Childhood adversity and COVID-19 outcomes in the UK Biobank

Jamie L Hanson ,[1,2] Kristen O'Connor,[3] Dorthea J Adkins,[2] Isabella Kahhale[1,2]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/jech-2023-221147).

[1]Psychology, University of Pittsburgh, Pittsburgh, PA, USA
[2]Learning, Research, & Development Center, University of Pittsburgh, Pittsburgh, PA, USA
[3]Saint Vincent College, Latrobe, Pennsylvania, USA

Correspondence to
Dr Jamie L Hanson, Learning, Research, & Development Center, University of Pittsburgh, Pittsburgh, PA 15260, USA; jamie.hanson@pitt.edu

Received 14 July 2023
Accepted 14 October 2023
Published Online First 1 November 2023

To cite: Hanson JL, O'Connor K, Adkins DJ, *et al*. *J Epidemiol Community Health* 2024;**78**:75–81.

ABSTRACT

Objectives This study aims to investigate the association between childhood adversity and COVID-19-related hospitalisation and COVID-19-related mortality in the UK Biobank.

Design Cohort study.

Setting UK.

Participants 151 200 participants in the UK Biobank cohort who had completed the Childhood Trauma Screen were alive at the start of the COVID-19 pandemic (January 2020) and were still active in the UK Biobank when hospitalisation and mortality data were most recently updated (November 2021).

Main outcome measures COVID-19-related hospitalisation and COVID-19-related mortality.

Results Higher self-reports of childhood adversity were related to greater likelihood of COVID-19-related hospitalisation in all statistical models. In models adjusted for age, ethnicity and sex, childhood adversity was associated with an odds ratio (OR) of 1.227 of hospitalisation (95% CI 1.153 to 1.306, childhood adversity z=6.49, p<0.005) and an OR of 1.25 of a COVID-19-related death (95% CI 1.11 to 1.424, childhood adversity z=3.5, p<0.005). Adjustment for potential confounds attenuated these associations, although associations remained statistically significant.

Conclusions Childhood adversity was significantly associated with COVID-19-related hospitalisation and COVID-19-related mortality after adjusting for sociodemographic and health confounders. Further research is needed to clarify the biological and psychosocial processes underlying these associations to inform public health intervention and prevention strategies to minimise COVID-19 disparities.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Disparities in COVID-19 outcomes are driven by numerous health and sociodemographic risk factors.
⇒ Childhood adversity is associated with lifelong physical health disparities and early mortality.
⇒ No known studies to date have examined the association between childhood adversity and COVID-19 mortality and morbidity.

WHAT THIS STUDY ADDS

⇒ In the UK Biobank, childhood adversity was significantly associated with COVID-19-related hospitalisation and COVID-19-related mortality.
⇒ For both morbidity and mortality, these links were seen in statistical models adjusted for important sociodemographic and physical health confounders.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Modifiable and more proximal psychosocial factors may impact adult health outcomes, including COVID-19-related mortality and hospitalisation.
⇒ Adversity may relate to depression, self-concept or self-regulation, cascading from childhood experiences to the outcomes that we investigated here.
⇒ Pinpointing these processes may allow for policy and interventions to lessen the negative impact of COVID-19 in those that have suffered childhood adversity.

INTRODUCTION

Since 2020, COVID-19 has claimed the lives of over 6.7 million people globally.[1] This pandemic has led to unprecedented global declines in life expectancy, with COVID-19 being the leading cause of death in the Americas and the third leading cause of death in Europe.[2 3] COVID-19 has also placed enormous burdens on healthcare systems, often requiring hospitalisation and intensive care for those with severe infections, in turn leading to billions of dollars in healthcare expenses.[4] While COVID-19 is a significant public health issue, the factors contributing to COVID-19 mortality and morbidity are still unclear. With this pandemic linked to significant long-term negative sequelae (eg, changes in brain structure and risk for heart conditions),[5 6] it is critical to increase knowledge about factors contributing to risk in order to guide public health intervention and prevention strategies.

While certain pre-existing medical conditions and unhealthy lifestyle patterns are linked to more severe COVID-19 infection,[7 8] disparities in COVID-19 outcomes have also been driven by numerous sociodemographic factors including age, sex, race, ethnicity, current socioeconomic status and occupation.[7 9 10] For example, compared with White individuals, COVID-19 hospitalisation in England is four times higher for black individuals and two times higher for Asian individuals.[9] Similarly increased risk has been noted for people from lower socioeconomic status backgrounds, with these effects persisting even after accounting for lifestyle risk factors and other potential confounders.[10] Interestingly, nearly all of this research has examined relations between COVID-19 outcomes and contemporaneous sociodemographic variables,

failing to consider early sociodemographic factors and neglecting developmental perspectives on the origins of health and disease.[11] To our knowledge, no studies have examined if COVID-19 outcomes are influenced by exposure to childhood adversity.

