## Sharing a household with children and risk of COVID-19: a study of over 300,000 adults living in healthcare worker households in Scotland

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.

# Abstract

#### Background

Children are relatively protected from novel coronavirus infection (COVID-19). The reasons for this protection are not well understood but differences in the immune response to Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) have been implicated. If such differences are due to differential exposure to non-SARS-CoV-2 infectious agents, adults who are close contacts of children may partly share in this protection. Such a protective effect would have important implications for the lives of children, not least in terms of schooling.

#### Methods

Using a Scotland-wide record-linkage based occupational cohort comprising healthcare workers and members of their households, we examined whether sharing a household with young children (aged 0 to 11) attenuated the risk of hospitalisation with COVID-19, and/or testing positive for COVID-19 infection of any severity (any case of Covid-19). All healthcare workers directly employed by the National health Service (NHS) in Scotland, or contracted to provide general practice services, were included. Outcome and covariate data were obtained via linkage to Scotland-wide microbiology, drug prescribing, hospitalisation and death data.

#### Results

241,266 adults did not share a household with young children; 41,198, 23,783 and 3,850 shared a household with 1, 2 and 3 or more young children respectively. The risk of hospitalisation with COVID-19 was lower in those with one child and lower still in those with two or more children, adjusting for age the hazard ratio (HR) was 0.83 per child (95% CI 0.70-0.99). On additionally adjusting for sex, socioeconomic deprivation, occupation, professional role, staff/non-staff status, the number of adults and adolescents in each household, and comorbidity, the HR was 0.89 per child (95% CI 0.74-1.06). An association of the same magnitude, but more precisely estimated, was obtained for any case of COVID-19 (fully adjusted model, HR per child 0.89; 95% CI 0.84-0.95).

#### Conclusion

Increased household exposure to young children was associated with an attenuated risk of testing positive for SARS-CoV-2 and appeared to also be associated with an attenuated risk of COVID-19 disease severe enough to require hospitalisation.

### Introduction

Children are relatively protected from Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2). When exposed, children are less likely to develop symptomatic infection (COVID-19), and when infected they are less like to become seriously ill.<sup>1</sup> This difference is large; in the UK over the peak 9 weeks of the epidemic, the mortality in the UK population for SARS-CoV-2 was 0.0005% among children aged 0 to 14, compared to 0.003% for adults aged 25-44 and 0.11% for adults aged 65 to 74.<sup>2</sup>

The reasons why COVID-19 is milder in childhood are not well understood, and differences in both the innate and acquired immune systems have been implicated.<sup>3</sup> While developmental factors alone may account for any differences, pre-exposure to antigenically-similar infectious agents may also be relevant. Evidence of B and T-cell cross-reactivity between endemic coronaviruses and SARS-CoV-2 has been demonstrated in independent studies,<sup>4–10</sup> and children may have higher levels of exposure to endemic coronaviruses than adults.<sup>11,12</sup> Alternatively, there may be non-specific "training" of the innate immune response as a result of increased exposure to childhood vaccinations and respiratory viruses.<sup>13</sup>

If differential exposure to infectious agents is an important mechanism, adults who are close contacts of children, such as childcare providers, teachers and parents may also benefit. Despite a lack of empirical evidence that children are important in the transmission of COVID-19, schools and nurseries throughout the world have been closed, resulting in substantial harms to the health and wellbeing of children,<sup>14</sup> while a substantial proportion of staff who work in schools have reported feeling unsafe about the reopening of educational establishments.<sup>15</sup> Consequently, if exposure to children was found to be protective, rather than harmful, this would have important implications for policy. Few studies, however, have examined this question.<sup>16</sup>

We recently reported the risk of hospitalisation for COVID-19 in around 160,000 healthcare workers and 250,000 members of their households in Scotland.<sup>17</sup> Using this cohort, who are at increased risk of exposure to SARS-CoV-2 and COVID-19, we now test the hypothesis that the risk of COVID-19 is attenuated where adults share households with children aged 11 and younger.

### Methods

#### Population, data sources and record linkage

The population studied is described in detail elsewhere. Briefly, we previously created a cohort of adults who were either healthcare workers (aged 18 to 65) or healthcare worker's household members (all ages). Healthcare workers were identified via a human resources database which includes all staff directly-employed by the NHS in Scotland on the 1<sup>st</sup> of March 2020, as well as via a database of doctors contracted to provide general practice services. Household members of these groups were identified via a common address using a complete listing of all individuals registered with general practices in Scotland (which includes almost the entire Scottish population). Individuals were assigned to the same household only if the address (including house and, if included, apartment number) was identical; fuzzy matching was not allowed. We linked these data to multiple Scotland-wide databases.<sup>17</sup> These included datasets containing individual level clinical information for virology testing for SARS-CoV-2, general hospitalisation data, community prescribing, critical care admissions and statutory death registration records.

#### Outcome

Outcome, exposure, and covariate information was examined for all adults aged 18 years or over living in a healthcare worker household. The primary outcome was COVID-19 requiring hospitalisation, defined as a first positive PCR test for SARS-CoV-2 up to 28 days prior to, or during, a hospital admission. We also report findings for the secondary outcomes of any COVID-19 (defined as any positive PCR test for SARS-CoV-2, regardless of hospitalisation or death status) and severe COVID-19 (defined as a first positive PCR test for SARS-CoV-2 up to 28 days prior to admission to intensive care or a high-dependency unit, or death). Any outcome event occurring between the 1<sup>st</sup> of March and 7<sup>th</sup> of July 2020 was included.

