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1 **Risk factors for PICU admission and death amongst children and young people**  
2 **hospitalized with COVID-19 and PIMS-TS in England during the first pandemic year**

3

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32 **Abstract**

33 Identifying which children and young people (CYP) are most vulnerable to serious SARS-CoV-  
34 2 infection is important to guide protective interventions.

35

36 To address this question we used data for all hospitalizations in England in 0-17 year olds  
37 from 1<sup>st</sup> Feb 2019 - 31<sup>st</sup> Jan 2021. We examined how sociodemographic factors and  
38 comorbidities may be risk factors for Pediatric Intensive Care Unit (PICU) admission within  
39 hospitalizations due to: COVID-19 and Paediatric Inflammatory Multisystem Syndrome  
40 Temporally Associated with SARS-CoV-2 (PIMS-TS) in the first pandemic year (2020-21), all  
41 other non-traumatic causes in 2020-21, all non-traumatic causes in 2019-20, and  
42 hospitalizations due to influenza in 2019-20.

43

44 Risk of PICU admission and death from COVID-19 or PIMS-TS amongst CYP was very low. We  
45 identified 6,338 COVID-19 hospitalizations, of which 259 were admitted to PICU and 8 died,  
46 and 712 PIMS-TS hospitalizations, of which 312 were admitted to PICU and < 5 died.  
47 Hospitalizations with COVID-19 and PIMS-TS were more common amongst males, older CYP,  
48 those from socio-economically deprived neighbourhoods, and those who were non-White  
49 ethnicity (Black, Asian, mixed or other).

50

51 Odds of PICU admission were: increased amongst CYP aged under 1 month and decreased  
52 amongst 15-17 year olds compared with 1-4 year olds with COVID-19; increased in older CYP  
53 and females with PIMS-TS, increased for Black compared with White ethnicity in COVID-19  
54 and PIMS-TS patients. Odds of PICU admission in COVID-19 were increased for CYP with  
55 comorbidities, and highest for CYP with multiple medical problems. Increases in odds of  
56 PICU admission associated with different comorbidities in COVID-19 showed a similar  
57 pattern to other causes of hospitalization examined, and so likely reflect background  
58 vulnerabilities. These findings identify distinct risk factors associated with PICU admission  
59 among CYP with COVID-19 or PIMS-TS that may aid treatment and prevention strategies.

60

61

62



64 **Main Text**

65 **Introduction**

66

67 Most children and young people (CYP) experience a mild disease following SARS-CoV-2  
68 infection compared with adults,<sup>1-3</sup> and asymptomatic infection is common.<sup>4</sup> However,  
69 severe clinical outcomes have been reported amongst CYP due to COVID-19 and to  
70 Paediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS-CoV-2  
71 (PIMS-TS) or Multisystem Inflammatory Syndrome in Children (MIS-C), including a small  
72 number of deaths.<sup>2,5-9</sup> Understanding which CYP are vulnerable to increased risk is  
73 important to guide clinicians, families and policymakers in relation to protective shielding  
74 and potential vaccination strategies.

75

76 Early in the pandemic, guidance from the UK Royal College of Paediatrics and Child Health  
77 (RCPCH) identified CYP with immunodeficiency or immunosuppression, and those with  
78 certain malignancies, as having the greatest vulnerability to COVID-19.<sup>10</sup> However, CYP with  
79 a broad range of other conditions have also been highlighted as being potentially clinically  
80 extremely vulnerable (CEV). CYP who are identified as CEV have been advised to take  
81 additional “shielding” precautions to reduce the risk of SARS-CoV-2 infection in many  
82 countries. These include measures that may result in harm to CYP and their families,  
83 including those associated with reduced social mixing and restriction of in-person schooling.

84

85 Clear guidance is urgently needed on which CYP are at higher risk of poorer outcomes of  
86 SARS-CoV-2 infection in order to limit harms due to inappropriate shielding. The rarity of  
87 severe and fatal COVID-19 in CYP means that large-scale population-based studies are  
88 needed to identify CYP at greatest risk. These analyses also need to take into account  
89 background risks for severe illness that preceded the pandemic; CYP who are at increased  
90 risk of severe disease due to SARS-CoV-2 infection may also be those who are vulnerable to  
91 other respiratory viruses such as influenza.<sup>11</sup>

92

93 We used national linked administrative health data (Secondary Use Services data (SUS),  
94 linked with the national SARS-CoV-2 database, pediatric intensive care data, and national  
95 mortality data) to analyse all hospital admissions due to COVID-19 or PIMS-TS amongst CYP

96 in England from Feb 2020 – Jan 2021. Among these admissions, we examined how  
97 sociodemographic factors and pre-existing conditions recorded over the previous 5 years  
98 (from 2015/16 to 2020/21) were associated with odds of admission to a Pediatric Intensive  
99 Care Unit (PICU), which we used as a proxy for serious disease, or death. To understand if  
100 these risk factors were specific to SARS-CoV-2, represented background vulnerabilities or  
101 reflected changes to healthcare activity caused by the pandemic, we then repeated this  
102 analysis amongst CYP admitted with other causes of admission that year, and admissions  
103 during 2019-20 including those due to influenza.

104

105

106 **Results**

107 There were 1,242,197 emergency non-traumatic hospital admissions in England (hereafter  
108 “admissions”) between 01 Feb 2019 and 31 Jan 2021 involving 892,906 CYP; 699,397 (78%)  
109 had only one admission. During 2020-21, there were 470,606 admissions: 6,338 with COVID-  
110 19 amongst 5,830 CYP; 712 with PIMS-TS amongst 690 CYP and 463,556 for other causes  
111 amongst 367,637 CYP. In comparison, there were 771,591 admissions for 587,115 CYP  
112 during 2019-20, of which 6968 were due to influenza in 6,780 CYP (see supplementary  
113 material 1 table S1 and S15). 69.8% of CYP admitted due to PIMS-TS had no prior hospital  
114 admissions, compared with 49.5-54.4% in all other cohorts.

115

116 The distribution of admissions by age, sex and ethnicity differed between the COVID-19,  
117 PIMS-TS, and other cohorts (Table 1). A higher proportion of the PIMS-TS cohort was male  
118 (63.5%) compared to the other cohorts (52.8-54%). Overall, 30.9% of admissions with  
119 COVID-19 were in infants (children aged under 1 year, including neonates under 1 month of  
120 age, and post neonatal infants aged 1-11 months), similar to other pandemic year  
121 admissions and total admissions in 2019-20, but more than for influenza (17.1%) during this  
122 time period. Amongst PIMS-TS, only 10.3% of admissions were in infants, whereas >85%  
123 were among 1-14 year-olds. CYP with non-White ethnicity made up 41.9% of COVID-19  
124 admissions, and 60.0% of PIMS-TS admissions, higher than the other hospitalization cohorts  
125 we examined. There were more admissions in CYP from more deprived neighbourhoods  
126 compared with least deprived in all cohorts, as assessed using Index of Multiple Deprivation  
127 (IMD) quintile category. Further description of how IMD is determined is available in the  
128 supplementary material.

