts of evolving complex inter-related factors upon changes in the phenotypes of pediatric SARS-CoV-2 related hospital admissions are unclear.

We used population-based electronic healthcare record (EHR) data to describe trends in hospital admissions caused or contributed to by SARS-CoV-2 infection among children and adolescents resident in England. Our study objectives were to explore any changes over time in the characteristics of hospital admissions caused or contributed to by SARS-CoV-2,

including severe admissions involving critical care[10] and in the demographics of affected children.

Methods

Study Design and Data Sources

This was a national English retrospective cohort study based on linked EHR data. We used National Health Service (NHS) England's secure data environment (SDE) accessed through the British Heart Foundation (BHF) Data Science Centre's CVD-COVID-UK/COVID-IMPACT Consortium to create a linked cohort comprising the following datasets[11]: a) national laboratory COVID-19 testing data from the UK Health Security Agency Second Generation Surveillance System (SGSS); b) primary care data from the General Practice Extraction Service Data for Pandemic Planning and Research (GDPPR); c) hospital episode statistics (HES), including admitted patient care, critical care, and outpatient data; d) deaths from the Office of National Statistics (ONS) Civil Registration of Death, including the causes of death listed in order; e) NHS England's record of COVID-19 vaccination status.

External Reference Sources

We described data from two important national sources of information for contextualization of the linked study cohort: a) SARS-CoV-2 prevalence as reported by the UK Office of National Statistics COVID Infection Survey up to its closure in March 2023.[5] This was a prospective observational study of SARS-CoV-2 prevalence ascertained by testing in a sample of people in private residential households in England. These data were available for two age groups of '2-11 years' and '12-16 years' old. b) deaths for which COVID-19 or PIMS-TS was listed as one of the causes on the death certificate as reported by the ONS for each one-year age group between July 2020 and August 2023.[12] Given the NHS rule that numbers

are rounded to multiples of 5 within a linked patient level research dataset and counts of less than 10 are not reported, in the context of very small numbers in specific groups, the unlinked ONS record of individual numbers of deaths provided the most complete picture.

Linked Cohort Creation

We used source datasets that had been linked By NHS Digital using the NHS number, a unique numeric persistent healthcare identifier assigned at first encounter with the healthcare system.

Inclusion Criteria for the Cohort

Children were included who met all the following criteria during the study period of July 1, 2020, to 31 August 31, 2023: a) age 0 - 17 years old at the time of ascertained SARS-CoV-2 infection, b) residence in England, c) a valid person pseudo-identifier enabling data linkage, d) alive at study start or born during the study period, e) known sex and f) experienced a SARS-CoV-2 related admission to hospital.

Criteria for Identifying SARS-CoV-2 Related Admission

We used peer reviewed methods to create a cohort of children who had a SARS-CoV-2 related hospitalization in England during the study period. [13, 2] Hence we considered for inclusion all hospitalizations where at least one of the following criteria was met: a) hospital Episode Statistics recorded the primary or non-primary cause of hospital admission with the ICD-10 codes U07.1 or U07.2, which are the codes for “COVID 19, with or without a positive test”; or b) the primary or non-primary cause for admission was an ICD-10 code used to identify PIMS-TS[14], which were ICD-10 code U07.5, newly available during 2021; and for 2020 and 2021 only, the ICD-10 codes R65 (‘Systemic Inflammatory Response Syndrome’), M30.3 ('Mucocutaneous lymph node syndrome [Kawasaki]’), with no exclusionary codes

that indicate an alternative diagnosis; or c) there was a positive SARS-CoV-2 test (in SGSS) from up to 14 days before hospitalization until the date of hospital discharge.[15]

Hospital Admission Types

Among SARS-CoV-2 associated hospitalizations in the cohort, we used a hierarchical approach to identify mutually exclusive hospitalization types, using a combination of the ICD-10 codes listed as a cause for admission[16] and positive SARS-CoV-2 tests. During this assignment of admission types we firstly identified those with incidental infection (in which SARS-CoV-2 infection is deemed as not causative to the hospital stay[17]), and then we removed these records from the study cohort. We report the admission types in the Box (See Supplementary Table 1).

Admission type	Definition
Hospitalizations with nosocomial infection	Where the first evidence of SARS-CoV-2 infection (either based on codes or a positive test) was present from day 8 of hospitalization onwards, consistent with definitions used by NHS England.[15] Although nosocomial SARS-CoV-2 is not on the causal pathway of the hospital admission, it may contribute to prolonged stay, therefore we considered these to be SARS-CoV-2 related hospitalizations.
Hospitalizations with incidental infection	Candidate reasons for incidental admission were identified in the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) prospective study of COVID-19 in children, such as trauma, poisoning, or elective surgery[17]. We included a wider range of primary reasons for admission than ISARIC, capturing also mental health disorders, eye conditions, dental conditions, injuries, assault, self-harm, and certain pregnancy related conditions.[2] These children may or may not have had a positive test. After identifying hospital admissions incidental to SARS-CoV-2 infection, we then excluded them from these analyses of SARS-CoV-2 related hospitalizations.
PIMS-TS hospitalizations	A code for PIMS-TS was present as a cause for hospitalization as detailed in 'criteria' and no exclusion codes were present indicating an alternative diagnosis.