COVID-19 requiring hospitalisation was chosen as the primary outcome rather than any COVID-19 as we were concerned that higher rates of acute respiratory infections in members of households containing small children may lead to increased testing for SARS-CoV-2 and hence ascertainment bias.

#### Exposure

The primary exposure was the number of children aged 0 to 11 (hereafter referred to as young children) in each household. In additional analyses, risks for household members of pre-school children (aged 0-4) and primary school-aged children (aged 5-11) were examined separately as were the risks of sharing a household with older children (aged 12-17) and with other adults.

#### Covariates

Data on age, sex and the Scottish Index of Multiple Deprivation (SIMD) quintile (an area-based measure of socioeconomic deprivation) were obtained from the linked databases. Pre-specified comorbidities (see Table S1) were defined using previous hospitalisation and prescribing data. Ethnicity was estimated using the ONOMAP algorithm, which estimates ethnicity based on forename and surname.<sup>18</sup>

Occupational covariates were defined at the household level based on the characteristics of the household member who was a healthcare worker. These included the healthcare worker's occupation (eg medical, nursing, allied health professional), exposure to patients (eg in a patient facing or non-patient facing role) seniority-level, length of service, immigration status, and full/part-time working status. Where more than one household member was a healthcare worker, the highest risk designation (eg patient facing rather than non-patient facing) was applied.

#### Statistical analysis

The cumulative incidence of hospitalisation for COVID-19 for adults was plotted according to the number of young children in their household. We modelled COVID-19 requiring hospitalisation using Cox regression, calculating robust standard errors to allow for clustering due to shared household membership and stratifying on groups of health board areas to allow for differences in baseline hazard. We present effect estimates for a minimal model adjusting for age, a full model including all the covariates and intermediate models to allow readers to judge the robustness of any findings to different model specifications. In addition to the primary outcome, we also produced estimates for two other outcomes – any COVID-19 and severe COVID-19. We also conducted a range of sensitivity analyses including additional covariates, and/or restricting the cohort to different populations (eg households where all adults were healthcare workers).

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### Results

Of the 310,097 adults living in a healthcare worker household, 241,266 (78%), 41,198 (13%), 23,783 (7.8%) and 3,850 (1.2%) shared a household with 0, 1, 2 and 3 or more young children respectively. The proportion of women were similar across these categories. Those who did not share a household with young children were on average 5-years older than those who did; were more likely to live in the most deprived areas. However, adults who were of non-white ethnicity were more likely to share a household with young children (Table 1) than were those of white ethnicity. Comorbidity was less common among adults sharing households with young children, and the proportion with comorbid diseases fell as the number of young children in the household increased (Table 1 and Supplementary Table S1).

Household composition differed according to the number of younger children. Households with more children were more likely to include 2 or more adults. More than a quarter of adults who shared a household with a single child under 12 also shared a household with a child aged 12-17. Fewer than 1 in 10 adults in a household with young children also shared a household with anyone over the age of 65 (Supplementary Table S2).

#### Testing for SARS-CoV-2

Testing for SARS-CoV-2 was low overall but was commoner among adults who shared a household with young children. The proportion of adults tested ranged from 6.11% among those who did not share a household with young children to 9.19% in those who shared a household 3 or more young children (Table 1).

#### COVID-19 requiring hospitalisation

Compared to those in households without children, the risk of COVID-19 requiring hospitalisation was lower in those with one child and lower still in those with two or more children (Figure 1). In unadjusted analyses, the hazard ratio (HR) for this association was 0.72 per child (95% CI 0.60-0.85, p <0.001, Table 2) - ie the risk of COVID-19 requiring hospitalisation fell, on average, by 0.72-fold per each additional young child in the household. On adjusting for the adult's own age (ie not the age of the children in the household), this association was attenuated (HR per child 0.83; 95% CI 0.70-0.99), with further smaller changes after adjusting for remaining pre-specified potential confounders (sex, socioeconomic deprivation, occupation, professional role, staff/non-staff status, the number of adolescents in the household, the number of adults in each household, and the comorbidity counts plus selected comorbidities - see Table S1) and for whether or not the healthcare worker in the adult's household was part-time or full time, which was not pre-specified. For this fully adjusted analysis, the confidence interval included the null, and so was consistent with no beneficial effect of sharing a household with young children (HR per child 0.89; 95% CI 0.74-1.06).

Similar, but slightly stronger associations were found when the analysis was restricted to households where at least one member of staff had a patient-facing role (fully adjusted model, HR per child 0.83; 95% CI 0.68-1.02, Supplementary Table S3), a group with greater occupational exposure to SARS-CoV-2 than non-patient facing healthcare workers, although on formally testing for an interaction between patient facing and non-patient facing groups, the coefficient included the null, (P-value for interaction = 0.80). There was also a clearer "dose response" across categories from 0 to  $\geq$ 3 children in both the unadjusted and adjusted models for adults in patient facing compared to adults in non-patients facing households (Supplementary Table S3).

