The potential of intervening on childhood adversity to reduce socioeconomic inequities in body mass index and inflammation among Australian and UK children: A causal mediation analysis

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/jech-2022-219617).

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Received 25 July 2022
Accepted 19 July 2023

To cite: Priest N, Guo S, Gondek D, *et al*. *J Epidemiol Community Health* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/jech-2022-219617

ABSTRACT

Background Lower maternal education is associated with higher body mass index (BMI) and higher chronic inflammation in offspring. Childhood adversity potentially mediates these associations. We examined the extent to which addressing childhood adversity could reduce socioeconomic inequities in these outcomes.

Methods We analysed data from two early-life longitudinal cohorts: the Longitudinal Study of Australian Children (LSAC; n=1873) and the UK Avon Longitudinal Study of Parents and Children (ALSPAC; n=7085). Exposure: low/medium (below university degree) versus high maternal education, as a key indicator of family socioeconomic position (0–1 year). Outcomes: BMI and log-transformed glycoprotein acetyls (GlycA) (LSAC: 11–12 years; ALSPAC: 15.5 years). Mediator: multiple adversities (≥2/<2) indicated by family violence, mental illness, substance abuse and harsh parenting (LSAC: 2–11 years; ALSPAC: 1–12 years). A causal mediation analysis was conducted.

Results Low/medium maternal education was associated with up to 1.03 kg/m^2 higher BMI (95% CI: 0.95 to 1.10) and up to 1.69% higher GlycA (95% CI: 1.68 to 1.71) compared with high maternal education, adjusting for confounders. Causal mediation analysis estimated that decreasing the levels of multiple adversities in children with low/medium maternal education to be like their high maternal education peers could reduce BMI inequalities by up to 1.8% and up to 3.3% in GlycA.

Conclusions Our findings in both cohorts suggest that slight reductions in socioeconomic inequities in children's BMI and inflammation could be achieved by addressing childhood adversities. Public health and social policy efforts should help those affected by childhood adversity, but also consider underlying socioeconomic conditions that drive health inequities.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Socioeconomic disadvantage is a key driver of inequities in childhood body mass index (BMI) and chronic inflammation. Empirical research also shows that childhood adversity may increase the risk of childhood obesity and chronic inflammation. However, little is known about the extent to which addressing childhood adversity could reduce socioeconomic inequities in children's BMI and chronic inflammation.

WHAT THIS STUDY ADDS

⇒ Using causal mediation analysis, we estimated that decreasing the levels of adversity among children with low/medium maternal education to be at levels like their peers with high maternal education would slightly reduce socioeconomic inequities in BMI and chronic inflammation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Action to address childhood adversity and associated health impacts remains imperative, however, this alone is unlikely to be sufficient to reduce socioeconomic inequities in childhood BMI and inflammation. Policy efforts should also consider opportunities to address more upstream socioeconomic conditions (eg, low education and occupation status) that drive these inequities.

INTRODUCTION

Non-communicable diseases (NCDs) are a leading cause of mortality, accounting for seven of 10 deaths globally.[1] By 2030, the total economic loss due to NCDs is estimated to be over US$2 trillion per annum globally.[2] NCDs typically manifest in adulthood yet risk factors such as obesity and chronic inflammation often begin to appear in childhood.[3] For example, the most recent national data showed that the prevalence of childhood obesity was 8.2% and 10.1%, respectively, in Australia and the UK.[4 5] Obesity and inflammation have a bidirectional and causal relationship and both are increased over the life course.[3 6] The United Nations Sustainable Development Goals include a specific target of

reducing one-third of premature deaths from NCDs through prevention and treatment by 2030.[1]

NCDs and their risk factors, including childhood obesity and inflammation, have stark social gradients with those from lower socioeconomic conditions experiencing a greater burden of disease and risk factors, throughout pre-conception, infancy and early childhood.[7 8] Yet early, primary prevention of NCDs remains limited by limited knowledge of optimal early-life intervention targets that reduce inequities in childhood NCD risk factors, such as obesity and inflammation. Identifying such intervention targets has substantial global public health implications.