129

130 Amongst COVID-19 admissions, 53.9% had a recorded comorbidity, and 18.0% had a life  
131 limiting comorbidity, higher than for other pandemic year admissions, all admissions in  
132 2019-20, and influenza admissions in 2019-20 (Supplementary Table S1). Patterns of  
133 comorbidities amongst admissions with PIMS-TS were different to the other cohorts, with  
134 68.3% having any comorbidity recorded, of which 20.6% were life-limiting. Due to the multi-  
135 system nature of PIMS-TS, and of limitations in how data are recorded within SUS, many of  
136 the comorbidities recorded could have been related to complications of the disease, rather  
137 than prior conditions. Although 40.2% of PIMS-TS admissions had a cardiovascular

138 comorbidity recorded, only 5.3% had a congenital cardiac condition, with remaining codes  
139 including arrhythmias and aneurysms, which may reflect the disease process. When non-  
140 congenital cardiac conditions, blood disorders and anemias were excluded, only 15.9% of  
141 PIMS-TS admissions had a comorbidity recorded, compared with 30-35% in the other  
142 cohorts.

143

#### 144 *Outcomes following admission*

145 Table 2 shows total numbers and proportions of PICU admissions within each cohort by  
146 comorbidity category, with additional data for all comorbidities examined in Supplementary  
147 material 1 Tables S3-S5. Across COVID-19 admissions, 259 (4.1%) were admitted to PICU,  
148 compared with 312 (43.8%) of PIMS-TS admissions, 5016 (1.1%) of other pandemic year  
149 admissions, 7282 (0.9%) of all admissions in 2019-20 and 161 (2.3%) of influenza admissions  
150 in 2019-20.

151

152 Twenty nine CYP admitted with COVID-19 died within 28 days of hospitalisation. Of these, 8  
153 were confirmed as likely caused by SARS-CoV-2 infection after reviewing case notes and  
154 death notification data. All had a comorbidity recorded and 7/8 had a life-limiting condition.  
155 Six CYP died within 28 days of an admission with PIMS-TS, of which < 5 were thought to be  
156 caused by the disease.

157

#### 158 *Sociodemographic factors*

159 In multivariable models adjusting for all factors and the presence of comorbidities, female  
160 sex was associated with increased odds of PICU admission for PIMS-TS, and reduced odds  
161 amongst all admissions 2019-20, with no associations found by sex for COVID-19 or the  
162 other cohorts (supplementary material 1, tables S11-S15). Compared with admissions  
163 amongst 1-4 year olds, odds of PICU admission for COVID-19 were increased amongst  
164 neonates (CYP aged less than 1 month) and decreased amongst 15-17 year olds, similar to  
165 patterns for other pandemic year admissions and all admissions 2019-20, (although odds  
166 were also decreased for 5-14 year olds in these cohorts). Odds of PICU admission for PIMS-  
167 TS increased with age in a stepwise fashion and were highest in 15-17 year olds. The odds of  
168 PICU admission within influenza admissions in 2019-20 were only higher amongst neonates  
169 compared with 1-4 year olds.



170

171 Compared with White CYP, odds of PICU admission were higher amongst Black CYP for  
172 COVID-19 and Black, Asian and CYP with unknown ethnicity for PIMS-TS. Other pandemic  
173 year admissions and all admissions 2019-20 showed a pattern of higher odds of PICU  
174 admission in non-White ethnic groups, with no evident differences by ethnicity amongst  
175 influenza admissions in 2019-20. There were no significant differences in odds of PICU  
176 admission by IMD category for COVID-19, all admissions in 2019-20 and influenza  
177 admissions in 2019-20. In contrast, odds of PICU admission were increased in less deprived  
178 categories amongst PIMS-TS admissions, and amongst other pandemic year admissions.

179

### 180 *Comorbidities*

181 The odds of admission to PICU were increased amongst CYP with any comorbidity compared  
182 with no comorbidity in all cohorts (supplementary material 2). The increases in odds of PICU  
183 admission associated with having each of any comorbidity, a life-limiting comorbidity, or  
184 comorbidities in more than one body system for COVID-19 (Figure 1), had overlapping  
185 confidence intervals with those for all admissions in 2019-20 and influenza admissions in  
186 2019-20, but were lower than for other pandemic year admissions. Odds ratios for PIMS-TS  
187 admissions were consistently the lowest of any cohort for each comorbidity category,  
188 although confidence intervals often overlapped.

189

190 For body system comorbidities (Figure 2), odds ratios for the increase associated with  
191 cancer/haematological conditions, neurological, respiratory, neurological with respiratory  
192 and respiratory with cardiovascular comorbidities in COVID-19 appeared comparable to  
193 influenza and all admissions in 2019-20 but not PIMS-TS (where the increase in odds was  
194 lower) or other pandemic year admissions (where the increase in odds was higher). The  
195 increase in odds for cardiovascular comorbidities within COVID-19 appeared similar to that  
196 seen in all admissions in 2019-20, but higher than influenza admissions 2019-20 and PIMS-  
197 TS, and lower than for other pandemic year admissions. A similar pattern was observed for  
198 combinations of body-system comorbidities (Figure 3), i.e. that the increase in odds for  
199 COVID-19 appeared similar to that for influenza and all admissions 2019-20, but was higher  
200 than for PIMS-TS and lower than in other pandemic year admissions.

201

202 Asthma, diabetes, epilepsy and trisomy 21 each increased risk of PICU admission for COVID-  
203 19, although sickle cell disease did not (Figure 4). Increases in odds for COVID-19 appeared  
204 broadly similar to those for other cohorts although confidence intervals were wide,  
205 particularly for PIMS-TS.

206

207 Results from sensitivity analyses where data were restricted to 11-17 year olds to guide  
208 vaccination policy are shown in supplementary material 1 figures S1-S4 and supplementary  
209 material 3. Patterns of odds ratios were similar, although female sex was associated with  
210 significantly reduced odds of PICU admission for COVID-19. Increases in odds of PICU  
211 admission associated with comorbidities for COVID-19 amongst 11-17 year olds were lower  
212 than when all CYP were included for some outcomes. However, due to low numbers,  
213 confidence intervals around these estimates were wide. We were not able to model  
214 associations within Influenza admissions in 11-17 year olds due to low numbers.