COVID-19 hospital admissions	Either the primary cause for admission was a code for COVID-19 (*definite COVID-19 admission*); OR the primary reason for hospital admission was a sign, symptom, or presentation consistent with COVID-19 (and did not definitively indicate an alternative diagnosis); AND a non-primary cause for hospital admission was COVID-19 AND there was no excluded code indicating a reason for hospital admission was an alternative or co-infection (*suspected COVID-19 admission*). These children may or may not have had a positive test. We detail the references and related information for this phenotype in our prior paper (referred to as Types A1 and A2).[2]

Hospitalizations where SARS-CoV-2 infection was a contributor	A non-primary reason for admission was COVID-19 AND the primary cause for admission was a condition known to co-occur with SARS-CoV-2 infection as a co or secondary infection, such as respiratory syncytial virus, parainfluenza, adenovirus, staphylococcal pneumonia, streptococcal pneumonia); OR was a condition that has been linked to SARS-CoV-2 infection in children (type 1 diabetes mellitus, status epilepticus or febrile seizures); OR was a condition associated with higher risk of severe illness with SARS-CoV-2 infection [17](conditions treated with immunosuppression, any cancer, neurodevelopmental conditions that may affect breathing, neonatal conditions such as poor feeding, respiratory diseases such as asthma). These children may or may not have had a positive test. We detail the references and related information for this phenotype in our prior paper (referred to as Types B1 and B2).[2]

Demographics and Underlying Health Conditions

Ages were grouped as < 1 (ie, Infants), 1 - 4, 5 - 11, 12 - 15, and 16 - 17 years, sex, ethnicity (coded via adapted ONS data dictionary): Asian / Asian British, Black / Black British, Chinese, Mixed, Other, Unknown, White, socioeconomic deprivation information derived by mapping patients' Lower Layer Super Output Areas (LLSOA) to the English Index of Multiple Deprivation (IMD)[18]; reported as quintiles (1: least deprived to 5: most deprived).

We identified two groups of medical and developmental underlying health conditions given their importance as risk factors for severe disease with SARS-CoV-2.[13, 17]

The Joint Committee for Vaccination and Immunisation (JCVI) of England identified certain health conditions as placing children at greater vulnerability of severe disease with SARS-CoV-2 infection: these are listed in the 'Green Book'.[19] Only groups listed in this guidance are offered COVID-19 vaccination in England.[8] As previously described,[2] the relevant conditions[19] were matched to ICD-10[16], and children and adolescents with any evidence of these conditions in hospital episode statistics (either outpatient or inpatient) were identified. We present numbers and percentages for these conditions throughout the results section.

Based on clinical consensus, using ICD-10 codes, we identified all medical and developmental health conditions that appeared in the hospital records of children with SARS-CoV-2 associated hospitalization prior to their date of infection; [2] we defined criteria for obesity based on weight-for-age and sex standard deviation score (SDS);[20] and World Health Organisation standards[21]; we defined pregnancy via the presence of associated ICD-10 codes within a 9-month time window to the date of infection.

Time Eras for SARS-CoV-2 Variants

We assigned a dominant SARS-CoV-2 variant to each admission using the following time eras: Original variant: 1st July 2020 to 7th December 2020 (5-months, 1-week); Alpha variant: 8th December 2020 to 17th May 2021 (7-months, 1-week); Delta variant 18th May 2021 to 13th December 2021 (7-months), Omicron variant 14h December 2021 to 30th September 2023 divided into three 7-month blocks to illustrates trends over this era.[22]

Vaccination Status

Vaccination status was coded as "unvaccinated", or first, second or third/booster dose ("vaccinated") determined by the number of vaccinations received ≥14 days prior to admission. Vaccine type was not reported as only Pfizer-BioNTech COVID-19 vaccine (Comirnaty) is approved for pediatric use in England.

Descriptive Statistics

This analysis was performed according to a pre-specified analysis plan published on GitHub, along with the phenotyping and analysis code (https://github.com/BHFDSC/CCU029_02).

We conducted a complete case analysis, reporting missing variables.

We described hospital admissions that were caused or contributed to by SARS-CoV-2 infection, stratified by the admission type over the study period. We defined severe outcomes as: SARS-CoV-2 associated hospital admission involving pediatric critical care and/or due to PIMS-TS, as specified by the UK Joint Committee for Vaccination and Immunisation (JCVI).[23] Among the children and adolescents with SARS-CoV-2 related hospitalization, we calculated the proportions in each of the 6 defined variant associated time eras over the study period (Original, Alpha, Delta and Omicron time periods), by hospital admission types and, by patient characteristics. We then explored temporal trends in the proportion of hospital admissions with each factor of interest, by fitting a linear

regression model to the 6 serial period proportions (each representing a time-period) and reporting the associated slope parameter p-value. After reviewing each linear trend, we summarized changes in characteristics by era for brevity, by reporting certain variables summarized by grouped eras of pre-Omicron (19.5 months) versus Omicron (21 months) using a chi square test.

Results

Over the three-year study period, among the estimated population of 11.9 million <18 years of age, there were 45,920 SARS-CoV-2 related hospital admissions (excluding incidental admissions) affecting 45,203 children and adolescents. There were 44,510 (98.5%) children with one admission; 665 (1.5%) with two admissions; and 25 (<0.1%) with ≥3 admissions. As shown in Figure 1 there were 34,870 (75.9%) admissions among children and adolescents with a diagnosis of COVID-19 (23,695 definite and 11,175 suspected); 1,845 (4.0%) with PIMS-TS; 8,330 (18.1%) with SARS-CoV-2 as contributor; and 875 (1.9%) were admitted then acquired nosocomial SARS-CoV-2 infection.

Trends in Characteristics of Hospital Admissions

SARS-CoV-2 infections as identified by ONS, which provides an indication of population prevalence during the relevant time-periods for '2-11' and '12-16' year olds, and SARS-CoV-2 associated hospital admissions identified in the linked dataset depicted in Figure 2, tracked together. We show all characteristics by each time-period in Table I. Over the observation period there was a trend towards a greater proportion of all SARS-CoV-2 related hospitalizations in children and adolescents being due to COVID-19: 1,150 (64.1%) Original, 2,260 (63.8%) Alpha, 6,150 (70.9%) Delta, 14,980 (79.1%) Omicron first 7-months, 6,740 (77.8%) Omicron second 7-months, 3,600 (83.8%) Omicron third 7-months (p<0.001).

Children and adolescents hospitalized with SARS-CoV-2 as a contributing factor and those with nosocomial SARS-CoV-2 infection made up a stable proportion of all admissions over the whole study period (p=0.22 and p=0.13 respectively). Conversely, the relative proportion of children and adolescents with a hospital admission due to PIMS-TS trended down despite a rise in Alpha: (240 (13.4%) Original, 565 (15.9%) Alpha, 770 (8.9%) Delta, 240 (1.3%) Omicron first 7-months, 20 (0.2%) Omicron second 7-months, 5 (0.1%) Omicron third 7-months (p=0.01)).