To explore whether there was residual confounding even after adjusting for part-time working (i.e. in case part-time workers with more children worked fewer hours and hence had less exposure to

people with COVID-19) we also stratified adults by whether or not they shared a household with a healthcare worker who worked part-time. We found an inverse association between the number of young children in the household and risk of COVID-19 requiring hospitalisation in the part-time stratum (HR per child 0.63; 95% CI 0.43-0.92) but not in the whole time stratum (1.04; 95% CI 0.84-1.28, P-interaction = 0.007). Separately, to examine for residual confounding by comorbidity, we restricted the analyses to adults who had no known comorbidities, finding similar effect measure estimates to those seen in the main analysis (HR per child on adjusting for demographic and occupational factors 0.83; 95% CI 0.68-1.03). Similar results were also obtained on restricting to adults who had 2 or fewer prescriptions within the previous 9 months (HR per child was 0.91; 95% CI 0.71-1.18, 1.34; 95% CI 0.84-2.15).

#### Any COVID-19

The point estimate for the inverse association between number of young children in the household and the risk of any COVID-19 was similar to that found for the risk of COVID-19 requiring hospitalisation (Table 3). However, reflecting the much larger number of outcome events when looking at any COVID-19 compared to COVID-19 requiring hospitalisation, confidence intervals were narrower for any COVID-19 and did not include the null (HR per child in fully adjusted models 0.89; 95% CI 0.84-0.95).

As with the primary outcome, we found similar inverse associations between number of young children in the household and the risk of any COVID-19 after restricting the analysis to participants without any known comorbidities (0.89; 95% CI 0.84-0.95) and to those who had 2 or fewer prescriptions within the previous 9 months (adjusting for demographic and occupational factors the HR per child was 0.89; 95% CI 0.83-0.96.). Compared to the primary outcome, the associations for any COVID-19 was more similar according to part-time working status (HR per child 0.85; 95% CI 0.77-0.92 for part-time and 0.92; 95% CI 0.84-1.00 non-part time, P-interaction = 0.75).

Adjusting for the same variables, we explored the risk of any COVID-19 after more finely categorising younger children into primary school and pre-school children. On formal testing, this separate categorisation improved the model fit (Chi-square = 5.74, df = 0.99, p = 0.02) and slightly stronger associations were observed in pre-school children than in primary school children (in age adjusted models, HR per pre-school child 0.82; 95% CI 0.74-0.91 versus HR per primary school child 0.94; 95% CI 0.88-1.00). In contrast there was no evidence of a lower risk where adolescents or adults 18 or older were present in the household (Table 4). Similar differences between the age-groups, but with wider 95% confidence intervals reflecting the smaller numbers of events, were also found for the primary outcome of COVID-19 requiring hospitalisation (Supplementary Appendix Table S4).

#### Additional analyses

We also examined associations for the much less common outcome, severe COVID-19, the results of which are shown in the supplementary appendix in Tables S5 and S6. The full set of regression coefficients and standard errors for all fitted models are provided at **github\_repository\_to\_be\_made\_public\_following peer\_review**.

#### Discussion

We found that among a cohort of over 300,000 adults living in a household containing a healthcare worker in Scotland, the risk of testing positive for SARS-CoV-2 during the first wave of the COVID-19 pandemic was lower for individuals living with young children (0-11 years), and that this persisted after adjusting for potential confounding variables. Risk of hospitalisation for COVID-19 (our primary outcome) was similarly lower for those living with young children, although this finding did not reach statistical significance.

To support decision making concerning the closure of schools during the COVID-19 pandemic, several studies have examined the transmission of COVID-19 from children to adults. A community surveillance study in England and Wales conducted by Public Health England found that children rarely tested positive for SARS-CoV-2, even when they had symptoms of acute respiratory infection; this was particularly true for younger children<sup>19</sup> Studies examining contacts of younger children with SARS-CoV-2 have also shown low rates of secondary cases, particularly in non-household settings, consistent with minimal or no transmission from children to adults.<sup>20</sup> Although we were mainly concerned with testing the hypothesis that contact with children might exert a protective effect in a high-risk population (healthcare workers), our study is also consistent with the findings that children do not pose a substantial risk of infection to adults with whom they share a household.

Our pre-specified hypothesis, that close contact with young children may actually protect against the risk of COVID-19 among adults, has not been extensively studied. We only found one study which touched on this question, a survey of exposures among people who had recovered from SARS-CoV-2.<sup>16</sup> Ours is the first cohort study of which we are aware to formally test this hypothesis, for which the findings provide a degree of support.

A number of limitations of this study should be acknowledged. First, the observed inverse association may be a chance finding. For the primary outcome, on including in our regression models the potential confounders which we had pre-specified, the confidence interval included the null. Although we knew that statistical power would be limited, we had decided, a priori, to use COVID-19 requiring hospitalisation as the primary outcome rather than any COVID-19 (which was much commoner), as we were concerned that high rates of (non-SARS-CoV-2) acute respiratory infection in households with small children may cause ascertainment bias, increasing the apparent rate of any COVID-19 in these groups as a result of increased testing. The level of testing was indeed higher among those adults who shared a household with young children, suggesting that there may be increased ascertainment. Despite this, in the fully adjusted models, we found similar point estimates regardless of whether the outcome was hospitalisation or any COVID-19. For the commoner outcome these estimates were more precise with confidence intervals that did not include the null, which suggests that the finding for the primary outcome may be real, rather than a chance observation.

Another possibility is that the identified association may have been confounded by part-time working. For the primary outcome, on stratifying the analysis into households where healthcare workers did and did not work part time, the association was evident in the former group but null in the latter. Since within part-time healthcare workers those with more children may work fewer hours (and therefore have lower exposure to SARS-CoV-2), and since we lacked accurate data on hours worked during the pandemic, the apparent effect of sharing a household with young children may be due to unmeasured confounding. Nonetheless, the association between the number of children and the risk of any case of COVID-19 – a much commoner outcome – did persist on

stratifying for part-time/whole-time status. Consequently, unmeasured confounding by time spent in high-risk occupational settings seems unlikely.