This knowledge gap is significant given that large-scale, epidemiological studies indicate that childhood adversity is associated with lifelong physical health disparities and early mortality.[12 13] For example, in a meta-analysis of 253 719 participants, those with high levels of childhood adversity were 2–3 times more likely to be diagnosed with heavy alcohol use, cancer, heart disease and respiratory disease, compared with those with low levels of childhood adversity.[13] Similarly, a population-based cohort study of over one million individuals between 16 and 34 years of age found that those with the highest levels of childhood adversity had an all-cause mortality risk 4.5 times higher than those with no adversity; this mortality risk corresponded to 10.3 additional deaths (per 10 000 person-years).[14] This increased mortality and morbidity risk is perhaps not surprising, given that childhood adversity relates to higher levels of inflammation and dysregulation of the hypothalamic pituitary adrenal axis.[15 16] With several studies now connecting excessive inflammation to COVID-19 disease severity and death,[17] childhood adversity could be related to heightened negative outcomes related to COVID-19 through proinflammatory pathways or potentially other indirect mechanisms (ie, unhealthy habits later in life[18]).

The current study seeks to investigate the association between early childhood adversity and COVID-19 mortality and morbidity in the UK Biobank (UKBB), a large-scale and well-characterised cohort. With childhood adversity being commonly linked to excessive inflammation and greater prevalence of negative health outcomes, we predicted that higher levels of adversity would be associated with higher rates of COVID-19-related hospitalisation. Additionally, given work finding childhood adversity is related to early mortality overall, we hypothesised that adversity would be related to higher rates of COVID-19-related mortality. Finally, we anticipated that adjusting for potential confounds would reduce the strength of relations, but that childhood adversity would still be significantly associated with COVID-19-related negative outcomes.

METHODS

Study design and participants

The UKBB is a large-scale, biomedical research project focused on identifying risk factors for common life-threatening and disabling conditions in middle-aged and older-aged individuals. The UKBB database contains in-depth demographic, behavioural and medical data from over half a million volunteer participants in the UK. At its onset in 2006, UKBB recruited residents between the ages of 40 and 69 that were registered with the United Kingdom's National Health Service (NHS) and lived within 25 miles of an assessment site. Across a total of 22 assessment sites, participants completed touch-screen questionnaires and face-to-face interviews to collect information about their demographic backgrounds and lifestyles, including their ethnicity, level of education, weight and height measurements, chronic health conditions, and other variables.[10 19] Recruitment was completed in 2010, along with consent for future contact and linkage to routinely collected health-related data, such as those produced by the NHS. All UK Biobank participants provided informed consent electronically and the study was approved by the North-west Multi-centre Research Ethics Committee. Demographics for participants with different relevant data are shown in table 1. Further details on data linkages, cleaning, validation and data availability (including summary statistics for all data fields) can be found on the UKBB data showcase webpage (https://biobank.ctsu.ox.ac.uk/crystal/).

Table 1 Demographic table of participants with usable data, listing age at recruitment, sex, ethnicity, socioeconomic status (Townsend Deprivation Index), body mass index (BMI), education and time between recruitment and the start of the COVID-19 pandemic

Variable	N=151 200*
Age at recruitment (years)	55.85 (7.73)
Sex	
Female	85 469 (57%)
Male	65 731 (43%)
Ethnicity	
White	146 443 (97%)
Other	2109 (1.4%)
Black or Black British	1059 (0.7%)
Asian	1589 (1.1%)
Townsend deprivation at recruitment	1.72 (2.83)
BMI at recruitment	26.8 (4.5)
Education	
A levels/AS levels or equivalent	20 369 (15%)
College or university degree	68 705 (49%)
CSEs or equivalent	5587 (4.0%)
NVQ or HND or HNC or equivalent	7558 (5.4%)
O levels/GCSEs or equivalent	29 809 (21%)
Other professional qualifications for example, nursing, teaching	7587 (5.4%)
Time between recruitment and start of pandemic (years)	10.91 (0.86)

Of note, all covariates (ie, age, BMI) were measured at baseline when individuals began participation in the UKBB.
*Mean (SD); n (%).
CSE, Certificate of Secondary Education; GCSE, General Certificate of Secondary Education; HNC, Higher National Certificate; HND, Higher National Diploma; NVQ, National Vocational Qualification; UKBB, UK Biobank.

For this study, we focused on four major data sources: (1) self-reports of childhood adversity; (2) COVID-19 outcomes, specifically hospitalisation or death connected to COVID-19 infection; (3) demographic covariates (eg age, ethnicity) and (4) additional health-related variables (eg, body mass index, BMI) for use in sensitivity modelling. We detail information about each of these data sources below. Limiting participants to those with usable data in these categories, the average age in our sample was 55.91 years (±SD=7.73), 43.68% male and majority white (97%). Related to migration, the vast majority of participants self-reported being born in the UK (93.18%). Additional demographics are listed in table 1. A flow diagram depicting the number of participants included in our analyses, as well as information about participant exclusion, is shown in figure 1.