The number requiring critical care (overall 2,565 (5.6%)), trended down over time, despite a rise in Alpha: (160 (8.9%) Original, 400 (11.3%) Alpha, 615 (7.1%) Delta, 750 (4.0%) Omicron first 7-months, 440 (5.1%) Omicron second 7-months, 200 (4.7%) Omicron third 7-months (p=0.048)). In line with the drop in severe admissions, the hospital length of stay among children and adolescents hospitalized reduced slightly: the median was consistent at 2 days, but interquartile (IQR) range dropped from [1, 4-5] days (Original, Alpha, Delta) to [1,3] days in the Omicron waves (p=0.02). The number of deaths attributed to SARS-CoV-2 infection were: 11 Original, 18 Alpha, 44 Delta, 42 Omicron first 7-month period, 20 Omicron second 7-month period and 16 Omicron third 7-month period: there was a fall in death rate among those hospitalized from 521 per 100,000 to 249 per 100,000.

Characteristics of Children and Adolescents Hospitalized

Notably, there was a shift to the dominance of infant-related admissions after 2021: infant admissions contributed 535 (29.8%) Original; 1,130 (31.9%) Alpha; 2,565 (29.6%) Delta; 8,000 (42.2%) Omicron first 7-months; 4,820 (55.7%) second 7-months; 2,745 (63.9%) third 7-months (p=0.008). This is illustrated in Figure 3 and by the median [IQR] ages in years of

children and adolescents of 4.8 [0.6, 12.4] Original, 3.7 [0.5, 11.2] Alpha, 5.1 [0.6, 12.6] Delta, with a sharp drop to 1.1 [0.3, 6.4] years for the Omicron period (p=0.009).

We present the prevalence of the different types of underlying health condition in Table 2. The proportion of children and adolescents with a pre-existing health condition fell as shown in Table 1; however, on closer inspection, this change was related to the rising proportion of admissions in infants. To illustrate this, pre-existing health conditions identified as vaccine eligible in England[19] occurred in 2,010/19,790 (10.2%) infants hospitalized versus 12,295/26,130 (47.1%) participants aged 1 - 17 years hospitalized; and 405/1,015 (39.9%) infants receiving critical care versus 930/1,550 (60.0%) participants aged 1 - 17 years receiving critical care, as shown in Figure 4. Among infants hospitalized, the proportion with an underlying health condition remained stable (p=0.09), whereas among children aged 1 through 17 years of age who were hospitalized, the proportion rose slightly through CoV periods, from: 585 (46.4%) Original, 1,055 (43.7%) Alpha, 2,660 (43.5%) Delta, 5,270 (48.1%) Omicron first 7 months, 1,900 (49.5%) Omicron second 7 months, 825 (53.2%) Omicron third 7 months (p=0.051).

Over the study period, boys made up a higher proportion of SARS-CoV-2 related admissions than girls, with this difference becoming slightly more pronounced over time (7,470 (53.3%) in the first three waves (Original, Alpha, Delta) to 17,610 (55.2%) in the Omicron period, p=0.05).

Throughout the study period, children and adolescents who had a SARS-CoV-2 related hospitalization were more likely to be of a minority ethnic background and to reside in areas

with higher deprivation indices than expected based on the English population (Asian or British Asian background accounts for 7.7% of children, Black or Black British background accounts for 3.7%,[24] and 24.0% of children live in high deprivation areas;[18]). Among children with a SARS-CoV-2 related hospitalization, 6,670 (14.5%) were of Asian or British Asian background; 2,525 (5.5%) were of Black or Black British background; and 12,640 (27.5%) resided in high deprivation areas. The over representation of these groups was most pronounced at the start of the pandemic (Original and Alpha) when 1,130 (21.2%) were of Asian or British Asian background; 450 (8.4%) were of Black or Black British background; and 1,690 (31.6%) resided in the most deprived areas (all p<0.001).

Discussion

A key finding from this population-based study of England's 11.9 million children and adolescents[1], is that among 45,920 SARS-CoV-2 related hospital admissions, the number involving infants increased from the start of the pandemic, did not fall as we emerged from the height of the pandemic, and mainly affected babies with no known underlying health conditions. The latest 12-month period is a potential illustration of the 'new normal' involving *6,300 SARS-CoV-2 related admissions in infants, of which only 655 (10.4%) had an underlying health condition identified as higher risk by the English vaccination programme*[8]*, 305 (4.8%) involved critical care, and 8 deaths were recorded.* Conversely, among children and adolescents aged 1 through 17 years, the number hospitalized due to SARS-CoV-2 fell to its lowest number, however there was an increasing likelihood that hospitalized children had a pre-existing health condition[8]: among 4,335 hospitalized children and adolescents aged 1 through 17 years, 2,235 (51.6%) had an underlying health condition identified as

higher risk by the English vaccination program, 235 (5.4%) received critical care and 9 died with COVID-19 as a cause. Underlying health conditions affected most of those aged 1 through 17 years who required critical care (60%) or who died with COVID-19 as a cause (>90%), and PMS-TS became highly unusual with only 20 recorded cases.

The current phenotype of SARS-CoV-2 related hospitalization in children reflects the fact that although waning of immunity occurs,[3] by 2022-2023, many children aged over 1-year were protected by acquired immunity, including immunity from COVID-19 vaccination, especially in teenagers.[6, 25] Conversely infants have the lowest likelihood of protection from previous infection or vaccination against SARS-CoV-2, and are in general most vulnerable to respiratory illnesses,[26] partially explaining their greater risk of needing hospital treatment when infected, irrespective of underlying health conditions. In our previous study of English children involving a linked dataset containing all ascertained SARS-CoV-2 infections inclusive of community testing and hospital admissions during the pandemic, infants were the most likely to be hospitalized while infected of all age groups at 7,225/41,360 (17.1%),[2] which can be compared with the estimated proportion of hospitalization when infected of 29%,[27] from a recent systematic analysis of respiratory syncytial virus (RSV). It is likely that changes in SARS-CoV-2 also contributed to both age groups affected, severity and disease syndromes, as hospitalization of young children was conspicuously low at the start of the pandemic, and PIMS-TS waned as predominant SARS-CoV-2 variant changed.