Residual confounding due to better health in those households with more children (perhaps affecting the decision to have more children) is also an unlikely explanation because the observed associations were also found on restricting the analyses to healthier adults.

From first principles, any protective effect of children on COVID-19 rate and severity in their household contacts would seem likely to involve cross-reactive immunity to endemic coronavirus infections acquired outside the home, e.g. at nursery or school. Evidence of antigenic similarity between N proteins of SARS-CoV-2 and those of endemic beta coronaviruses (strains Cov-OC43 and Cov-NL63) have now been shown in studies of cell-mediated immunity, and there is also evidence of cross-reactivity in antibody-mediated immunity, although it is currently uncertain how well this protects against COVID-19.<sup>4–9</sup> Secondly, children who had respiratory samples (sputum, broncho-alveolar washings etc) obtained for clinical reasons (e.g. respiratory tract infection) have previously been found to have high levels of seasonal coronavirus, was commonest in children under 5.<sup>12</sup> Thirdly, as well as having higher rates of infection (or asymptomatic carriage) children must also be capable of transmitting seasonal coronaviruses to adults with whom they share households. Younger adults (aged 15-44) which includes those ages most likely to share households with young children, have higher levels of antibodies to N proteins of COV-OC43 than do older adults,<sup>21</sup> but whether this reflects exposure at home via contact with children, or elsewhere, is unknown.

Alternatively, children could exert a protective effect through stimulation of the innate immune system of adults with whom they are close contacts<sup>13</sup> Children positive for seasonal coronaviruses often test positive for unrelated respiratory viruses. It is likely that any such effect would be shorter-term than one based on changes in specific acquired immunity. Two clinical trials are currently underway involving vaccination with BCG for COVID-19,<sup>22,23</sup> which will help determine whether such an effect is plausible.

Notwithstanding possible mechanisms, our findings provide sufficient evidence of a potentially interesting protective effect against COVID-19 infection in households with young children to warrant further study in other settings. High exposure settings, such as occupational groups or populations which have had increased exposure to SARS-CoV-2, would be of particular interest. Other adults that could usefully be studied are those who have had contact with large numbers of children, such as those who work in primary schools and nurseries, particularly in geographical settings where exposure to SARS-CoV-2 has also been common. As reliable population screening for antibodies to SARS-CoV-2 becomes widespread, another interesting test of our hypothesis would be to compare the prevalence of antibodies to SARS-CoV-2, and in parallel antibodies to seasonal antibodies *viz*. Cov-OC43, in those with and without substantive exposure to children of different age groups.

Our findings also raise intriguing questions around the design and evaluation of future vaccination programmes against SARS-CoV-2. For example, it would be important to examine the differential production of IgM and IgG antibodies to SARS-CoV-2 in adults and children to evaluate the possibility that children might 'pre-immunize' adults with endemic coronaviruses. Subsequent vaccination could then trigger a more rapid secondary immune response. This is an important practical point, since recent studies of antibody kinetics following natural infection with SARS-CoV-2 have indicated that antibodies are generally not detectable for 10-14 days, and in some patients are never detectable.<sup>24</sup> This lag time may be too long to ensure protection against severe COVID-19. Could

exposure to children perhaps enhance the efficacy of SARS-CoV-2 vaccines? Further, although longterm studies are not yet feasible with SARS-CoV-2, follow-up after experimental Cov-OC43 infection indicates that seropositivity wanes fairly rapidly over time, with many volunteers becoming negative

within a year.<sup>10</sup> This raises the possible risk of re-infection, and the consequent need for follow-up vaccination, in which case any possible role of children acting as 'natural vaccine boosters;' should be taken into consideration.

#### Conclusion

In a large occupational cohort, increased household exposure to young children was associated with an attenuated risk of testing positive for SARS-CoV-2 and appeared to also be associated with (nonstatistically-significant) attenuated risk of COVID-19 disease severe enough to require hospitalisation. Verification of this finding is needed in other settings where both exposure to SARS-CoV-2 and contact with young children are common. These findings have potentially important implications for future control of the COVID-19 pandemic, for example through informing policy on nursery and school closure and vaccination.

### References

1. Swann OV, Holden KA, Turtle L, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. *BMJ*. 2020;370. doi:10.1136/bmj.m3249

2. Spiegelhalter D. What have been the fatal risks of Covid, particularly to children and younger adults? Medium. Published June 16, 2020. Accessed August 10, 2020.

https://medium.com/wintoncentre/what-have-been-the-fatal-risks-of-covid-particularly-to-childrenand-younger-adults-a5cbf7060c49

3. Cristiani L, Mancino E, Matera L, et al. Will children reveal their secret? The coronavirus dilemma. *Eur Respir J*. 2020;55(4):2000749. doi:10.1183/13993003.00749-2020

4. Le Bert N, Tan AT, Kunasegaran K, et al. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. *Nature*. Published online July 15, 2020:1-10. doi:10.1038/s41586-020-2550-z

5. Grifoni A, Weiskopf D, Ramirez SI, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. *Cell*. 2020;0(0). doi:10.1016/j.cell.2020.05.015

6. Lv H, Wu NC, Tsang OT-Y, et al. Cross-reactive Antibody Response between SARS-CoV-2 and SARS-CoV Infections. *Cell Rep.* 2020;31(9):107725. doi:10.1016/j.celrep.2020.107725