Self-reports of childhood adversity

UKBB participants completed the Childhood Trauma Screener (CTS),[20] a shortened version of the Childhood Trauma Questionnaire, in an online follow-up after initial recruitment. The CTS is a five-item questionnaire that asks about multiple forms of child maltreatment including physical abuse, physical neglect, emotional abuse, emotional neglect and sexual abuse. Participants rated the frequency with which they felt loved or hated, were physically abused or sexually molested, and if someone took them to a doctor when they were children. Responses were made on a 5-point Likert scale from 0 ('never true') to

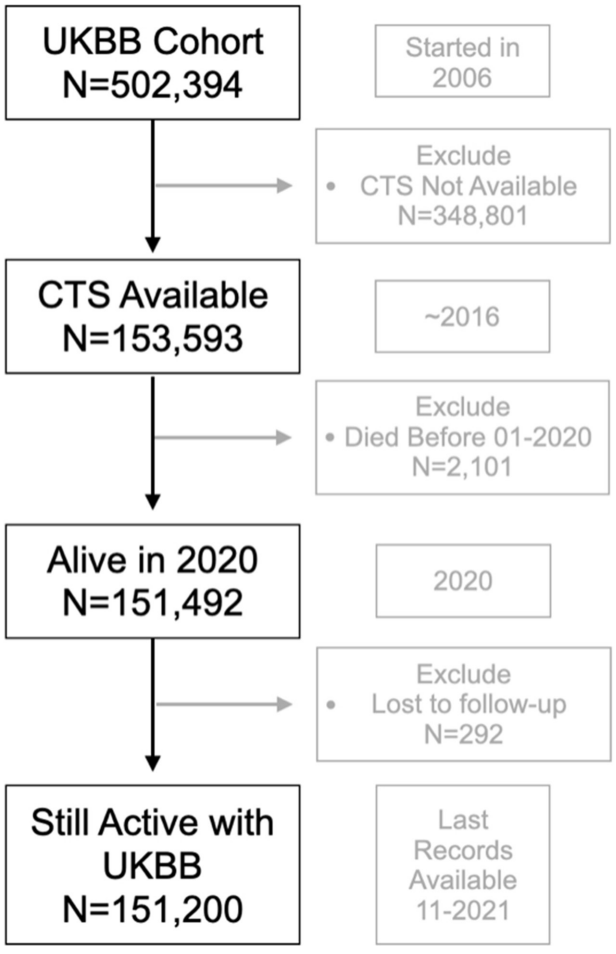

Figure 1 Flow diagram showing participants that were included (or excluded) from analyses based on data availability. The largest source of data loss was the lack of childhood adversity variables (the Childhood Trauma Screen, CTS). UKBB, UK Biobank.

4 ('very often true'). Participants could also select 'prefer not to answer' for any of the items. The CTS has been validated against other retrospective measures of child maltreatment and shows strong criterion and convergent validity, as well as good internal consistency.[20] The exact items of the CTS are noted in our online supplemental materials. Of note, the original UKBB sample is 502 394 participants, but only 151 200 individuals had valid data for this questionnaire, were alive at the start of the COVID-19 pandemic and still active in the UKBB. As noted in our online supplemental materials, participants in our analytical sample tended to be younger and more affluent (as indexed by lower Townsend Deprivation Index Scores). Our analytical subsample also was less diverse (including more white participants), more educated and included more females than the full UKBB cohort. Full details about these analyses are included in our online supplemental materials.

COVID-19-related health outcomes

We examined two classes of health outcomes related to COVID-19: (1) death where COVID-19 was reported as a primary or contributory cause and (2) inpatient hospitalisation where NHS data indicated COVID-19 occurrence. Both of these outcomes are related to International Classification of Diseases (ICD) code of U07.1: Confirmed COVID-19 case.[21] Deaths were recorded through linkage to national death registries (NHS Digital, NHS Central Register, National Records of Scotland).

Of the 502 394 volunteers enrolled in the UKBB study, 69 444 died before January 2020, the start of the COVID-19 pandemic as demarcated by the WHO. These participants were, therefore, excluded from all analyses. Among the 432 950 participants alive at the start of the pandemic, 151 200 had previously completed the CTS and were the focus of analysis. Filtering for any occurrence of 'COVID-19' in causes of death, 176 participants with complete childhood adversity data died due to COVID-19. In regard to hospitalisation, 693 participants with complete childhood adversity data had an inpatient hospitalisation related to COVID-19 (ICD Code U07.1). Health records were available up until November 2021.

Demographic covariates

Different potential confounding factors were included in our statistical models. Initially, these included sex, ethnicity, and age at recruitment. Sex was classified as male or female; categories for ethnicity were white, black or black British, Asian or Asian British, multiracial and other ethnic group. Three additional sociodemographic and physical health factors were also examined: (1) Townsend Deprivation Index, an aggregated measure of socioeconomic status that quantifies the poverty level of an individual's neighbourhood using data on unemployment, car and home ownership, and household overcrowding that are associated with a particular postal code[22 23]; (2) BMI, derived from participants' weight and height measurements and (3) Chronic health conditions, a binary count of 10 self-reported diseases or serious medical issues. These included high blood pressure, diabetes, angina, hay fever, rhinitis or eczema, asthma, heart attack, emphysema/chronic bronchitis, deep-vein thrombosis (blood clot in leg) and stroke. Because the timing varied in regard to when participants were recontacted by UKBB and when information about potential confounding factors was available, we used sociodemographic and health data collected at recruitment. This was to minimise missing data, as only a portion of the sample would have updated data available (ie, only deceased or hospitalised participants would have updated age data).