Of concern, as shown in prior studies, children with ethnic minority background and residence in the most deprived areas, remain most vulnerable to severe illness due to SARS-CoV-2[2, 13]. This proclivity has has been shown with a range of respiratory viruses causing

critical illnesses, including RSV, and has been attributed to family characteristics, socioeconomic and environmental factors.[28] Their vulnerability was particularly pronounced in 2020, suggesting that children from high deprivation areas and ethnic minority background experienced pandemic specific health inequalities as do their adult family members. The Royal College of Paediatrics in England noted that health inequalities based on ethnicity, income, housing, climate change, and being looked after by local authorities are important contributors of acute and long-term illnesses among children in 2024.[29]

Our study is strengthened by use of population-scale EHR data, peer reviewed methods of case ascertainment[2] and reasonably consistent testing of children with respiratory symptoms in hospital settings. Limitations are related to potential influence by the quality of coding in the EHR, which is undertaken based on national guidance in England. Additionally, our study only considered acute illness related to SARS-CoV-2 and did not aim to capture post-COVID-syndrome, which also can affect young children. [30]

Our findings strongly emphasize the importance of protection conferred on young infants under 6 months of age by maternal COVID-19 immunization during pregnancy.[31] Pregnant persons should counselled about the risk for young infants of hospital admission with SARS-CoV-2 infection and protection afforded to their infants as well as to themselves by maternal immunization.

COVID-19 vaccine is available for children aged from 6 months to 5 years, and in randomized studies was found to be safe, immunogenic, and efficacious against symptomatic infection.[32, 33] However, severe disease cases were too few to contribute to these studies, thus emphasizing the importance of observational population-based data in documenting these. The Centers for Disease Control and Prevention (CDC) considered benefits and harms,

value, acceptability, feasibility, and resource use, in their recommendation for COVID-19 vaccination to all persons aged over 6 months in the United States.[34]

The recent number of infant hospitalizations (6,300) per year and the burden of these hospitalizations expressed in terms of the length of stay (median 2 days) may be used to inform future decisions about the use of COVID-19 vaccination for children aged 6 months to 5 years. For context, we note that the Joint Committee for Vaccination and Immunisation (JCVI) in England, which does not recommend COVID-19 for healthy children, recommended a year-round passive immunization of infants against RSV using nirsevimab or maternal immunization, to protect all infants against RSV in 2023. JCVI was informed by a model assumption of 20,000 hospitalized with RSV, 900 (4.5%) intensive care admissions and 22 deaths in infants per annum.[35] These figures are similar to the findings of an English study that used hospital episode statistics between 1999-2012, which recorded an average of 20,000 hospital admissions and 900 critical care admissions annually in children with bronchiolitis of all causes.[26] Furthermore, JCVI considered the burdensome nature of hospital admission for RSV expressed as an estimated 11,000 infants per annum needing nasogastric feeding and low flow oxygen[35] which mean hospital stays of at least a week (ie, greater than 2 days).

In the absence of further changes in SARS-CoV-2 severity and health protection policies, the National Health Service and pediatric clinical care teams in England should be prepared for the likely ongoing burden of SARS-CoV-2 related hospital admissions in previously healthy infants .

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Author contributions

HW did the analysis and created the figures, KB and HW wrote the paper, CT and DS supported the analysis and data management, BM, SD, SF, SV, CP, HW and KB designed the study, KB and HK wrote the clinical coding maps. All authors contributed to and approved the paper.

Transparency statement

All authors meet the ICMJE criteria for authorship. The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and

that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Declaration of interests statement

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Ethical approval and data availability

The North East - Newcastle and North Tyneside 2 research ethics committee provided ethical approval for the CVD-COVID-UK/COVID-IMPACT research program (REC No 20/NE/0161) to access, within secure trusted research environments, unconsented, whole-population, de-identified data from electronic health records collected as part of patients' routine healthcare.

The data used in this study are available in NHS England's Secure Data Environment (SDE) service for England, but as restrictions apply they are not publicly available

(https://digital.nhs.uk/services/secure-data-environment-service). The CVD-COVID-UK/COVID-IMPACT program, led by the BHF Data Science Centre (https://bhfdatasciencecentre.org/), received approval to access data in NHS England's SDE service for England from the Independent Group Advising on the Release of Data (IGARD) (https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/independent-group-advising-on-the-release-of-data) via an application made in the Data Access Request Service (DARS) Online system (ref. DARS-NIC-381078-Y9C5K) (https://digital.nhs.uk/services/data-access-request-service-dars/dars-products-and-services). The CVD-COVID-UK/COVID-IMPACT Approvals & Oversight Board (https://bhfdatasciencecentre.org/areas/cvd-COVID-uk-COVID-impact/) subsequently granted approval to this project to access the data within NHS England's SDE service for England. The de-identified data used in this study were made available to accredited researchers only. Those wishing to gain access to the data should contact bhfdsc@hdruk.ac.uk in the first instance.

Table I. Cohort characteristics identified SARS-CoV-2-related admissions stratified by viral variant period. Note that all variables are derived from the linked cohort except for the figures for deaths, which are derived from publicly available ONS data and aim to provide contextual comparison.

* Counted only when a positive test date occurs in the period of 14 days before admission up to discharge, the presence of this test defines an admission as SARS-CoV-2-related, but may not be the sole reason for their inclusion in the cohort (ie, diagnostic codes may also be present).

Table II. Pre-existing health conditions for all ascertained SARS-CoV-2 related admissions, stratified by variant period.

Figure 1: Flow chart illustrating the hierarchy of categorization for ascertained hospitalisations in the study cohort.

Figure 2: Key trends in SARS-CoV-2 related hospital admissions in children and adolescents during study period July 2020 to August 2023.