7. van der Heide V. SARS-CoV-2 cross-reactivity in healthy donors. *Nat Rev Immunol*. 2020;20(7):408-408. doi:10.1038/s41577-020-0362-x

8. Ng KW, Faulkner N, Cornish GH, et al. Pre-existing and de novo humoral immunity to SARS-CoV-2 in humans. *bioRxiv*. Published online July 23, 2020:2020.05.14.095414. doi:10.1101/2020.05.14.095414

9. Pia L. SARS-CoV-2-reactive T cells in patients and healthy donors. *Nat Rev Immunol*. 2020;20(6):353-353. doi:10.1038/s41577-020-0333-2

10. Huang AT, Garcia-Carreras B, Hitchings MDT, et al. A systematic review of antibody mediated immunity to coronaviruses: antibody kinetics, correlates of protection, and association of antibody responses with severity of disease. *medRxiv*. Published online April 17, 2020. doi:10.1101/2020.04.14.20065771

11. Gaunt ER, Hardie A, Claas ECJ, Simmonds P, Templeton KE. Epidemiology and Clinical Presentations of the Four Human Coronaviruses 229E, HKU1, NL63, and OC43 Detected over 3 Years Using a Novel Multiplex Real-Time PCR Method. *J Clin Microbiol*. 2010;48(8):2940-2947. doi:10.1128/JCM.00636-10

12. Nickbakhsh S, Ho A, Marques DFP, McMenamin J, Gunson RN, Murcia PR. Epidemiology of Seasonal Coronaviruses: Establishing the Context for the Emergence of Coronavirus Disease 2019. *J Infect Dis*. 2020;222(1):17-25. doi:10.1093/infdis/jiaa185

13. Blok BA, Arts RJW, Crevel R van, Benn CS, Netea MG. Trained innate immunity as underlying mechanism for the long-term, nonspecific effects of vaccines. *J Leukoc Biol*. 2015;98(3):347-356. doi:10.1189/jlb.5RI0315-096R

14. Viner RM, Russell SJ, Croker H, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. *Lancet Child Adolesc Health*. 2020;4(5):397-404. doi:10.1016/S2352-4642(20)30095-X

15. Reopening Schools Survey Results. Accessed August 17, 2020. https://www.eis.org.uk/Coronavirus/ReopeningSchoolsSurvey

16. Dugas M, Schrempf IM, Ochs K, et al. Association of contact to small children with mild course of COVID-19. *medRxiv*. Published online July 26, 2020:2020.07.20.20157149. doi:10.1101/2020.07.20.20157149

17. Shah AS, Wood R, Gribben C, et al. *Risk of Hospitalisation with Coronavirus Disease 2019 in Healthcare Workers and Their Households: A Nationwide Linkage Cohort Study*. Epidemiology; 2020. doi:10.1101/2020.08.03.20164897

18. Onomap. Accessed August 17, 2020. https://www.onomap.org/

19. Ladhani SN, Amin-Chowdhury Z, Davies HG, et al. COVID-19 in children: analysis of the first pandemic peak in England. *Arch Dis Child*. Published online August 12, 2020. doi:10.1136/archdischild-2020-320042

20. COVID-19 in children and the role of school settings in COVID-19 transmission. European Centre for Disease Prevention and Control. Published August 6, 2020. Accessed August 10, 2020. https://www.ecdc.europa.eu/en/publications-data/children-and-school-settings-covid-19-transmission

21. Gao X, Zhou H, Wu C, et al. Antibody against nucleocapsid protein predicts susceptibility to human coronavirus infection. *J Infect*. 2015;71(5):599-602. doi:10.1016/j.jinf.2015.07.002

22. Assistance Publique - Hôpitaux de Paris. *Randomized Controlled Trial Evaluating the Efficacy of Vaccination With Bacillus Calmette and Guérin (BCG) in the Prevention of COVID-19 Via the Strengthening of Innate Immunity in Health Care Workers*. clinicaltrials.gov; 2020. Accessed August 16, 2020. https://clinicaltrials.gov/ct2/show/study/NCT04384549

23. BCG Vaccine for Health Care Workers as Defense Against COVID 19 - Full Text View -ClinicalTrials.gov. Accessed August 17, 2020. https://clinicaltrials.gov/ct2/show/NCT04348370

24. Kellam P, Barclay W. The dynamics of humoral immune responses following SARS-CoV-2 infection and the potential for reinfection. *J Gen Virol*. 2020;101(8):791-797. doi:10.1099/jgv.0.001439

#### Table 1 - Baseline characteristics of adults living in healthcare worker households by number of young children in household