Statistical modelling

To understand the impact of childhood adversity on COVID-19 outcomes, we used mixed effects logistic regression analysis to generate ORs with 95% CIs. As noted previously, our final analytical sample was 151 200 participants. These individuals had valid measurements of childhood adversity, were alive at the start of the COVID-19 pandemic, and still active in the UKBB. With each outcome (COVID-19-related hospitalisation; COVID-19-related mortality), four model variations were used: (a) sex, age and ethnicity were included as independent variables, without inclusion of childhood adversity (model 1); (b) sex, age, ethnicity and childhood adversity as independent variables (model 2); (c) sex, age, ethnicity, current socioeconomic status (Townsend Deprivation Index) and childhood adversity as independent variables (model 3) and (d) sex, age, ethnicity, current socioeconomic status, physical health history (Chronic health conditions) and childhood adversity as independent variables (model 4). This allowed us to first understand risks caused by childhood adversity (model 2), while iteratively eliminating the effects of potential confounders and/or mediators (models 3 and 4) to understand the role of demographic and physical comorbidities in attenuating risks. The outcome variable in each model (COVID-19-related hospitalisation or COVID-19-related mortality) was a

Table 2 The multivariate output for models where COVID-19-related hospitalisation was the dependent variable (both panels) and sex, age and ethnicity were the independent variables (left panel) or sex, age, ethnicity and childhood adversity were the independent variables (right panel)

	Base model (without adversity): predicting hospitalisation			Model without adversity predicting hospitalisation		
Variable	**ORs**	**95% CI**	**P value**	**ORs**	**95% CI**	**P value**
Intercept	0.00	0.00 to 0.00	**<0.001**	0.00	0.00 to 0.00	**<0.001**
Ethnicity: other (white ref.)	2.54	1.64 to 3.95	**<0.001**	2.28	1.47 to 3.55	**<0.001**
Ethnicity: black (white ref.)	3.60	2.09 to 6.20	**<0.001**	3.06	1.77 to 5.29	**<0.001**
Ethnicity: Asian (white ref.)	2.13	1.24 to 3.64	**0.006**	1.93	1.13 to 3.31	**0.017**
Sex (female reference)	2.10	1.80 to 2.45	**<0.001**	2.15	1.84 to 2.51	**<0.001**
Age (at recruitment)	1.26	1.17 to 1.36	**<0.001**	1.28	1.18 to 1.38	**<0.001**
Childhood adversity				1.23	1.15 to 1.31	**<0.001**
Random effects						
σ^2	3.29			3.29		
τ_{00}	0.10_{site}			0.10_{site}		
ICC	0.03			0.03		
N	22_{site}			22_{site}		
Observations	151 200			151 200		
Marginal R^2/conditional R^2	0.061/0.090			0.073/0.100		

Bold values are statistically significant at p<0.05.
ICC, Intraclass Correlation Coefficient.

binary indicator of the occurrence of that negative health outcome (1=COVID-19-related hospitalisation, or COVID-19-related mortality; 0=no hospitalisation, or mortality). Independent variables were deemed significant based on their p values, as well as 95% CIs of ORs that crossed 1. When appropriate, we also compared different models using binomial analysis of variances with p values calculated using a χ^2 test and χ^2 distribution.

For statistical modelling, we used R V.4.2.2 and the following R packages: aod V.1.3.2, broom.mixed V. 0.2.9.4, car V.3.1.1, cowplot V.1.1.1, gt V.0.8.0, gtsummary V.1.6.3, hrbrthemes V.0.8.0, jtools V.2.2.1, lme4 V.1.1.31, modelbased V.0.8.6, performance V.0.10.1, plyr V.1.8.8 and tidyverse V.1.3.2.

RESULTS

Across multiple statistical models, we observed an association between childhood adversity and COVID-19-related hospitalisation. For all models, higher self-reports of childhood adversity were related to greater likelihood of COVID-19-related hospitalisation. In our model adjusted for age, ethnicity and sex (model 2), childhood adversity was associated with an OR of 1.227 of hospitalisation (95% CI 1.153 to 1.306, childhood adversity z=6.49, p<0.005). Notably, compared with our model that only included age, ethnicity and sex (model 1), inclusion of childhood adversity improved model fit ($\chi^2(1, N=151200)=36.5$, p<0.005) with an improvement in R^2 (model 1 conditional R^2: 0.090, Akaike information criterion (AIC)=8669.9; model 2 conditional R^2: 0.100, AIC=8635.4, as noted in table 2). Receiver operating characteristic curves and regression coefficient plots for these models are shown in figure 2.

Adjustment for potential confounds attenuated this association, but still suggested a connection between childhood adversity and COVID-19-related hospitalisation. In models adjusting for age, ethnicity, sex and current socioeconomic status (model 3), childhood adversity was associated with an OR of 1.20 of hospitalisation (95% CI 1.13 to 1.28, childhood adversity z=5.80, p<0.005). When we also include chronic health conditions (model 4), the association between childhood adversity and COVID-19-related hospitalisation remains mostly unchanged (OR 1.193, 95% CI 1.121 to 1.269, childhood adversity z=5.55, p<0.005).