From top panel to bottom panel:

ONS' reported modelled population infection prevalence;

number of SARS-CoV-2 associated hospital admissions by type;

number of SARS-CoV-2 associated hospital admissions by age group;

proportion of SARS-CoV-2 associated hospital admissions by ethnic group;

proportion of SARS-CoV-2 associated hospital admissions by deprivation quintile;

proportion of SARS-CoV-2 associated hospital admissions by underlying health condition recognized by the English vaccination program and listed in the 'Green Book'[30];

proportion of SARS-CoV-2 associated hospital admissions by nth admission;

number of admissions.

The bottom panel shows the count directly and the other panels show 14 day rolling averages of daily counts.

Figure 3: Heatmap illustrating the age of children among those with a SARS-CoV-2 related admission to hospital over time. The bar charts on each axis illustrate the overall counts of admissions by month and year of age appropriately. The top line chart illustrates the increasing concentration of <1's in the cohort, to explain the difficulty in viewing the bimodality in the age of admissions when viewed over time.

Figure 4: The proportion of children and adolescents in different age groups who had an underlying health condition recognized by the English vaccination program and listed in the 'Green Book'[30]. The top panel shows all children and adolescents admitted to hospital and the lower panel shows the subset receiving critical care.

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Time period and relevant variant	Overall	Original 2020-07-01 to 2020-12-07	Alpha 2020-12-08 to 2021-05-17	Delta 2021-05-18 to 2021-12-13	Omicron 1 2021-12-14 to 2022-07-13	Omicron 2 2022-07-14 to 2023-02-13	Omicron 3 2023-02-14 to 2023-09-30
Number of admissions	45,920	1,795	3,545	8,680	18,945	8,660	4,295
Sex							
Male	25,080 (54.6)	950 (52.9)	1,940 (54.7)	4,585 (52.8)	10,370 (54.7)	4,835 (55.8)	2,405 (56.0)
Female	20,840 (45.4)	845 (47.1)	1,605 (45.3)	4,095 (47.2)	8,580 (45.3)	3,825 (44.2)	1,890 (44.0)
Age (median [IQR])	1.66 [0.31, 8.84]	4.79 [0.60, 12.40]	3.69 [0.53, 11.24]	5.12 [0.58, 12.62]	1.72 [0.33, 8.22]	0.73 [0.25, 4.09]	0.53 [0.24, 2.73]
Age category							
< 1	19,790 (43.1)	530 (29.6)	1,130 (31.9)	2,565 (29.6)	7,995 (42.3)	4,815 (55.7)	2,745 (63.9)
1 - 4	9,995 (21.8)	385 (21.4)	795 (22.4)	1,745 (20.1)	4,415 (23.3)	1,900 (21.9)	750 (17.5)
5 - 11	8,260 (18.0)	400 (22.3)	820 (23.1)	2,000 (23.0)	3,625 (19.1)	965 (11.1)	460 (10.7)
12 - 15	4,960 (10.8)	315 (17.5)	485 (13.7)	1,570 (18.1)	1,825 (9.6)	565 (6.5)	205 (4.8)
16 - 17	2,915 (6.3)	165 (9.2)	315 (8.9)	800 (9.2)	1,085 (5.7)	415 (4.8)	135 (3.1)
Ethnic group							
Asian or Asian British	6,670 (14.5)	440 (24.5)	695 (19.7)	1,145 (13.2)	2,410 (12.7)	1,275 (14.7)	700 (16.2)
Black or Black British	2,525 (5.5)	130 (7.2)	320 (9.0)	510 (5.9)	920 (4.9)	410 (4.7)	235 (5.5)
Chinese	185 (0.4)	<10 (<0.6)	10 (0.3)	35 (0.4)	65 (0.3)	50 (0.6)	20 (0.5)
Mixed	2,470 (5.4)	90 (5.0)	210 (5.9)	495 (5.7)	1,000 (5.3)	465 (5.4)	215 (5.0)
Other	1,395 (3.0)	65 (3.6)	145 (4.1)	255 (2.9)	540 (2.9)	250 (2.9)	140 (3.3)
Unknown	355 (0.8)	10 (0.6)	40 (1.1)	55 (0.6)	140 (0.7)	70 (0.8)	40 (0.9)
White	32,320 (70.4)	1,055 (58.8)	2,125 (59.9)	6,185 (71.3)	13,870 (73.2)	6,140 (70.9)	2,945 (68.6)
IMD Quintile							
1 (most deprived)	12,640 (27.6)	600 (33.4)	1,090 (30.7)	2,460 (28.4)	4,900 (25.9)	2,370 (27.4)	1,215 (28.3)
2	10,110 (22.0)	415 (23.1)	880 (24.8)	1,870 (21.5)	4,070 (21.5)	1,910 (22.1)	965 (22.5)
3	8,655 (18.8)	330 (18.4)	645 (18.2)	1,625 (18.7)	3,585 (18.9)	1,700 (19.6)	775 (18.0)
4	7,685 (16.7)	265 (14.8)	495 (14.0)	1,415 (16.3)	3,360 (17.7)	1,455 (16.8)	695 (16.2)
5 (least deprived)	6,830 (14.9)	185 (10.3)	435 (12.3)	1,310 (15.1)	3,030 (16.0)	1,225 (14.1)	645 (15.0)
Presence of a risk factor linked to clinical vulnerability by the vaccination program	14,440 (31.4)	685 (38.2)	1,210 (34.1)	2,940 (33.9)	6,090 (32.1)	2,420 (27.9)	1,095 (25.5)
Presence of any medical or developmental risk factor	22,715 (49.5)	990 (55.2)	1,890 (53.3)	4,505 (51.9)	9,405 (49.6)	4,025 (46.5)	1,900 (44.2)