Childhood adversity has been proposed as one promising intervention target to reduce the population burden of NCDs as well as addressing socioeconomic inequities in NCDs.[9] Children from socioeconomically disadvantaged families are exposed to more adversities than their non-disadvantaged peers.[10] Ensuring socioeconomic disadvantage is not conflated with childhood adversity is essential to ensure clear identification of causal pathways and potential intervention targets.[11] Childhood adversity typically refers to any exposure to abuse, neglect or family dysfunction rather than socioeconomic conditions themselves.[12] Separately, socioeconomic disadvantage is frequently measured using indicators such as low levels of parental education, income and occupational class,[13] with maternal education considered a particularly important indicator of assets and resources linked to child health and development.[14]

Associations have previously been established between maternal education and childhood obesity and chronic inflammation[15] through possible pathways such as greater exposure to stressful family relationships and reduced access to resources. Children from families with low maternal education are more likely to experience adversities than their peers with high maternal education due to poor material, psychosocial and behavioural conditions. For example, UK data show that 19.9% of children with low maternal education (eg, did not complete secondary education) were exposed to two or more adversities by age 5 compared with 14.4% of children with medium/high maternal education (eg, advanced level).[16] Empirical evidence from population studies and systematic reviews also suggests that childhood adversity itself may increase the risk of childhood obesity[17] and chronic inflammation[12 18] through multiple biological, psychological and behavioural exposures (eg, diet, stress, blood pressure).[9]

There is emerging evidence showing the feasibility and effectiveness of interventions to prevent and reduce adversities in childhood.[19 20] In the present study, we focused on four childhood adversities (family violence, household member mental illness, household member substance abuse and harsh parenting), given they occur in the family environment and are more often targeted than other adversities (eg, parent legal problems, parental divorce, household member death).[21] Currently, considerable policy and practice opportunities in Australia and the UK now focus on reducing family adversity through schools, health services and communities.[19 21] If childhood adversity substantially mediates socioeconomic inequities in childhood obesity and chronic inflammation, this would present even more compelling evidence for childhood adversity as a priority intervention target for reducing NCD risk factors.

To further inform policy action, we aimed to investigate the potential benefit of addressing childhood adversity to reduce socioeconomic inequities in children's body mass index (BMI) and chronic inflammation. To explore whether our findings are consistent across different settings and cohort samples,[22] we examined this issue in both Australia and the UK, as potential levers for reducing the socioeconomic gradient in NCDs risk factors continue to gain significant attention in both contexts.[16 23 24]

METHODS

Data sources

We draw on high-quality prospective data from the Longitudinal Study of Australian Children (LSAC) and the UK Avon Longitudinal Study of Parents and Children (ALSPAC).

Longitudinal Study of Australian Children

LSAC recruited a nationally representative early-life longitudinal cohort of 5107 infants, which commenced in May 2004. The LSAC design and sampling methodology are documented elsewhere.[25] In short, a two-stage clustered design was used to select a sample that was broadly representative of all Australian children, except those living in remote areas. All families who completed Wave 6 were invited, and approximately half of the Wave 6 sample participated in the Child Health CheckPoint,[26] conducted between LSAC Waves 6 and 7, when children were 11–12 years of age. The LSAC (ID 13–04) and CheckPoint (ID 14–26) methodologies were approved by the Australian Institute of Family Studies Human Research Ethics Review Board, and the CheckPoint additionally by The Royal Children's Hospital Melbourne Human Research Ethics Committee (33225D).

Avon Longitudinal Study of Parents and Children

ALSPAC is a prospective prenatal cohort from the Avon region of South-West England.[27 28] This study recruited 14 541 women during pregnancy with expected delivery dates of 1 April 1991 to 31 December 1992. The sample was boosted when the cohort children were approximately 7 years old with children with eligible birth dates who were not previously included in the study, resulting in a total of 15 454 pregnancies and 15 589 fetuses. Of these, 14 901 children were alive at 1 year of age. Due to the demographic profile of the catchment area population and differential attrition, the most disadvantaged groups and ethnic minority groups are under-represented in ALSPAC.[28] The study website contains a fully searchable data dictionary (http://www.bristol.ac.uk/alspac/researchers/our-data/). Consent for biological samples has been collected in accordance with the Human Tissue Act (2004). Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees.

Measures

Our conceptual model (figure 1) depicts the hypothesised pathway from maternal education to BMI and inflammation respectively, informed by current knowledge (see online supplemental appendix 1 for details). Figure 1 was used to guide the selection of measures (table 1) and inform the analytic approach.