215

216 **Discussion**

217

218 We found that very few CYP admitted to hospital in England due to COVID-19 or PIMS-TS  
219 went on to develop severe disease or die. Of the 12.02 million 0-17 year olds in England  
220 during 2020, 1 in 2062 (n= 5830) were admitted to hospital due to COVID-19, and 1 in  
221 47,903 (n=251) were admitted to PICU. This represented only 1.3% of all secondary care  
222 admissions in the pandemic year and less than 5% of non-traumatic emergency PICU  
223 admissions. Eight of these CYP died within 28 days of admission to hospital. For PIMS-TS, 1  
224 in 17,425 (n=690) of CYP in England were admitted to hospital, 1 in 38,911 (n=309) were  
225 admitted to PICU, and fewer than 5 children died. This likely represents all PIMS-TS cases  
226 nationally over the study period, as the vast majority will have required hospitalisation.

227 CYP admitted to hospital with COVID-19 and PIMS-TS were older and more likely to be non-  
228 white than in the other cohorts examined. For COVID-19, we found the odds of PICU  
229 admission increased amongst neonates compared with 1-4 year-olds, and those who were  
230 Black compared with White ethnicity, but found no associations by deprivation. Female sex  
231 was associated with significantly lower odds of PICU admission for COVID-19, but only in  
232 sensitivity analyses where data were restricted to 11-17 year olds. For PIMS-TS, the odds of  
233 PICU admission were increased amongst females, older CYP and those from non-White  
234 ethnic groups.

235 Of the 251 CYP admitted to PICU with COVID-19, 91% (n=229) had an underlying condition  
236 or comorbidity. The odds of PICU admission due to COVID-19 were increased in all  
237 comorbidity categories tested except sickle cell disease. We found that CYP with complex  
238 medical problems across multiple body systems, and those with neurodisability, were at  
239 greatest risk. This pattern is described in previous work,<sup>12</sup> and is consistent with our meta-  
240 analysis of the published data, where each increase in number of pre-existing conditions  
241 was associated with increased odds of PICU admission and death for COVID-19 [R.  
242 Hardwood et. Al, unpublished<sup>13</sup>]. Increases in odds of PICU admission associated with  
243 comorbidities in PIMS-TS were lower than for COVID-19, but are difficult to interpret; coding  
244 of PIMS-TS admissions suggested two-thirds had a comorbidity, whilst three quarters had no  
245 prior admissions to hospital. When codes which include known cardiac and haematological  
246 complications of PIMS-TS were excluded, estimates for comorbidities in these admissions

247 dropped to around 15%, similar to work from the UK and US showing the majority of CYP  
248 admitted with PIMS-TS or MIS-C were previously healthy.<sup>8,14</sup>

249 Our comparison with other causes of admission allowed us to assess whether these risk  
250 factors are specific to COVID-19 or PIMS-TS, or reflect background vulnerability to serious  
251 illness. Our findings that non-White ethnic groups (ie CYP who were of Asian and Black  
252 ethnicity) was associated with increased odds of serious disease was similar to findings from  
253 other cohorts except for influenza. However, a high proportion of admissions for COVID-19  
254 and PIMS-TS were from non-White ethnic groups, consistent with previous work,<sup>15-17</sup> and  
255 increases in odds associated with non-White ethnicity were greater in these cohorts, similar  
256 to findings in adults.<sup>18,19</sup> Age-patterns for COVID-19, and particularly for PIMS-TS admission,  
257 were notably shifted towards older age-groups in comparison with other cohorts, including  
258 influenza. We only found significant sex differences in risk for COVID-19 amongst 11-17 year  
259 olds, unlike other pandemic-year admissions and all admissions in 2019-20, where female  
260 sex was associated with lower odds of PICU admission in all models. Almost two thirds of  
261 PIMS-TS admissions were amongst males, higher than in all other cohorts, but odds of PICU  
262 admission were greater amongst females.

263 We found broadly similar increases in odds for PICU admission associated with number of  
264 body systems or type of comorbidities across COVID-19, all 2019-20 admissions and  
265 influenza admissions. Increases in odds were highest for combinations of body system  
266 comorbidities e.g. neurological and respiratory, neurological and cardiovascular and  
267 respiratory and cardiovascular. Similarly, for the specific conditions examined, odds ratios  
268 overlapped with those for other pandemic year, all admissions 2019-20 and influenza, with  
269 the exception of sickle cell disease which was not associated with an increased odds of PICU  
270 admission for COVID-19 or influenza.

271 When absolute risk was examined, the increases in risk associated with comorbidities were  
272 relatively small in the COVID-19, other pandemic year, all admissions 2019-20 and influenza  
273 cohorts, although greater for COVID-19 than other groups. For example, for the 229 CYP  
274 with comorbidity in one body system admitted to PICU with COVID-19, the increase in risk  
275 above those without comorbidities was 2% for COVID-19, 0.75% for all admissions in 2019-  
276 20 and 1.3% for influenza. Combinations of comorbidities increased risk the most, although

277 again numbers were very small. Amongst the 414 admissions with respiratory and  
278 neurological comorbidities, the increase in risks were 18.6% for COVID-19 compared with  
279 12.3% for influenza and 7-8% for other cohorts. Whilst this greater increase in absolute risk  
280 with COVID-19 appeared significant for body system comorbidities and their combinations,  
281 confidence intervals overlapped for all specific conditions.

282 Our finding that the pattern of risks for severe COVID-19 related to comorbidities is similar  
283 to that for other reasons for admission suggests these reflect underlying vulnerabilities to  
284 illness and infection. A similar observation has been made in adults when risks were  
285 examined across COVID-19 and non-COVID deaths during the pandemic.<sup>20</sup> However, whilst  
286 the pattern of risks was very similar and absolute risks remained relatively small, increases  
287 in absolute risk of PICU admission were often higher for COVID-19 than for other cohorts  
288 including influenza. This suggests that SARS-CoV-2 infection may magnify underlying risks  
289 faced by CYP with chronic and life-threatening conditions. It is also possible that these  
290 findings reflect changes in health system factors during the pandemic, although other  
291 studies have suggested there was no overall change in thresholds for PICU admission in  
292 England.<sup>21</sup>

293 Patterns within admissions due to COVID-19 amongst CYP, (older age, non-White ethnicity  
294 and presence of comorbidities), are very similar to those identified for adults.<sup>18,19</sup> This  
295 suggests that the strong age-related risk of severe disease in adult COVID-19<sup>19,22</sup> extends  
296 across the early life-course, but has previously been difficult to uncover in CYP due to the  
297 extreme rarity of severe disease.