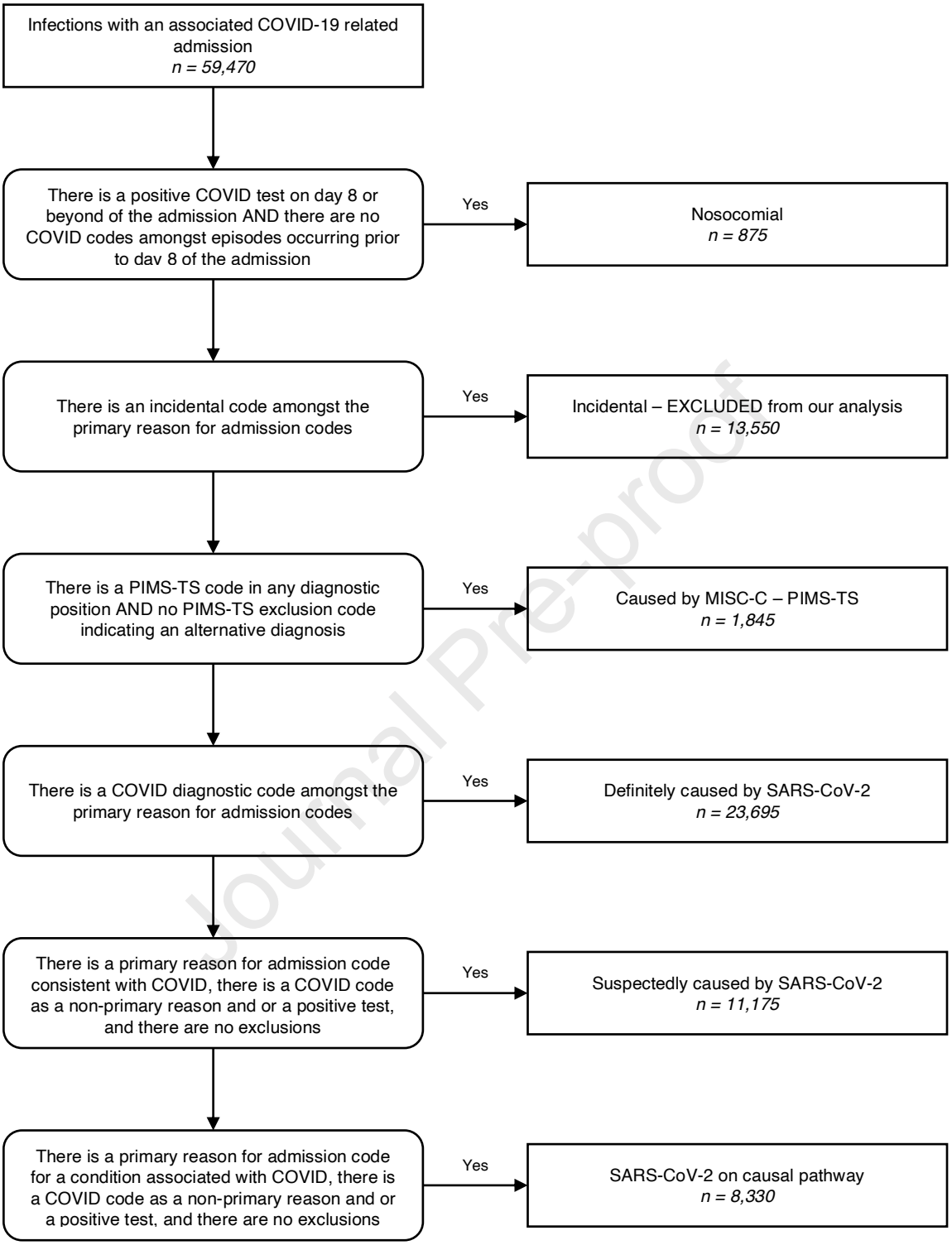
COVID positive test in window *	34,710 (75.6)	1,360 (75.8)	2,680 (75.6)	6,885 (79.3)	14,680 (77.5)	6,110 (70.6)	2,995 (69.7)
Length of stay (median, [IQR])	2.00 [1.00, 3.00]	2.00 [1.00, 4.00]	2.00 [1.00, 5.00]	2.00 [1.00, 4.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]
Still in hospital	105 (0.2)	<10 (<0.6)	<10 (<0.3)	20 (0.2)	45 (0.2)	15 (0.2)	10 (0.2)
Critical care provided	2,565 (5.6)	160 (8.9)	400 (11.3)	615 (7.1)	750 (4.0)	440 (5.1)	200 (4.7)
Type of admission							
Nosocomial SARS-CoV-2	875 (2.0)	50 (2.7)	90 (2.5)	130 (1.4)	350 (1.9)	185 (2.2)	65 (1.5)
PMS-TS diagnosis	1,845 (4.0)	240 (13.4)	565 (15.9)	770 (8.9)	240 (1.3)	20 (0.2)	<10 (<0.2)
Covid-19 as definite cause	23,695 (51.6)	710 (39.6)	1,410 (39.8)	4,110 (47.4)	9,860 (52.0)	4,965 (57.3)	2,645 (61.6)
Covid-19 suspected as causal	11,175 (24.3)	440 (24.5)	850 (24.0)	2,040 (23.5)	5,120 (27.0)	1,775 (20.5)	955 (22.2)
SARS-CoV-2 on causal pathway	8,330 (18.1)	355 (19.8)	630 (17.8)	1,630 (18.8)	3,375 (17.8)	1,715 (19.8)	625 (14.6)
Vaccination status 14 days prior to infection							
Unvaccinated	43,215 (94.1)	1,795 (100.0)	3,540 (99.9)	8,455 (97.4)	17,340 (91.6)	8,050 (93.0)	4,040 (94.1)
First Dose	1,305 (2.8)	0 (0.0)	<10 (<0.3)	170 (2.0)	855 (4.5)	200 (2.3)	70 (1.6)
Second Dose	990 (2.2)	0 (0.0)	0 (0.0)	50 (0.6)	535 (2.8)	280 (3.2)	125 (2.9)
Booster Dose	410 (0.9)	0 (0.0)	0 (0.0)	<10 (<0.1)	215 (1.1)	130 (1.5)	60 (1.4)
Nth Infection							
First	43,550 (94.8)	1,785 (99.4)	3,515 (99.2)	8,605 (99.1)	17,925 (94.6)	7,785 (89.9)	3,935 (91.6)
Second	2,285 (5.0)	<10 (<0.6)	30 (0.8)	70 (0.8)	1,010 (5.3)	835 (9.6)	325 (7.6)
> Second	85 (0.2)	0 (0.0)	<10 (<0.3)	<10 (<0.1)	<10 (<0.1)	40 (0.5)	35 (0.8)
Deaths involving COVID-19 (ONS)	133	2	18	40	41	21	11
Deaths due to COVID-19 (ONS)	93	2	15	34	22	15	5

Table 1: Cohort characteristics for all identified SARS-CoV-2-related admission amongst the study group, stratified by variant period. Note that all variables are derived from the linked cohort except for the figures for deaths, which are derived from publicly available ONS data and aim to provide contextual comparison.