Related to COVID-19-related mortality, childhood adversity was associated with an OR of 1.25 of a COVID-19-related death (95% CI 1.11 to 1.424, childhood adversity z=3.50, p<0.005) in our models adjusting for age, ethnicity and sex (model 2). Notably, compared with our model that only included age, ethnicity and sex (model 1), inclusion of childhood adversity improved model fit ($\chi^2(1)=10.5$, p=0.001) with an improvement in R^2 (model 1 conditional R^2=0.231 AIC=2606.0; model 2 conditional R^2=0.241, AIC=2597.5, as noted in table 3). Receiver operating characteristic curves and regression coefficient plots for these models are shown in figure 3.

Again, confound adjustment attenuated associations, but statistical models still suggested a connection between childhood adversity and COVID-19-related mortality. In models adjusting for age, ethnicity, sex and current socioeconomic status (model 3), childhood adversity was associated with an OR of 1.214 of hospitalisation (95% CI 1.069 to 1.379, childhood adversity z=2.99, p=0.003). When we also include chronic health conditions (model 4), the association between childhood adversity and COVID-related mortality remains mostly unchanged (OR 1.204, 95% CI 1.061 to 1.367, childhood adversity z=2.88, p=0.004). Additional sensitivity models examining additional confounding factors and interactions between chronic conditions and childhood adversity are noted in our online supplemental materials. In our Supplement, we also completed exploratory analyses examining the potential mechanisms linking childhood adversity to COVID-19 outcomes. This involved indirect ('mediation') models where we tested whether statistical associations between adversity (X) and COVID-19 mortality or hospitalisation outcomes (Y) were reduced when accounting for current socioeconomic status or pre-existing health conditions (M).

DISCUSSION

In a large-scale, well-characterised cohort, we found links between childhood adversity and COVID-19-related outcomes. Specifically, we found significant associations between childhood adversity and both COVID-19-related hospitalisation and COVID-19-related mortality. For both morbidity and mortality, these links were seen in statistical models adjusted for important sociodemographic and physical health confounders, underscoring the significance of childhood adversity in predicting mortality and morbidity risk.

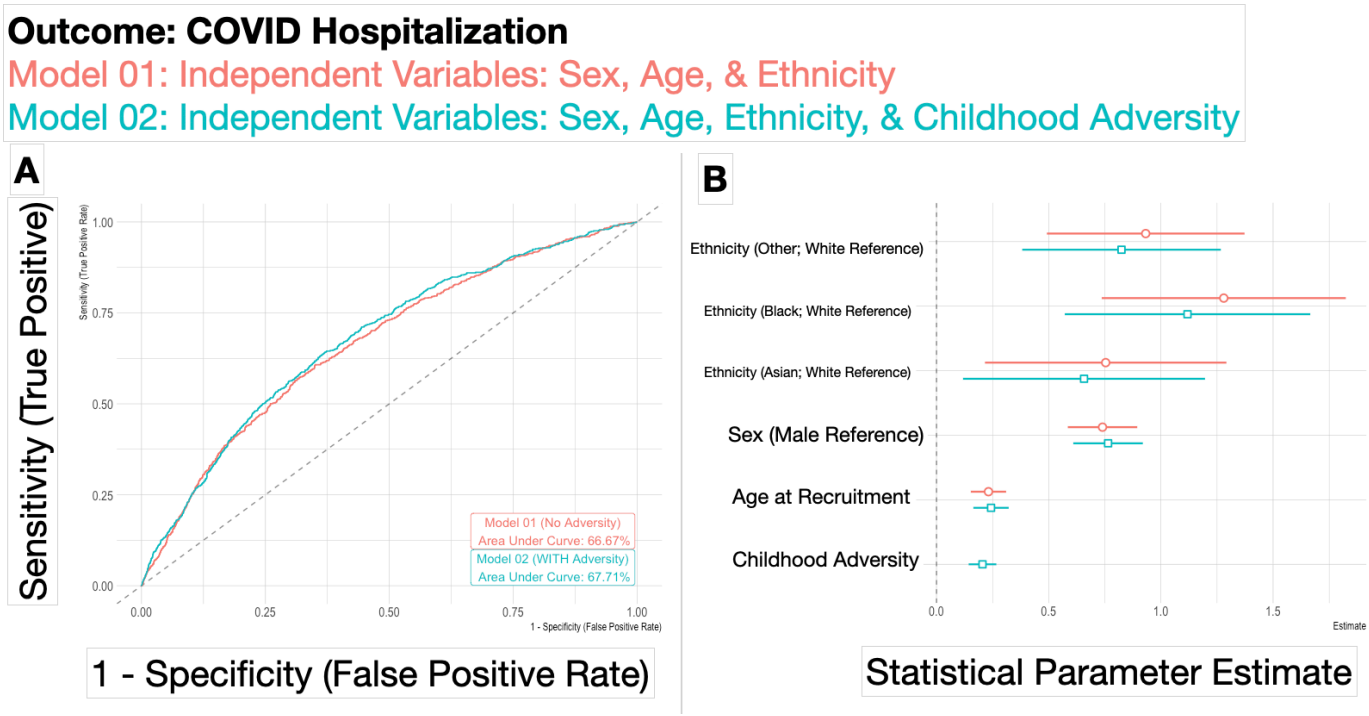

Figure 2 This two-panel figure shows results for COVID-19 hospitalisation. Panel (A) shows a receiver operating characteristic curve for two models (Model 01: age, sex and ethnicity predicting hospitalisation, but no measure of childhood adversity included in our mixed effects logistic regression analysis; model 2: age, sex, ethnicity and childhood adversity predicting hospitalisation). Panel (B) shows regression coefficients from these mixed effects logistic regression analysis, with sex, age and childhood adversity depicted. Model 01 is coloured orange, while model 02 is coloured teal.