	0 children	1 child	2 children	3+ children
	aged 0-11	aged 0-11	aged 0-11	aged 0-11
Number of adults	241266	41198	23783	3850
Adults who are healthcare workers	121004 (50.15)	22025 (53.46)	13179 (55.41)	2237 (58.10)
Age, mean (standard deviation)	44.53 (15.04)	39.82 (10.58)	39.01 (8.08)	38.47 (6.62)
Male	105116 (43.57)	17639 (42.82)	10803 (45.42)	1783 (46.31)
Scottish index of multiple deprivation				
1 - most deprived	37242 (15.44)	5655 (13.73)	2447 (10.29)	373 (9.69)
2	46147 (19.13)	7700 (18.69)	3599 (15.13)	582 (15.12)
3	48659 (20.17)	7491 (18.18)	4280 (18.00)	706 (18.34)
4	52847 (21.90)	9701 (23.55)	6102 (25.66)	999 (25.95)
5 - least deprived	56371 (23.36)	10651 (25.85)	7355 (30.93)	1190 (30.91)
Race/ethnicity - Non-white	7768 (3.22)	2088 (5.07)	1162 (4.89)	259 (6.73)
Comorbidity count				
None	207796 (86.13)	37315 (90.57)	21924 (92.18)	3564 (92.57)
One	24897 (10.32)	3231 (7.84)	1579 (6.64)	252 (6.55)
Two or more	8573 (3.55)	652 (1.58)	280 (1.18)	34 (0.88)
Occupation of healthcare worker in				
household				
Nursing and midwifery	102514 (42.49)	18688 (45.36)	10085 (42.40)	1530 (39.74)
Administrative services	44929 (18.62)	6710 (16.29)	3236 (13.61)	404 (10.49)
Support services	27294 (11.31)	3232 (7.85)	1386 (5.83)	236 (6.13)
Medical and dental	20836 (8.64)	4326 (10.50)	3586 (15.08)	849 (22.05)
Allied health profession	20007 (8.29)	3798 (9.22)	2974 (12.50)	442 (11.48)
Other	25686 (10.65)	4444 (10.79)	2516 (10.58)	389 (10.10)
Occupational role of healthcare worker in household				
Non-patient facing	50441 (20.91)	7453 (18.09)	3667 (15.42)	471 (12.23)
Patient facing	137697 (57.07)	25461 (61.80)	15485 (65.11)	2627 (68.23)
Undetermined	53128 (22.02)	8284 (20.11)	4631 (19.47)	752 (19.53)
Part time working in healthcare worker in				
household				
Whole time	147608 (61.18)	19482 (47.29)	8296 (34.88)	1206 (31.32)
Part time	88351 (36.62)	20329 (49.34)	14183 (59.64)	2281 (59.25)
Not recorded	5307 (2.20)	1387 (3.37)	1304 (5.48)	363 (9.43)
Tested for SARS-CoV-2	14736 (6.11)	2835 (6.88)	1823 (7.67)	354 (9.19)

Statistics are the number (percentage) of adults with each characteristic except for age, which is given as the mean and standard deviation.

# Table 2 - Risk and hazard ratios for COVID-19 requiring hospitalisation for adults living in healthcare worker households by number of young children in household

	No children aged 0- 11	1 child aged 0-11	2 children aged 0-11	3+ children aged 0-11	Per child
N adults with COVID-19 requiring hospitalisation	356	52	15	2	-
Total N adults	241266	41198	23783	3850	-
Risk per 10,000	14.8	12.6	6.3	5.2	-
Unadjusted	1	0.86	0.41	0.36	0.72
		(0.64-1.16)	(0.25-0.69)	(0.09-1.45)	(0.60-0.85)
Model 1	1	1.07	0.54	0.50	0.83
		(0.79-1.45)	(0.32-0.91)	(0.12-2.00)	(0.70-0.99)
Model 2	1	1.10	0.57	0.49	0.85
		(0.81-1.50)	(0.34-0.96)	(0.12-2.00)	(0.72-1.01)
Model 3	1	1.12	0.58	0.50	0.86
		(0.82-1.52)	(0.35-0.98)	(0.12-2.02)	(0.72-1.02)
Model 4	1	1.15	0.62	0.55	0.89
		(0.84-1.58)	(0.37-1.05)	(0.14-2.21)	(0.74-1.06)

Hazard ratios obtained from Cox proportional hazard models. Model 1 adjusts for age using a penalised spline function. Model 2 additionally adjusts for sex, Scottish Index of Multiple Deprivation, occupation (eg nursing, medical), occupational role (patient facing, non-patient facing, undetermined), healthcare worker (yes/no), length of service, number of children aged 12 to 17 in household, number of adults in household. Model 3 additionally adjusts for the comorbidity count and specific conditions (ischaemic heart disease, other heart disease, other circulatory system diseases, advanced chronic kidney disease, asthma and chronic lower respiratory disease, neurological disorders, decompensated liver disease, any immunological condition, malignant neoplasms, disorders of oesophagus, stomach and duodenum, type 1 diabetes and type 2 diabetes). Model 4 additionally adjusts for part-time status.

# Table 3 - Risk and hazard ratios for any COVID-19 for adults living in healthcare worker households by number of young children in household

	No children aged 0-11	1 child aged 0- 11	2 children aged 0-11	3+ children aged 0-11	Per child
N adults with any COVID-19	3222	507	268	52	-
Total N adults	241266	41198	23783	3850	-
Risk per 10,000	133.5	123.1	112.7	135.1	-
Unadjusted	1	0.92	0.84	1.02	0.94
		(0.83-1.01)	(0.73-0.96)	(0.75-1.37)	(0.89-0.99)
Model 1	1	0.84	0.75	0.89	0.88
		(0.75-0.93)	(0.65-0.86)	(0.66-1.21)	(0.83-0.93)
Model 2	1	0.84	0.74	0.85	0.88
		(0.75-0.93)	(0.65-0.86)	(0.63-1.15)	(0.83-0.93)
Model 3	1	0.83	0.75	0.85	0.88
		(0.75-0.93)	(0.65-0.86)	(0.63-1.15)	(0.83-0.93)
Model 4	1	0.85	0.77	0.89	0.89
		(0.77-0.95)	(0.67-0.89)	(0.66-1.20)	(0.84-0.95)

Model fitting and covariates as per footnote of Table 2.