* Counted only when a positive test date occurs in the period of 14 days before admission up to discharge, the presence of this test defines an admission as SARS-CoV-2-related, but may not be the sole reason for their inclusion in the cohort (i.e. diagnostic codes may also be present).

Time period	Overall	Original	Alpha	Delta	Omicron 1	Omicron 2	Omicron 3
Number	45,920	1,795	3,545	8,680	18,945	8,660	4,295
Presence of a health condition linked to greater vulnerability recognized by the English vaccination program (Green Book[30])	14,305 (31.2)	675 (37.6)	1,195 (33.7)	2,890 (33.3)	6,050 (31.9)	2,405 (27.8)	1,090 (25.4)
Cancer (Excluding Benign Tumors)	2,185 (4.8)	65 (3.6)	160 (4.5)	345 (4.0)	985 (5.2)	425 (4.9)	205 (4.8)
Blood Disorders and Immune Deficiencies	1,775 (3.9)	100 (5.6)	165 (4.7)	315 (3.6)	765 (4.0)	290 (3.3)	135 (3.1)
Endocrine Conditions	2,195 (4.8)	105 (5.8)	185 (5.2)	460 (5.3)	940 (5.0)	365 (4.2)	135 (3.1)
Severe Neurological and Developmental Conditions	3,995 (8.7)	185 (10.3)	330 (9.3)	780 (9.0)	1,720 (9.1)	675 (7.8)	305 (7.1)
Hypertension, Cardiac Valves and Cardiomyopathy	2,100 (4.6)	95 (5.3)	215 (6.1)	350 (4.0)	855 (4.5)	395 (4.6)	185 (4.3)
Severe Respiratory Diseases	3,580 (7.8)	215 (12.0)	300 (8.5)	840 (9.7)	1,445 (7.6)	540 (6.2)	245 (5.7)
Digestive, Liver and Renal Diseases	1,280 (2.8)	55 (3.1)	100 (2.8)	300 (3.5)	590 (3.1)	155 (1.8)	85 (2.0)
Arthritis and Connective Tissue Diseases	545 (1.2)	20 (1.1)	50 (1.4)	125 (1.4)	245 (1.3)	75 (0.9)	30 (0.7)
Congenital Syndromes and Anomalies	5,375 (11.7)	215 (12.0)	420 (11.8)	885 (10.2)	2,260 (11.9)	1,075 (12.4)	525 (12.2)
Obesity (>16 Years of Age)	220 (0.5)	15 (0.8)	35 (1.0)	65 (0.7)	65 (0.3)	25 (0.3)	10 (0.2)
Pregnancy	60 (0.1)	<10 (<0.6)	<10 (<0.3)	15 (0.2)	25 (0.1)	<10 (<0.1)	<10 (<0.2)
A wider range of all medial and developmental underlying health conditions identified in our cohort July 2020-March 2022	22,355 (48.7)	970 (54.0)	1,850 (52.2)	4,395 (50.6)	9,295 (49.1)	3,965 (45.8)	1,880 (43.8)
Cancer and Neoplasms (Excluding Benign Tumors)	2,340 (5.1)	80 (4.5)	175 (4.9)	360 (4.1)	1,050 (5.5)	450 (5.2)	220 (5.1)
Blood Disorders and Immune Deficiencies	4,260 (9.3)	205 (11.4)	370 (10.4)	725 (8.4)	1,865 (9.8)	740 (8.5)	360 (8.4)
Endocrine Conditions	5,025 (10.9)	240 (13.4)	460 (13.0)	1,040 (12.0)	2,095 (11.1)	840 (9.7)	355 (8.3)
Neurological and Developmental Conditions	9,365 (20.4)	395 (22.0)	750 (21.2)	1,770 (20.4)	4,055 (21.4)	1,655 (19.1)	740 (17.2)
Respiratory Conditions	4,885 (10.6)	260 (14.5)	400 (11.3)	1,025 (11.8)	2,000 (10.6)	835 (9.6)	365 (8.5)
Congenital Hypertension and Heart Disease (Congenital and Acquired)	5,905 (12.9)	265 (14.8)	545 (15.4)	1,080 (12.4)	2,350 (12.4)	1,110 (12.8)	555 (12.9)
Digestive and Liver Conditions	3,485 (7.6)	135 (7.5)	235 (6.6)	630 (7.3)	1,585 (8.4)	610 (7.0)	285 (6.6)
Muscle, Skin and Arthritic Conditions	3,380 (7.4)	145 (8.1)	260 (7.3)	605 (7.0)	1,460 (7.7)	610 (7.0)	305 (7.1)
Renal and Genitourinary Conditions	2,995 (6.5)	120 (6.7)	245 (6.9)	560 (6.5)	1,265 (6.7)	530 (6.1)	270 (6.3)
Prematurity and Low Birth Weight	5,480 (11.9)	165 (9.2)	345 (9.7)	790 (9.1)	2,160 (11.4)	1,350 (15.6)	670 (15.6)
Obesity defined based on World Health Organisation thresholds	1,660 (3.6)	90 (5.0)	210 (5.9)	465 (5.4)	565 (3.0)	225 (2.6)	105 (2.4)
Pregnancy identified in medical record	60 (0.1)	<10 (<0.6)	<10 (<0.3)	15 (0.2)	25 (0.1)	<10 (<0.1)	<10 (<0.2)

Table 2: Pre-existing health conditions for all ascertained admissions, stratified by variant period.