Our data fills in important knowledge gaps both in terms of childhood adversity and health, as well as risk factors related to COVID-19-related hospitalisation and mortality. The results detailed here align with past work linking higher childhood adversity to poor physical health, including heavy alcohol use, cancer, heart disease and respiratory disease. Similarly, previous studies have found that particularly high levels of adversity are connected to higher all-cause mortality risk. Related to these two bodies of work, multiple meta-analyses suggest childhood adversity connects to higher levels of inflammation. While this investigation was unable to speak to potential mechanisms, it is likely that higher levels of inflammation, as well as alterations in the hypothalamic pituitary adrenal axis, related to childhood adversity are connected to the increased mortality and hospitalisation observed here. Alternatively, childhood adversity may exacerbate the multitude of stressors associated with the pandemic, such as social isolation, economic hardship and health concerns, further increasing COVID-19-related mortality and morbidity.

Table 3 The multivariate output for models where COVID-19-related mortality was the dependent variable (both panels) and sex, age and ethnicity were the independent variables (left panel) or sex, age, ethnicity and childhood adversity were the independent variables (right panel)

	Base model (without adversity): predicting mortality			Model without adversity predicting mortality		
Variable	**ORs**	**95% CI**	**P value**	**ORs**	**95% CI**	**P value**
Intercept	0.00	0.00 to 0.00	**<0.001**	0.00	0.00 to 0.00	**<0.001**
Ethnicity: other (white ref.)	1.08	0.27 to 4.35	0.918	0.97	0.24 to 3.93	0.966
Ethnicity: black (white ref.)	4.56	1.44 to 14.46	**0.010**	3.93	1.23 to 12.51	**0.021**
Ethnicity: Asian (white ref.)	2.10	0.67 to 6.63	0.204	1.90	0.60 to 6.00	0.273
Sex (female reference)	2.42	1.76 to 3.32	**<0.001**	2.48	1.81 to 3.41	**<0.001**
Age (at recruitment)	2.34	1.93 to 2.82	**<0.001**	2.36	1.95 to 2.86	**<0.001**
Childhood adversity				1.25	1.11 to 1.42	**<0.001**
Random effects						
σ^2	3.29			3.29		
τ_{00}	0.02_{site}			0.02_{site}		
ICC	0.01			0.01		
N	22_{site}			22_{site}		
Observations	151 200			151 200		
Marginal R^2/conditional R^2	0.226/0.231			0.236/0.241		

Bold values are statistically significant at p<0.05.
ICC, Intraclass Correlation Coefficient.