# Table 4 - Hazard ratios for any COVID-19 for adults living in healthcare worker households by number of persons in household of different ages

	Per child aged 0 to 4	Per child aged 5 to 11	Per child aged 12 to 17	Per adult aged 18 or above
Unadjusted	0.86	0.98	1.05	0.81
	(0.78-0.95)	(0.92-1.05)	(0.98-1.12)	(0.78-0.84)
Model 1	0.83	0.91	1.00	0.97
	(0.74-0.92)	(0.85-0.97)	(0.93-1.07)	(0.89-1.06)
Model 2	0.80	0.92	1.02	1.04
	(0.72-0.89)	(0.86-0.99)	(0.95-1.09)	(1.01-1.08)
Model 3	0.80	0.92	1.02	1.04
	(0.72-0.89)	(0.86-0.99)	(0.95-1.09)	(1.01-1.08)
Model 4	0.82	0.94	1.02	1.04
	(0.74-0.91)	(0.88-1.00)	(0.96-1.10)	(1.01-1.07)

Model specification and covariates as per footnote of Table 2. The unadjusted models and model 1 were fitted separately for each exposure (eg aged 0 to5, aged 6 to 11 etc) but all exposures were included in models 2, 3 and 4. The effect estimates corresponds to "per child" column in Tables 2-3, where the counts of children and adults were treated as continuous variables, which assumes that any association between the number of children (or adults) and the hazard rate is log-linear.

# Figure 1 Risk of COVID-19 requiring hospitalisation in adults living in healthcare worker households by number of young children (aged 0 to 11) in household

Cumulative incidence (risk) plots of COVID-19 requiring hospitalisation by number of young children (aged 0 to 11) in household.



# Table S1 Comorbidity among adults living in healthcare worker households by number of young children in household

, ,	0 children aged 0-11	1 child aged 0-11	2 children aged 0-11	3 or more children aged 0-11
Any comorbidity	33470	3883	1859	286 (7.43)
	(13.87)	(9.43)	(7.82)	200 (7:10)
Ischaemic heart disease	4067 (1.69)	256	74 (0.31)	13 (0.34)
	(	(0.62)	(	( ')
Other heart disease	7298 (3.02)	604	250 (1.05)	38 (0.99)
		(1.47)		
Other circulatory system diseases	4386 (1.82)	494	237 (1.00)	49 (1.27)
		(1.20)		
Advanced chronic kidney disease	224 (0.09)	30 (0.07)	14 (0.06)	0
Asthma and chronic lower	5311 (2.20)	745	394 (1.66)	65 (1.69)
respiratory disease		(1.81)		
Neurological disorders	1249 (0.52)	161	91 (0.38)	11 (0.29)
		(0.39)		
Decompensated liver disease	203 (0.08)	13 (0.03)	8 (0.03)	0
Any immunological condition	217 (0.09)	25 (0.06)	13 (0.05)	0
Malignant Neoplasms	7854 (3.26)	819	443 (1.86)	52 (1.35)
		(1.99)		
Disorders of oesophagus, stomach	5707 (2.37)	676	325 (1.37)	50 (1.30)
and duodenum		(1.64)		
Diabetes, type 1	1617 (0.67)	274	160 (0.67)	17 (0.44)
		(0.67)		
Diabetes, type 2	7660 (3.17)	618	205 (0.86)	32 (0.83)
		(1.50)		
Diabetes, unknown type	470 (0.19)	57 (0.14)	24 (0.10)	6 (0.16)

# Tables S2a to S2d Number of adults living in healthcare worker households according household composition

#### Table S2a Number of adults aged ≥18 by number of young children and children aged 12-17 in household

	0 children aged	1 child aged 0-11	2 children aged	3 or more
Number of	0-11		0-11	children aged 0-
children aged 12				11
to 17 in				
household				
0 aged 12-17	208714 (86.51)	29855 (72.47)	21470 (90.27)	3559 (92.44)
1 aged 12 to 17	24359 (10.10)	9521 (23.11)	2051 (8.62)	215 (5.58)
2 aged 12 to 17	7596 (3.15)	1677 (4.07)	244 (1.03)	61 (1.58)
3+ aged 12 to 17	597 (0.25)	145 (0.35)	18 (0.08)	15 (0.39)

#### Table S2b Number of adults aged ≥18 by number of young children and adults aged 18 or older in household

Number of adults aged 18 or older in household	0 children aged 0-11	1 child aged 0-11	2 children aged 0-11	3 or more children aged 0- 11
1 aged ≥18	39395 (16.33)	5026 (12.20)	2041 (8.58)	365 (9.48)
2 aged ≥18	78980 (32.74)	23042 (55.93)	17499 (73.58)	3273 (85.01)
3+ aged ≥18	122891 (50.94)	13130 (31.87)	4243 (17.84)	212 (5.51)

#### Table S2c Number of adults aged $\geq$ 18 by number of young children and adults aged 65 to 74 in household

	0 children aged	1 child aged 0-11	2 children aged	3 or more
Number of adults	0-11		0-11	children aged 0-
aged 65 to 74 in				11
household				
0 aged 65-74	219469 (90.97)	39659 (96.26)	23208 (97.58)	3797 (98.62)
1 aged 65-74	17701 (7.34)	1310 (3.18)	509 (2.14)	43 (1.12)
2 aged 65-74	3925 (1.63)	229 (0.56)	66 (0.28)	10 (0.26)
3+ aged 65-74	171 (0.07)	0	0	0