Variant Period

Pre−Alpha | Alpha | Journal Pre-proof | Omicron 3

% of Monthly Admissions in <1s

100%
75%
50%
25%
0%

Total Monthly Admissions

4000
3000
2000
1000
0

Number of Admissions

0 500 1000 1500 2000

Age

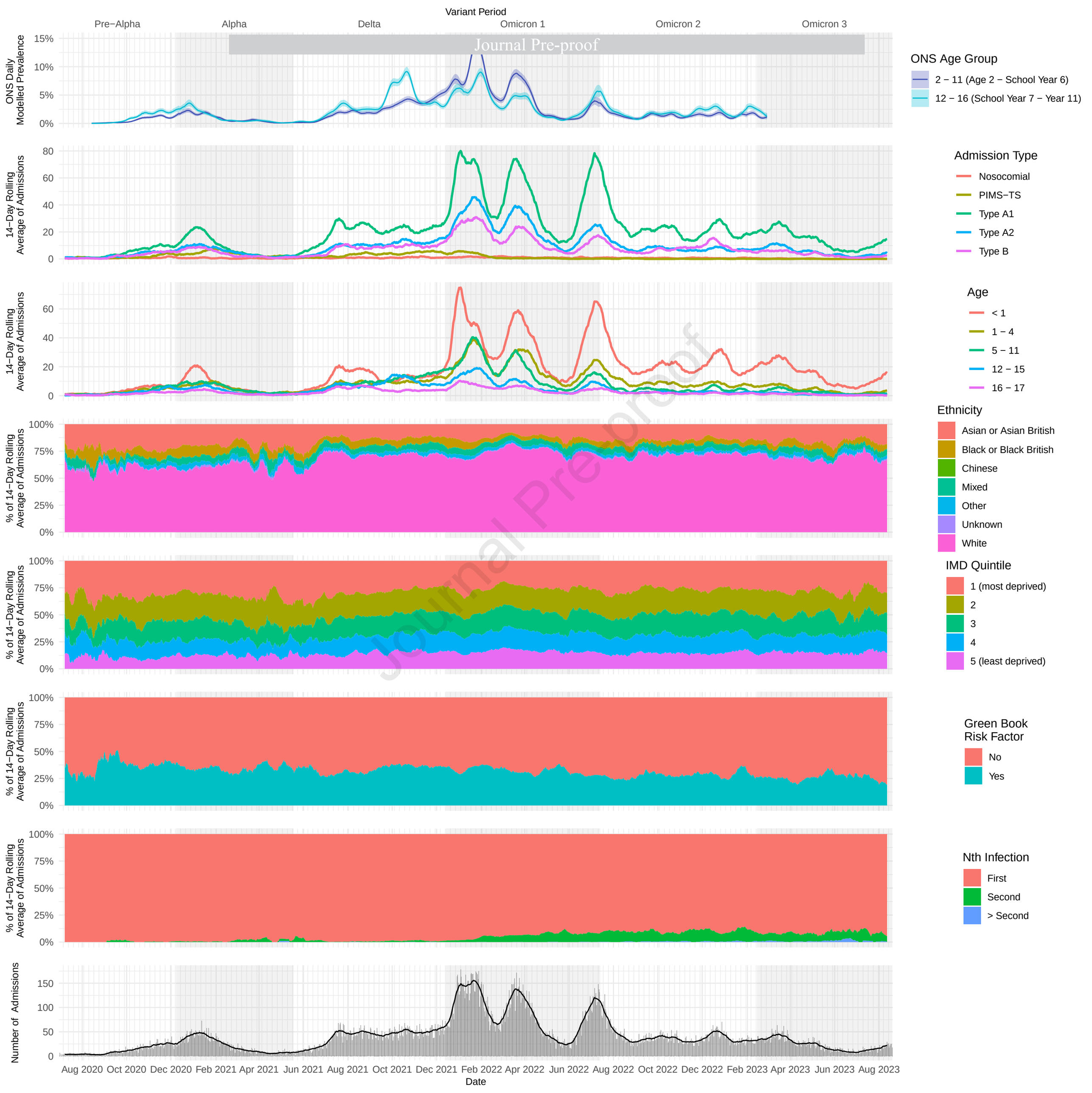
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0

Aug 2020 Oct 2020 Dec 2020 Feb 2021 Apr 2021 Jun 2021 Aug 2021 Oct 2021 Dec 2021 Feb 2022 Apr 2022 Jun 2022 Aug 2022 Oct 2022 Dec 2022 Feb 2023 Apr 2023 Jun 2023 Aug 2023

Month

0 5000 10000 15000 20000

Total Admissions in Age Year


Variant Period
Pre−Alpha
Alpha
Delta
Omicron 1
Omicron 2
Omicron 3
Journal Pre-proof
ONS Daily Modelled Prevalence
15%
10%
5%
0%
14−Day Rolling Average of Admissions
80
60
40
20
0
% of 14−Day Rolling Average of Admissions
100%
75%
50%
25%
0%
Number of Admissions
150
100
50
0
Aug 2020
Oct 2020
Dec 2020
Feb 2021
Apr 2021
Jun 2021
Aug 2021
Oct 2021
Dec 2021
Feb 2022
Apr 2022
Jun 2022
Aug 2022
Oct 2022
Dec 2022
Feb 2023
Apr 2023
Jun 2023
Aug 2023
Date
ONS Age Group
2 − 11 (Age 2 − School Year 6)
12 − 16 (School Year 7 − Year 11)
Admission Type
Nosocomial
PIMS−TS
Type A1
Type A2
Type B
Age
< 1
1 − 4
5 − 11
12 − 15
16 − 17
Ethnicity
Asian or Asian British
Black or Black British
Chinese
Mixed
Other
Unknown
White
IMD Quintile
1 (most deprived)
2
3
4
5 (least deprived)
Green Book Risk Factor
No
Yes
Nth Infection
First
Second
> Second