## 298 Strengths and Limitations

299 Previous work examining risk factors for severe disease and death from SARS-CoV-2 in CYP  
300 have predominantly used dedicated reporting systems, and analysed data in the first  
301 months of the pandemic.<sup>8,9,15,16</sup> In contrast, our study utilises unique population level data  
302 from a large country with a high burden of disease due to COVID-19, and includes all CYP  
303 admissions over the first pandemic year. We also uniquely examine data from previous  
304 years to provide context to our risk estimates. Our study is subject to a number of  
305 limitations. We are unable to account for the effect of protective shielding on differential  
306 exposure to SARS-Cov-2 among CYP thought to be vulnerable, which may have affected our

307 estimates. However, our findings relate to risk factors for severe disease once hospitalised,  
308 whereas shielding is likely to bias estimates of risk factors for infection, which we did not  
309 examine.

310 As the pandemic progresses and variants continue to emerge, the risks posed by SARS-CoV-  
311 2 amongst CYP may change. Our data included children infected with the Alpha variant  
312 (from November 2020 onwards) but did not include children infected with the Delta  
313 (B.1.617.2) variant, dominant in the UK since May 2021. The Delta variant has higher  
314 transmissibility, and prevalence, and there have been suggestions of greater severity in CYP,  
315 although the evidence for this is mixed.<sup>23</sup> Further population-level analyses are needed to  
316 explore the effect of this and other factors on disease severity in CYP as new data become  
317 available.

318

319 Although use of Secondary Uses Service (SUS) data allowed us to examine the burden of  
320 severe disease associated with SARS-CoV-2 and risk factors in CYP at population level, there  
321 are a number of limitations to SUS data. Missing or inaccurate data fields within SUS or  
322 other datasets, and incomplete data linkage, may have affected our findings. We included  
323 both cause of admission and PCR testing for SARS-Cov-2 to identify CYP with COVID-19 to  
324 ensure we capture all likely cases, but this will have affected our case definition specificity.  
325 Identifying PIMS-TS cases was particularly problematic, as ICD-10 codes for this condition  
326 were only introduced several months into the pandemic. We included CYP coded with  
327 Kawasaki disease and systemic inflammatory response syndrome when examining PIMS-TS,  
328 some of whom will not have had PIMS-TS (note that not all PIMS-TS cases had evidence of  
329 previous SARS-CoV-2 infection by PCR). Coding for PIMS-TS is likely to improve as knowledge  
330 of the condition increases, which will benefit future analyses of PIMS-TS admissions using  
331 hospital administrative data. There is also variation in case definition used for diagnosing  
332 post inflammatory syndromes related to SARS-CoV-2 (e.g. MIS-C and PIMS-TS), which may  
333 affect the generalizability of our results. However, in practice the vast majority of CYP will  
334 have fulfilled both criteria.<sup>8,15</sup>

335 We were unable to fully distinguish between admissions *with* COVID-19 and those *due to*  
336 COVID-19, and some of the admissions we classify as COVID-19 will include those with

337 incidental positive PCR tests. We used admission to PICU as an indicator for disease severity  
338 and were not able to examine the level of intensive support needed whilst in critical care.  
339 Our results may also have been affected by changes to thresholds for PICU admission, and  
340 coding practices, as the pandemic progressed and in comparison to the previous years. Our  
341 estimate for number of deaths due to COVID-19 and PIMS-TS only include hospitalised CYP,  
342 and so will not include those who died at home or in an emergency department prior to  
343 admission. Note that our linked study of all CYP deaths up to 28<sup>th</sup> Feb 2021 identified 25  
344 deaths across all places of death, and provides a more complete analysis of mortality risk  
345 associated with SARS-CoV-2.<sup>24</sup>

346 We use ICD-10 codes developed to identify chronic conditions across five years of admission  
347 data, and may have missed diagnoses recorded prior to this. We were not able to account  
348 for the wide range of disease severity included within the diagnostic groups used for coding  
349 purposes in our analysis. Further, the ICD-10 codes we used included some diagnoses which  
350 may relate to complications of acute disease, rather than pre-existing conditions only, as  
351 highlighted with PIMS-TS. We were unable to only include comorbidities prior to the index  
352 case to investigate this further as many CYP had no prior records, and this approach would  
353 not account for incomplete coding in previous admissions or diagnoses made in primary  
354 care. Linking SUS data with national primary care records would improve identification of  
355 pre-existing conditions for these analyses, but these data are currently not available. Our  
356 analysis of individual or body system comorbidities does not account for CYP with both the  
357 comorbidity of interest and other conditions. However, we do assess odds of PICU by  
358 number of body systems involved, which does address identifying CYP with multiple medical  
359 problems. Finally, due to incomplete coding we were unable to examine some important  
360 risk factors for severe disease in adults in these analyses, including obesity,<sup>25</sup> which should  
361 be the focus of future study.

362 In conclusion, in marked contrast to adults, CYP were at very low risk of severe disease and  
363 death from COVID-19 or PIMS-TS during the first pandemic year. In the rare instances when  
364 CYP did require hospitalisation, risk factors for severe disease were similar to those reported  
365 for adults. Additionally, the pattern of comorbidities was similar to that seen with influenza  
366 and all admissions in 2019-20, reflecting underlying vulnerabilities to infection, although  
367 COVID-19 magnified these risks to a small degree. We identified important demographic

368 factors which were associated with PICU admission due to PIMS-TS, although associations  
369 between comorbidities and PICU admission in this group were difficult to interpret.

370

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377 analysis.

#### 378 Author contribution statement

379 Study design was developed by all authors. Data cleaning and analysis was undertaken by  
380 JLW, LKF and RMV. Data interpretation was undertaken by all authors. The first draft was  
381 written by JLW. All authors contributed to editing and reviewing the final manuscript.