#### Table S2d Number of adults aged ≥18 by number of young children and adults aged 75 or older in household

Number of adults aged 75 or older in household	0 children aged 0-11	1 child aged 0-11	2 children aged 0-11	3 or more children aged 0- 11
0 aged ≥75	231223 (95.84)	40226 (97.64)	23387 (98.33)	3817 (99.14)
1 aged ≥75	8290 (3.44)	827 (2.01)	361 (1.52)	17 (0.44)
2 aged ≥75	1674 (0.69)	145 (0.35)	35 (0.15)	16 (0.42)
3+ aged ≥75	79 (0.03)	0	0	0

Table S3 Risk and hazard ratios for COVID-19 requiring hospitalisation for adults living in patient-facing healthcare worker households\* by number of young children in household.

	0 children aged 0- 11	1 child aged 0- 11	2 children aged 0-11	3 or more children aged 0-11	Per child
Events	252	36	13	1	-
Ν	137697	25461	15485	2627	-
Risk per 10,000	18.3	14.1	8.4	3.8	-
Unadjusted	1	0.78	0.44	0.21	0.69
		(0.55-	(0.26-	(0.03-1.53)	(0.57-
		1.12)	0.76)		0.84)
Model 1	1	0.90	0.52	0.26	0.76
		(0.63-	(0.30-	(0.04-1.85)	(0.62-
		1.29)	0.91)		0.92)
Model 2	1	0.95	0.59	0.29	0.80
		(0.66-	(0.33-	(0.04-2.03)	(0.65-
		1.36)	1.03)		0.97)
Model 3	1	0.96	0.59	0.29	0.80
		(0.67-	(0.34-	(0.04-2.05)	(0.66-
		1.38)	1.04)		0.98)
Model 4	1	1.00	0.64	0.32	0.83
		(0.69-	(0.36-	(0.05-2.27)	(0.68-
		1.44)	1.13)		1.02)

Model fitting and covariates as per footnote of Table 2 in the main manuscript

\* Households where at least one healthcare worker occupies a patient facing role.

# Table S4 Hazard ratios for COVID-19 requiring hospitalisation for adults living in healthcare worker households by number of persons in household of different ages

	Per child	Per child	Per child	Per adult
	aged 0 to 4	aged 5 to 11	aged 12 to 17	aged 18 or above
Unadjusted	0.59 (0.41-0.84)	0.79 (0.65-0.97)	1.01 (0.81-1.25)	0.95 (0.87-1.03)
Model 1	0.79 (0.56-1.13)	0.85 (0.69-1.05)	1.00 (0.81-1.24)	0.97 (0.89-1.06)
Model 2	0.80 (0.56-1.14)	0.87 (0.71-1.08)	1.02 (0.82-1.27)	1.04 (0.94-1.13)
Model 3	0.81 (0.57-1.15)	0.88 (0.71-1.09)	1.03 (0.83-1.27)	1.04 (0.95-1.14)
Model 4	0.84 (0.59-1.20)	0.91 (0.73-1.12)	1.04 (0.84-1.29)	1.03 (0.94-1.13)

Model specification and covariates as per footnote of Table 4.

# Table S5 Risks and hazard ratios for severe COVID-19 for adults living in healthcare worker households by number of young children in household

	0 children aged 0-11	1 child aged 0-11	2 children aged 0-11	3 or more children aged 0- 11	Per child
N adults with severe COVID-19	83	11	3	0	-
Total N adults	241266	41198	23783	3850	-
Risk per 10,000	3.4	2.7	1.3	0.0	-
Unadjusted	1	0.78 (0.42- 1.46)	0.37 (0.12- 1.18)	<0.01	0.65 (0.44- 0.95)
Model 1	1	1.30 (0.69- 2.46)	0.75 (0.24- 2.36)	<0.01	0.94 (0.66- 1.34)
Model 2	1	1.35 (0.72- 2.52)	0.75 (0.23- 2.38)	<0.01	0.94 (0.67- 1.34)
Model 3	1	1.39 (0.74- 2.60)	0.73 (0.23- 2.38)	<0.01	0.93 (0.66- 1.31)
Model 4	1	1.44 (0.77- 2.71)	0.80 (0.24- 2.60)	<0.01	0.99 (0.69- 1.40)

Model fitting and covariates as per footnote of Table 2 in the main manuscript.

# Table S6 Hazard ratios for severe COVID-19 for adults living in healthcare worker households by number of persons in household of different ages

	Per child	Per child	Per child	Per adult
	aged 0 to 5	aged 6 to 11	aged 12 to 17	aged 18 or above
Unadjusted	0.41 (0.14-1.20)	0.78 (0.51-1.19)	0.62 (0.36-1.08)	1.23 (1.05-1.45)
Model 1	0.75 (0.27-2.05)	1.02 (0.67-1.54)	0.68 (0.39-1.17)	1.22 (1.02-1.46)
Model 2	0.70 (0.25-1.95)	1.06 (0.71-1.57)	0.68 (0.39-1.17)	1.22 (1.01-1.48)
Model 3	0.67 (0.24-1.87)	1.05 (0.71-1.56)	0.68 (0.39-1.17)	1.23 (1.02-1.48)
Model 4	0.72 (0.27-1.96)	1.11 (0.74-1.66)	0.68 (0.40-1.18)	1.23 (1.02-1.48)

Model specification and covariates as per footnote of Table 4.