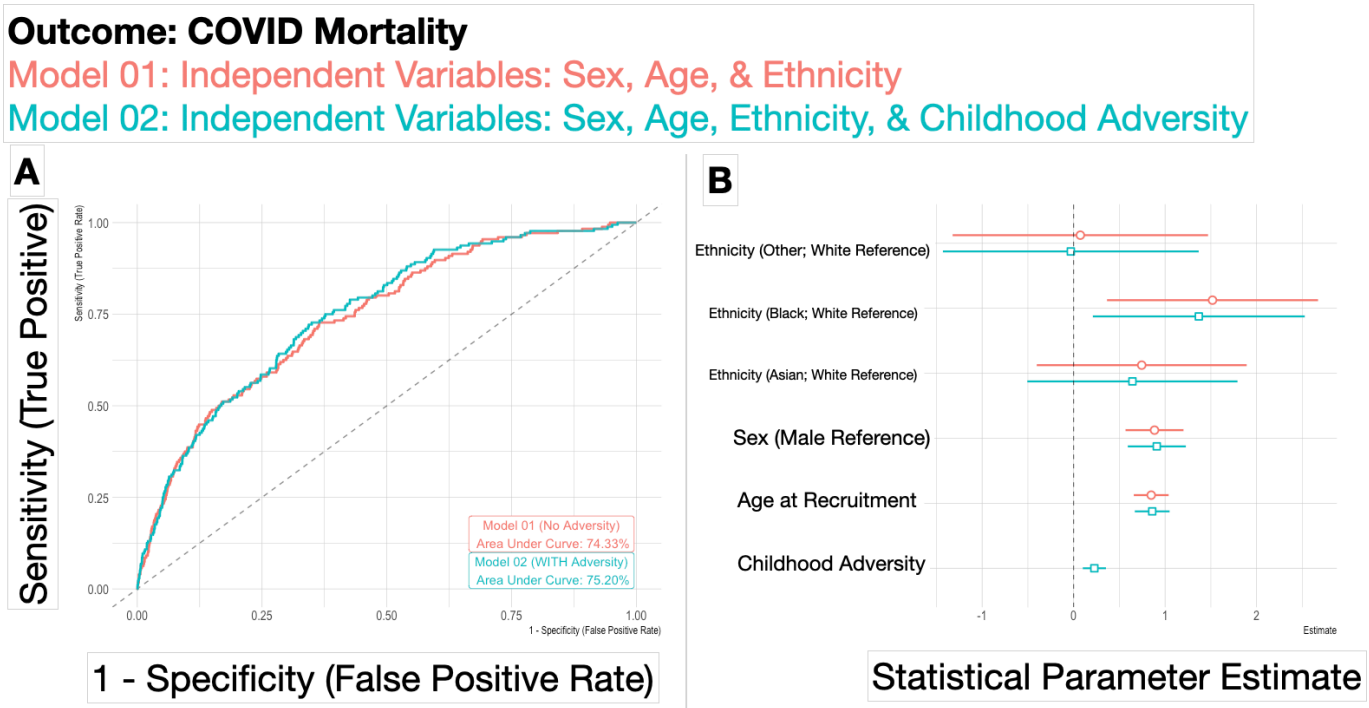

Figure 3 This two-panel figure shows results for COVID-19 mortality. Panel (A) shows a receiver operating characteristic curve for two models (model 01: age, sex and ethnicity predicting mortality, but no measure of childhood adversity included in our mixed effects logistic regression analysis; Model 2: age, sex, ethnicity and childhood adversity predicting mortality). Panel (B) shows regression coefficients from these mixed effects logistic regression analysis, with sex, age and childhood adversity depicted. Model 01 is coloured orange, while model 02 is coloured teal.

While this is the first study to examine links between childhood adversity and COVID-19-related outcomes in a large cohort, this project is not without limitations. First, our measure of childhood adversity was only available on a modest proportion of the overall UKBB sample (~30.1%). This may skew results as perhaps only certain individuals completed this measure. In addition, the UKBB is not truly a nationally representative cohort, with a response rate of ~5.5%. Participants tend to live in less socioeconomically deprived areas and are predominantly Caucasian. Associations between childhood adversity and COVID-19-related outcomes could differ in socioeconomically deprived areas, as well as in communities of colour. Second, while we controlled for many important, potential confounds, these were measured at the baseline assessment of the UKBB cohort. Baseline assessments were conducted multiple years before the COVID-19 pandemic and participants' current health or lifestyle may differ from when they started in the study. Notably, previous studies suggest UKBB baseline data can accurately rank participants years later,[24] but this has only been investigated for a few outcomes in the project. Third, the examination of morbidity and mortality may be an imperfect assessment of COVID-19-related outcomes. Hospitalisation data, for example, listed COVID-19 as a primary reason for admittance, but there may have been other diseases driving hospitalisation (eg, pneumonia). There may also be misclassification of deaths and hospitalisations due to COVID; future work could potentially probe multiple indices of health to understand if COVID-19 is the true cause of hospitalisation or mortality. Of note, COVID-19 infection was not necessarily confirmed in each case. Furthermore, data were only present until the end of 2021; different strains of COVID-19 have surged around the globe and may be associated with differential mortality and morbidity, a possibility these data are unable to address. Lastly, in considering our statistical models, links between adversity and COVID-19-related mortality were modest in magnitude, though still statistically significant.

These results also further delineate the sociodemographic and psychological factors contributing to COVID-19-related negative outcomes. Clear from past work is that certain pre-existing medical conditions and unhealthy lifestyle patterns are linked to more severe COVID-19 infection, which subsequently contributes to an increased likelihood of hospitalisation and mortality. Notably, our work extends past studies that have shown that sociodemographic risk factors are significant drivers of COVID-19 disparities. While previous projects have found that age, sex, race and ethnicity, and current socioeconomic status increase negative outcomes related to COVID-19, we believe this is the first project to examine how childhood adversity may further amplify risk. While the medical and public health communities have raised awareness about how sociodemographic variables may influence the impact of COVID-19, our work underscores that it is also critical to consider how an individual's developmental history may heighten the impact of the pandemic.

The association between experiences of childhood adversity and COVID-19 morbidity and mortality emphasise the need for further work considering modifiable and more proximal psychosocial factors. Future work could investigate if psychological processes related to adversity, such as depression, self-concept or self-regulation, cascade from childhood experiences to the adult health outcomes that we investigated here. Pinpointing these processes may allow for policy and interventions to lessen the negative impact of COVID-19 in those that have suffered childhood adversity. Further work in this space will be critical to reduce adversity-related negative outcomes with COVID-19, particularly as this disease becomes endemic, and to limit adversity-related negative outcomes with future pandemics.

Contributors Conceptualisation: JLH designed the study and developed the initial research question. Methodology: JLH, KO'C, DJA and IK designed the study methodology and aided in identified relevant data collection instruments. Data curation: JLH and IK collected and organised the data. Formal analysis: JLH conducted the statistical analysis and interpreted the results. Writing—original draft: JLH drafted the manuscript. Writing—review and editing: KO'C, DJA and IK reviewed and edited the manuscript. Visualisation: JLH and DJA created the figures and tables. Funding acquisition: JLH secured funding for the project. JLH acts as guarantor of the study.