#### 382 Competing Interest Statement

383 The authors declare there are no competing interests

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#### 394 Tables



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**Table 1** Number and proportion of admissions by sociodemographic characteristics within each cohort (COVID-19, PIMS-TS, other pandemic year admissions; all admissions in 2019-20; influenza admissions in 2019/20)

		2020/21						2019/20			
		COVID-19		PIMS TS		Other pandemic year admission		All admissions 2019/20		Influenza 2019/20	
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Total		6338	(100.0)	712	(100.0)	463556	(100.0)	771591	(100.0)	6968	(100.0)
Sex	Male	3347	(52.8)	452	(63.5)	247299	(53.3)	416830	(54.0)	3733	(53.6)
	Female	2991	(47.2)	260	(36.5)	216257	(46.7)	354761	(46.0)	3235	(46.4)
Age	Neonates	741	(11.7)	<5	.	69230	(14.9)	89822	(11.6)	151	(2.2)
	Post neonatal	1216	(19.2)	71	(10.0)	71560	(15.4)	135195	(17.5)	1036	(14.9)
	1 to 4	1281	(20.2)	217	(30.5)	126426	(27.3)	262511	(34.0)	3189	(45.8)
	5 to 9	840	(13.3)	216	(30.3)	71255	(15.4)	116951	(15.2)	1274	(18.3)
	10 to 14	1188	(18.7)	175	(24.6)	72256	(15.6)	97662	(12.7)	871	(12.5)
	15 to 17	1072	(16.9)	31	(4.4)	52829	(11.4)	69450	(9.0)	447	(6.4)
Ethnicity	White	3685	(58.1)	285	(40.0)	329358	(71.1)	544460	(70.6)	4653	(66.8)
	Mixed	279	(4.4)	51	(7.2)	20426	(4.4)	33397	(4.3)	259	(3.7)
	Asian	1203	(19.0)	155	(21.8)	49217	(10.6)	88615	(11.5)	1063	(15.3)
	Black	395	(6.2)	109	(15.3)	17388	(3.8)	30948	(4.0)	333	(4.8)
	Other	298	(4.7)	40	(5.6)	13160	(2.8)	22381	(2.9)	197	(2.8)
	Unknown	478	(7.5)	72	(10.1)	34007	(7.3)	51790	(6.7)	463	(6.6)
IMD Quintile Category	Most deprived	1662	(26.2)	163	(22.9)	108096	(23.3)	188391	(24.4)	1906	(27.4)
	2nd most deprived	1533	(24.2)	182	(25.6)	96386	(20.8)	163405	(21.2)	1497	(21.5)
	3rd most deprived	1218	(19.2)	164	(23.0)	92034	(19.9)	152297	(19.7)	1278	(18.3)
	4th most deprived	1087	(17.2)	98	(13.8)	87873	(19.0)	142097	(18.4)	1197	(17.2)
	Least deprived	838	(13.2)	105	(14.7)	78982	(17.0)	125167	(16.2)	1090	(15.6)
	Missing	0	(0.0)	0	(0.0)	185	(0.0)	234	(0.0)	0	(0.0)

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**Table 2** Total admissions and proportion resulting in pediatric critical care admission (PICU) by selected comorbidity groups within each cohort (COVID-19, PIMS-TS, other pandemic year admissions; all admissions in 2019/20; influenza admissions in 2019/20)

		COVID 19			PIMS TS			Other pandemic year admission			All admissions 2019/20			Influenza 2019/20		
		n	PICU	% PICU	n	PICU	% PICU	n	PICU	% PICU	n	PICU	% PICU	n	PICU	% PICU
	Total	6338	259	(4.1)	712	312	(43.8)	463556	5016	(1.1)	771591	7282	(0.9)	6968	161	(2.3)
Any comorbidity	No comorbidity	2923	22	(0.8)	258	50	(19.4)	242245	358	(0.1)	417842	811	(0.2)	3859	30	(0.8)
	Comorbidity present	3415	237	(6.9)	454	262	(57.7)	221311	4658	(2.1)	353749	6472	(1.8)	3109	131	(4.2)
Number of body systems	1 body system	1396	35	(2.5)	182	76	(41.8)	114597	1015	(0.9)	185453	1436	(0.8)	1449	29	(2.0)
	More than 1 body system	2019	202	(10.0)	272	186	(68.4)	106714	3643	(3.4)	168296	5036	(3.0)	1660	102	(6.1)
Life limiting or non-life limiting comorbidity	Non-life-limiting comorbidity	2272	79	(3.5)	307	157	(51.1)	169415	1701	(1.0)	272959	2323	(0.9)	2065	43	(2.1)
	Life-limiting comorbidity	1143	158	(13.8)	147	105	(71.4)	51896	2957	(5.7)	80790	4149	(5.1)	1044	88	(8.4)

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404

405 **Figure captions**

406 **Figure 1** Odds ratios and percentage point difference in predicted probability with 95% confidence intervals for admission to PICU by comorbidity groups  
407 within each cohort, adjusted for age, sex, IMD category, ethnicity

408  
409 Legend: Output from Generalised Estimation Equation models. Each mark and line represents odds ratios with 95% confidence intervals of PICU admission  
410 within each admission cohort amongst admission with each comorbidity group compared to those without any comorbidity adjusted for age, sex, IMD  
411 category and ethnicity. Percentage point difference in predicted probability of PICU admission with 95% confidence intervals are shown in the right panel.  
412 Observations: n=6338 COVID-19 admissions; n=710 PIMS-TS admissions; n= 463371 other pandemic year admissions; n=771357 all admissions 2019-20;  
413 n=influenza admissions 2019-20. These results are available in full in supplementary material part 2.  
414  
415

416 **Figure 2** Odds ratios and percentage point difference in predicted probability with 95% confidence intervals for admission to PICU by body system  
417 comorbidities within each cohort, adjusted for age, sex, IMD category, ethnicity

418  
419 Legend: Output from Generalised Estimation Equation models. Each mark and line represents odds ratios with 95% confidence intervals of PICU admission  
420 within each admission cohort amongst admission with each comorbidity group compared to those without any comorbidity adjusted for age, sex, IMD  
421 category and ethnicity. Percentage point difference in predicted probability of PICU admission with 95% confidence intervals are shown in the middle panel.  
422 Number of observations in each model is shown in the right panel. These results are available in full in supplementary material part 2.  
423  
424

425 **Figure 3** Odds ratios and predicted probability with 95% confidence intervals for admission to PICU by comorbidity combinations within each cohort, adjusted  
426 for age, sex, IMD category, ethnicity

427  
428 Legend: Output from Generalised Estimation Equation models. Each mark and line represents odds ratios with 95% confidence intervals of PICU admission  
429 within each admission cohort amongst admission with each comorbidity group compared to those without any comorbidity adjusted for age, sex, IMD  
430 category and ethnicity. Percentage point difference in predicted probability of PICU admission with 95% confidence intervals are shown in the middle panel.  
431 Number of observations in each model is shown in the right panel. These results are available in full in supplementary material part 2.  
432

433 **Figure 4** Odds ratios and predicted probability with 95% confidence intervals for admission to PICU by selected diagnoses within each cohort, adjusted for  
434 age, sex, IMD category, ethnicity

435  
436 Legend: Output from Generalised Estimation Equation models. Each mark and line represents odds ratios with 95% confidence intervals of PICU admission  
437 within each admission cohort amongst admission with each comorbidity group compared to those without any comorbidity adjusted for age, sex, IMD

438 category and ethnicity. Percentage point difference in predicted probability of PICU admission with 95% confidence intervals are shown in the middle panel.  
439 Number of observations in each model is shown in the right panel. These results are available in full in supplementary material part 2.

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518

## 519 **Methods**

### 520 Data

521 We used Secondary Use Services (SUS), an administrative national database covering ~98%  
522 of National Health Service (NHS) hospital activity in England.<sup>26</sup> Data were available for  
523 admissions due to any cause in CYP aged 0-17 years in England between March 1<sup>st</sup> 2015 to  
524 Feb 28<sup>th</sup> 2021 (n=11,467,027). Note this does not include accident and emergency  
525 attendances not resulting in hospital admission. Coded fields included reason for hospital  
526 admission, co-morbidities, and sociodemographic characteristics. We primarily examined  
527 admissions occurring from 1<sup>st</sup> Feb 2019 – 31<sup>st</sup> Jan 2021, but to account for variable quality  
528 and completeness of coding within SUS, we used all available data (2015-2021) from all  
529 types of admission (emergency, elective and maternal) to populate socio-demographic and  
530 comorbidity data for CYP.

531

532 As clinical details are limited in SUS, and to aid identification of COVID-19 and PIMS-TS  
533 admissions, these data were deterministically linked using unique patient NHS numbers to  
534 the following healthcare datasets:

535

536 1) Paediatric Intensive Care Audit Network (PICANet) data containing all Paediatric Intensive  
537 Care (PICU) admissions in England.

538 2) Death registrations provided by the Office for National Statistics (ONS).

539 3) National Child Mortality Database (NCMD), which collects preliminary notification data  
540 within 48 hours of death of a CYP death in England and Wales

541 4) SARS-CoV-2 PCR-testing data provided by Public Health England (PHE).

542

### 543 **Outcomes and Exposures**

544 We examined associations between severity outcomes (PICU admission or death) and the  
545 following exposures: reason for hospital admission (COVID-19, PIMS-TS, other),  
546 sociodemographic factors and presence of comorbidities.

547

548 We linked hospitalisations in SUS to PICANet data if the PICU admission date occurred  
549 during or within one day of the SUS admission or discharge date, to account for coding error  
550 in either dataset. We defined admissions resulting in death as the last admission for each

551 CYP that occurred within 28 days of death identified through ONS or NCMD. All NCMD  
552 deaths during the pandemic were clinically reviewed as part of a separate analysis [Smith, C  
553 et al 2021 (currently under peer review)] to identify the contribution of SARS-CoV-2  
554 infection and PIMS-TS to death.

555

#### 556 *Reason for admission*

557 We used primary and secondary diagnoses coded to International Classification of Diseases  
558 10 (ICD 10) to define all hospital admissions between 1<sup>st</sup> Feb 2019 and 31<sup>st</sup> Jan 2021. We  
559 excluded all traumatic admissions (where the primary cause of admission was an external  
560 cause in ICD-10), and non-emergency admissions (i.e. elective or maternity/newborn) from  
561 the analysis, and classified the remainder into five cohorts:

- 562 • admissions due to COVID-19 (1<sup>st</sup> Feb 2020 – 31<sup>st</sup> Jan 2021);
- 563 • admissions due to PIMS-TS (1<sup>st</sup> Feb 2020 – 31<sup>st</sup> Jan 2021);
- 564 • all other admissions during the pandemic year (1<sup>st</sup> Feb 2020 – 31<sup>st</sup> Jan 2021);
- 565 • all admissions in the year prior to the pandemic (1<sup>st</sup> Feb 2019 – 31<sup>st</sup> Jan 2020);
- 566 • all admissions where the primary diagnosis was influenza in the year prior to the  
567 pandemic (1<sup>st</sup> Feb 2019 – 31<sup>st</sup> Jan 2020).

568

569 We defined COVID-19 admissions as those occurring after Feb 1<sup>st</sup> 2020 with relevant ICD-10  
570 codes recorded as reason for admission, or (using linked data) where there was a positive  
571 PCR test for SARS-CoV-2 within 7 days of admission or discharge, (unless this occurred at  
572 least 7 days after admission to PICU, and nosocomial infection was likely).

573

574 We defined PIMS-TS admissions those occurring after 1<sup>st</sup> Feb 2020 with ICD-10 codes  
575 recorded as reason for admission for either PIMS-TS (introduced November 2020), or  
576 Kawasaki disease or systemic inflammatory response syndrome, (used as proxies for PIMS-  
577 TS prior to November 2020).

578

579 To improve the identification of COVID-19 and PIMS-TS, we also reviewed details of all PICU  
580 admissions during the first pandemic year held within PICANet. Where treating specialists  
581 determined the PICU admission was due to either COVID-19 or PIMS-TS, we recoded the



582 SUS admission accordingly. Hospital admissions identified as both due to COVID-19 and  
583 PIMS-TS were defined as being due to PIMS-TS, as we assumed the COVID-19 diagnosis was  
584 part of the same disease process.

585

#### 586 *Socio-demographic exposures*

587 Age was categorised as neonates (admission within 1 month of birth), post-natal infants  
588 (admission between 1 – 11 months of birth), 1-4 years, 5-9 years, 10-14 years and 15-17  
589 years. We defined ethnicity as: White, Mixed, Asian, Black, Other and unknown. We used  
590 Index of Multiple Deprivation (IMD) 2019 quintile category (hereafter IMD category) to  
591 define area level socioeconomic status of CYP. Further details of how IMD is defined are  
592 available in supplementary material 1.

593

#### 594 *Co-morbidities*

595 We used published literature and guidance on shielding to identify co-morbidities likely to  
596 increase risk of severe SARS-CoV-2 disease.<sup>10,13</sup> We identified CYP with chronic medical  
597 conditions by body system, those with life-limiting conditions, and those with asthma,  
598 diabetes, epilepsy, sickle cell disease and trisomy 21, using recognised ICD-10 code lists.<sup>27,28</sup>

599 Note that admissions amongst CYP with specific conditions were also included in the  
600 broader body system diagnostic categories. We then defined additional co-morbidity groups  
601 to examine vulnerability associated with multiple medical problems. These were defined as:  
602 comorbidities in more than one body system; comorbidities in both neurological and  
603 respiratory, neurological and cardiovascular, or respiratory and cardiovascular body  
604 systems. We compared admissions amongst CYP with each comorbidity category to CYP  
605 with no comorbidities in any category in all analyses.

606

#### 607 **Statistics and Reproducibility**

608 First we described the characteristics of each of the five cohorts: admissions due to COVID-  
609 19, admissions due to PIMS-TS, other non-traumatic admissions in 2020/21 (hereafter  
610 “other pandemic year admissions”), all non-traumatic admissions in 2019/20, and  
611 admissions due to influenza in 2019/20. We suppressed cell counts with small numbers  
612 (where  $n < 5$ ) due to the risk of identification of individuals, in line with guidance from data  
613 providers used in this study.