Funding This work was funded by internal grants provided to JLH by the University of Pittsburgh.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and this work was approved by the University of Pittsburgh's IRB (under protocol STUDY22080014). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data are available through the UK Biobank (http://www.ukbiobank.ac.uk/) upon application and with permission of UKBB's Research Ethics Committee.

ORCID iD

Jamie L Hanson http://orcid.org/0000-0002-0469-8886

REFERENCES

1 World Health Organization. WHO coronavirus (COVID-19) dashboard. 2023. Available: https://covid19.who.int
2 Schöley J, Aburto JM, Kashnitsky I, *et al*. Life expectancy changes since COVID-19. *Nat Hum Behav* 2022;6:1649–59.
3 Wang H, Paulson KR, Pease SA. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21. *Lancet* 2022;399:1513–36.
4 Bartsch SM, Ferguson MC, McKinnell JA, *et al*. The potential health care costs and resource use associated with COVID-19 in the United States: a simulation estimate of the direct medical costs and health care resource use associated with COVID-19 infections in the United States. *Health Aff* 2020;39:927–35.
5 Douaud G, Lee S, Alfaro-Almagro F, *et al*. SARS-CoV-2 is associated with changes in brain structure in UK Biobank. *Nature* 2022;604:697–707.
6 Xie Y, Xu E, Bowe B, *et al*. Long-term cardiovascular outcomes of COVID-19. *Nat Med* 2022;28:583–90.
7 Elliott J, Bodinier B, Whitaker M, *et al*. COVID-19 mortality in the UK Biobank cohort: revisiting and evaluating risk factors. *Eur J Epidemiol* 2021;36:299–309.
8 Ko JY, Danielson ML, Town M, *et al*. Risk factors for coronavirus disease 2019 (COVID-19)–Associated hospitalization: COVID-19–associated hospitalization surveillance network and behavioral risk factor surveillance system. *Clin Infect Dis* 2021;72:e695–703.
9 Lassale C, Gaye B, Hamer M, *et al*. Ethnic disparities in hospitalisation for COVID-19 in England: the role of socioeconomic factors, mental health, and inflammatory and pro-inflammatory factors in a community-based cohort study. *Brain Behav Immun* 2020;88:44–9.
10 Foster HME, Ho FK, Mair FS, *et al*. The association between a lifestyle score, socioeconomic status, and COVID-19 outcomes within the UK Biobank cohort. *BMC Infect Dis* 2022;22:273.
11 Gluckman PD, Hanson MA, Cooper C, *et al*. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med* 2008;359:61–73.
12 Elsenburg LK, Rieckmann A, Nguyen T-L, *et al*. Mediation of the parental education gradient in early adult mortality by childhood adversity: a population-based cohort study of more than 1 million children. *Lancet Public Health* 2022;7:e146–55.
13 Hughes K, Bellis MA, Hardcastle KA, *et al*. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *Lancet Public Health* 2017;2:e356–66.
14 Rod NH, Bengtsson J, Budtz-Jørgensen E, *et al*. Trajectories of childhood adversity and mortality in early adulthood: a population-based cohort study. *Lancet* 2020;396:489–97.
15 Chiang JJ, Lam PH, Chen E, *et al*. Psychological stress during childhood and adolescence and its association with inflammation across the LifeSpan: a critical review and meta-analysis. *Psychological Bulletin* 2022;148:27–66.
16 Kuhlman KR, Horn SR, Chiang JJ, *et al*. Early life adversity exposure and circulating markers of inflammation in children and adolescents: a systematic review and meta-analysis. *Brain Behav Immun* 2020;86:30–42.
17 Merad M, Martin JC. Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. *Nat Rev Immunol* 2020;20:355–62.
18 Brugiavini A, Buia RE, Kovacic M, *et al*. Adverse childhood experiences and unhealthy lifestyles later in life: evidence from SHARE countries. *Rev Econ Household* 2023;21:1–18.
19 Jani BD, Hanlon P, Nicholl BI, *et al*. Relationship between multimorbidity, demographic factors and mortality: findings from the UK Biobank cohort. *BMC Med* 2019;17:74.
20 Grabe HJ, Schulz A, Schmidt CO, *et al*. A brief instrument for the assessment of childhood abuse and neglect: the childhood trauma screener (CTS). *Psychiatr Prax* 2012;39:109–15.
21 World Health Organization. Emergency use ICD codes for COVID-19 disease outbreak. Available: https://www.who.int/standards/classifications/classification-of-diseases/emergency-use-icd-codes-for-covid-19-disease-outbreak [Accessed 14 Feb 2023].
22 Mackenbach JP. Health and deprivation. inequality and the North. *Health Policy* 1988;10:207.
23 Townsend P. Deprivation. *J Soc Pol* 1987;16:125–46.
24 Bradbury KE, Young HJ, Guo W, *et al*. Dietary assessment in UK Biobank: an evaluation of the performance of the touchscreen dietary questionnaire. *J Nutr Sci* 2018;7:e6.