614

615 We then modelled the association between sociodemographic factors and co-morbidities  
616 with PICU admission within each cohort separately. Sample sizes for these analyses were  
617 determined by the number of admissions identified within the SUS data, after non-  
618 emergency admissions, or those due to trauma, were excluded. Investigators were not  
619 blinded, and experiments were not randomized. All analyses were performed in Stata 16  
620 (StataCorp, College Station TX). Models employed generalized estimation equations (GEE)  
621 using the *xtgee* command in order to account for multiple admissions within the same CYP  
622 across and within different cohorts. Models used a logit link, specifying the covariance  
623 structure as “exchangeable” (i.e. we assumed equal correlations between any two  
624 admissions within one CYP). We then calculated the difference in predicted probability for  
625 PICU admission amongst those with and without each comorbidity category using the  
626 *margins* post estimation command. We used univariable and then multivariable models to  
627 estimate the odds of PICU admission within each cohort by the presence of specific  
628 comorbidities compared with CYP with no comorbidities across any diagnostic category  
629 (dichotomous or ordinal variable), adjusted for: age group (categorized as: infant, 1-4, 5-9,  
630 10-14, 15-17 years), sex, ethnic group (categorized as: White, Mixed, Asian, Black, Other)  
631 and IMD category (categorized as lowest – highest quintile category). Comparisons between  
632 cohorts were not tested; significance was inferred if 95% confidence intervals did not  
633 overlap. We were unable to model death as an outcome in these analyses due to low  
634 numbers. In sensitivity analyses, we repeated analyses to only include secondary school age  
635 CYP to inform vaccination policy (i.e. ages 11-17).

636

### 637 **Ethics approval and legal basis for data linkage and analyses**

638 Ethics approval was provided after review by Yorkshire and the Humber, South Yorkshire  
639 NHS Research Ethics Committee on 10<sup>th</sup> June 2021 (Reference 21/YH/0127).

640

641 Informed consent was not obtained to use hospital administrative data for research  
642 purposes. Patients have the ability to opt out of their personal/confidential information  
643 being shared by NHS Digital and Public Health England, and all other health and care  
644 organisations included in this analysis, for purposes not related to their own direct care.

645 Further information regarding the national opt-out can be found at:  
646 <https://www.nhs.uk/your-nhs-data-matters/manageyour-choice/> Current Control Of Patient  
647 Information (COPI) regulations provide a legal basis for linking datasets used in this study  
648 without consent.<sup>29</sup> Low numbers (n <5) are suppressed to reduce risk of identification of  
649 patients.

650

#### 651 **NCMD**

652 The NCMD legal basis to collect confidential and personal level data under the Common Law  
653 Duty of Confidentiality has been established through the Children Act 2004 Sections M - N,  
654 Working Together to Safeguard Children 2018 ([https://consult.education.gov.uk/child-  
655 protection-safeguarding-and-family-law/working-together-to-safeguard-children-revisions-  
656 t/supporting\\_documents/Working%20Together%20to%20Safeguard%20Children.pdf](https://consult.education.gov.uk/child-protection-safeguarding-and-family-law/working-together-to-safeguard-children-revisions-t/supporting_documents/Working%20Together%20to%20Safeguard%20Children.pdf)) and  
657 associated Child Death Review Statutory & Operational  
658 Guidance [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/att  
659 achment\\_data/file/859302/child-death-review-statutory-and-operational-guidance-  
660 england.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/859302/child-death-review-statutory-and-operational-guidance-england.pdf)). The NCMD legal basis to collect personal data under the General Data  
661 Protection Regulation (GDPR) without consent is defined by GDPR Article 6 (e) Public task  
662 and 9 (h) Health or social care (with a basis in law).

#### 663 **PICANet**

664 Processing of personally identifiable data for the purposes of service evaluation, audit, and  
665 research was approved by the Patient Information Advisory Group (now the Health  
666 Research Authority Confidentiality Advisory Group) in 2002 under Section 60 of the Health  
667 and Social Care Act (subsequently Section 251 of the National Health Service Act 2006)  
668 (reference: PIAG 4-07(c) 2002). Permissions to use these data were amended and approved  
669 specifically to collect additional data relating to COVID-19 for confirmed and suspected  
670 cases.

671

#### 672 **Data availability Statement**

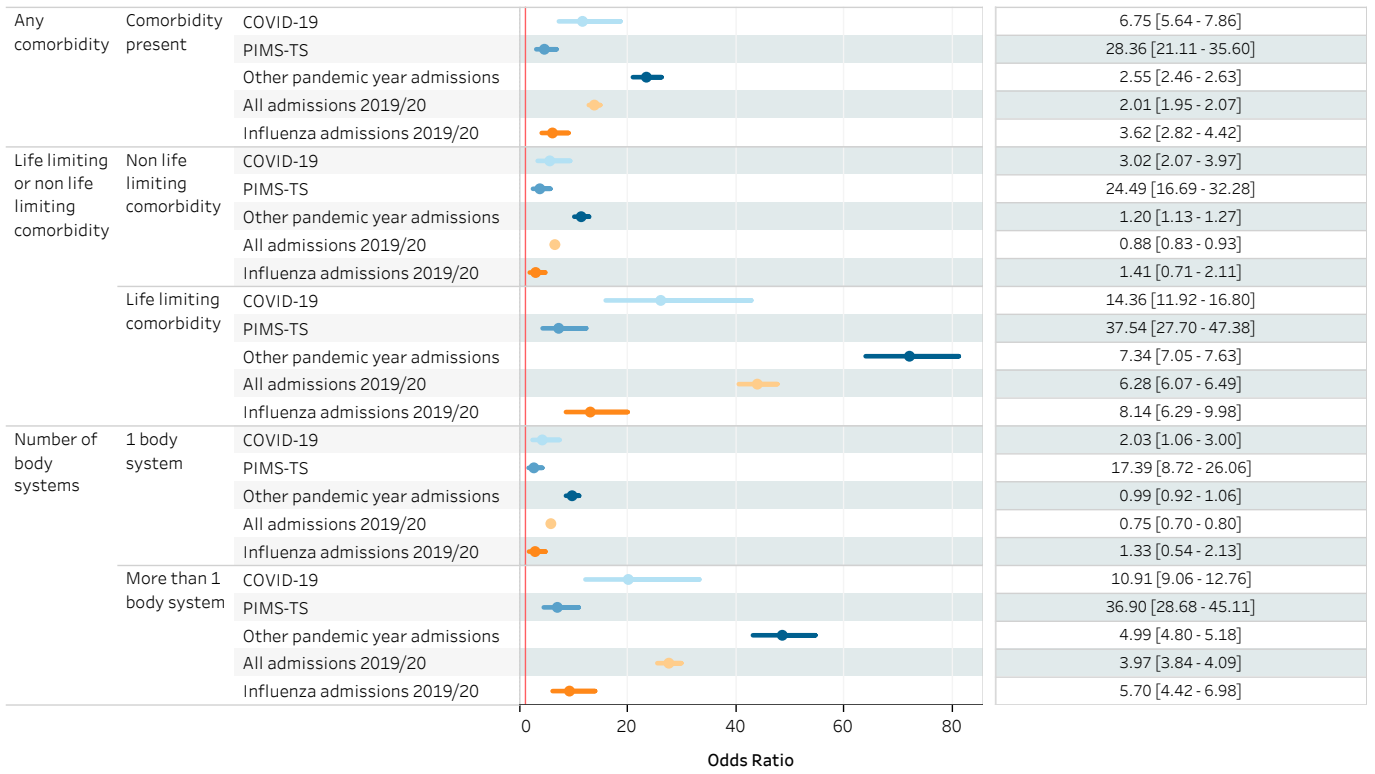
673

674 These analyses were undertaken using datasets held by NHS England for the use of ongoing  
675 service evaluation, held within the National Commissioning Data Repository. Access to these

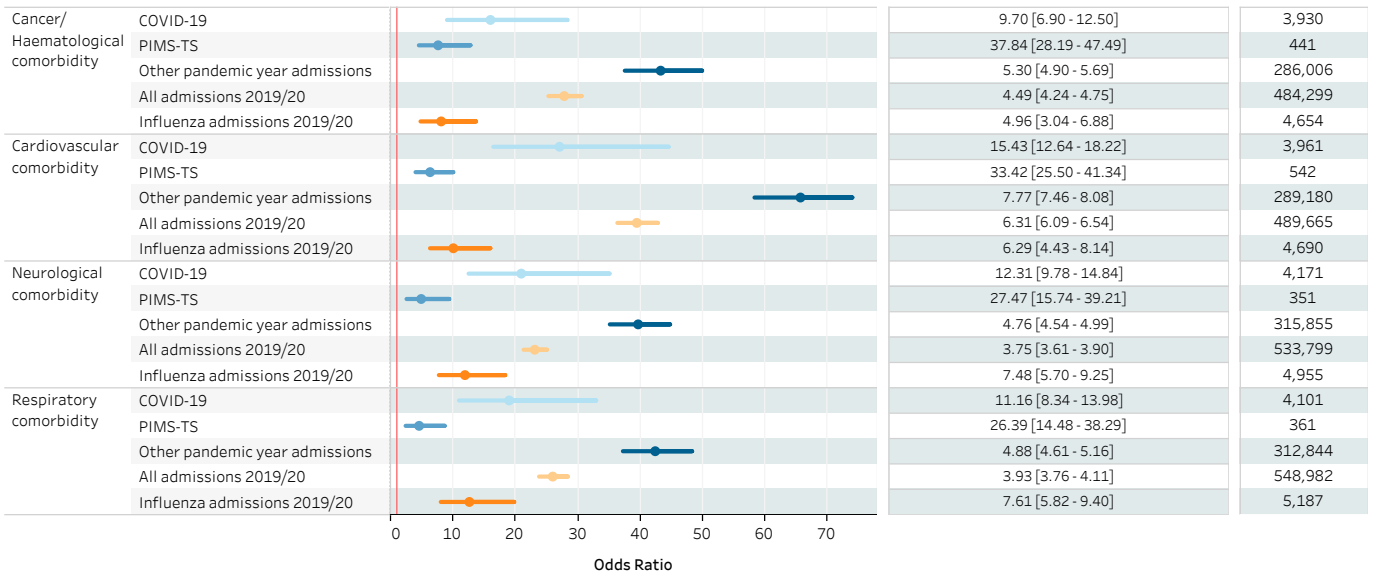
676 data at individual level are restricted, as described in data sharing agreements between NHS  
677 England and specific data providers, and within the application for ethical approval provided  
678 for this study. We were able to access and analyse these data as employees of NHS England.  
679 Researchers wishing to access the individual level data used in this analysis are able to apply  
680 to do so via NHS Digital. Aggregated, non-identifiable data used for this study are provided  
681 in the supplementary material.  
682

Odds ratios

% difference in predicted probability

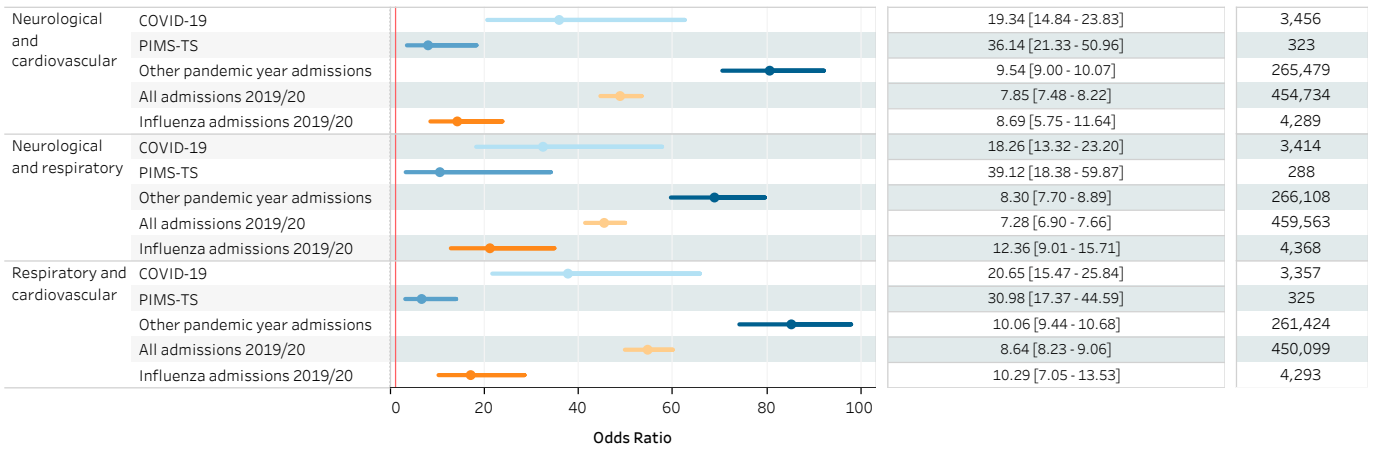


Odds ratios



Odds ratios

% difference in predicted probability observations



Odds ratios

% difference in predicted probability

observations