Statistical analysis

Our analytic samples consisted of children who had outcome data on either BMI or GlycA (LSAC: n=1873; ALSPAC: n=7085). All analyses were conducted using Stata V.17.0.[29] Participant characteristics were first summarised overall and by maternal education. Both cohort analytic samples had missing data in exposure, mediator, outcome and confounders,

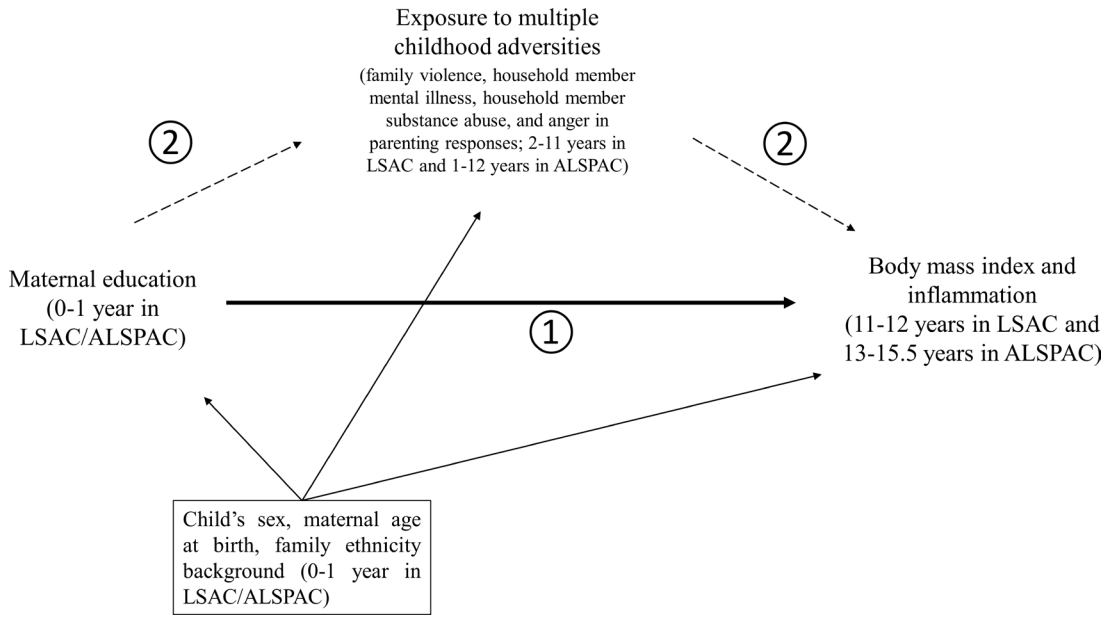

Figure 1 The conceptual model for the pathway from maternal education to BMI and inflammation respectively, via exposure to multiple childhood adversities (indicated by two or more). Path ① (bold line) represents the direct pathway from maternal education to BMI and inflammation, not through exposure to multiple adversities. Path ② (dashed line) represents the indirect pathway through exposure to multiple childhood adversities. In the box below are the potential confounders (child's sex, maternal age at birth and family ethnicity) that were adjusted for in analyses. ALSPAC, Avon Longitudinal Study of Parents and Children; BMI, body mass index; LSAC, Longitudinal Study of Australian Children.

therefore multiple imputation was used to handle missing data in all subsequent analyses (see details below). LSAC analyses also accounted for clustering by residential postcode due to the sample design.

To provide a preliminary examination of the strength of the pathways depicted in figure 1, we used a series of linear/logistic regression analyses to examine the associations between maternal education, multiple adversities and BMI/GlycA, unadjusted as well as adjusted for relevant confounders according to figure 1. Estimates from regression models were expressed as unit (kg/m^2) difference in means for BMI and percentage (%) difference in geometric means for GlycA between exposure groups.

Next, we conducted a counterfactual-based causal mediation analysis[30] to estimate the extent to which socioeconomic differences in children's BMI and GlycA could be reduced by decreasing the levels of multiple adversities (see online supplemental appendix 8 for technical details). We decomposed the total effect of maternal education on BMI/GlycA into direct (ie, effect of maternal education on BMI/GlycA not via multiple adversities) and indirect (ie, effect of maternal education on BMI/GlycA via multiple adversities) effects. The indirect effect can be interpreted as the benefit of a hypothetical intervention that would be able to effectively change the prevalence of the mediator (multiple adversities) in the exposed (low/medium maternal education) to be like that in the unexposed (high maternal education).[31 32] In this case, it would be a hypothetical intervention able to decrease the levels of multiple adversities among children with low/medium maternal education to be like their high maternal education peers. From the indirect effect estimate, we can estimate the so-called 'proportion mediated', which expresses the change in inequities after the hypothetical intervention as a proportion of the inequities before the intervention. In other words, it quantifies the proportion of the socioeconomic gap that is closed by the intervention.

Handling missing data

The percentage of missing data across all study variables ranged from 0 to 37.0% in LSAC and 0.2% to 52.5% in ALSPAC (online supplemental appendix 9). Multiple imputation by chained equations was conducted to handle these missing values.[33] The imputation model included all study variables and two auxiliary variables (child's birth weight z-scores, child's age at the outcome assessment). Fifty imputed data sets were created for both cohorts, with final results obtained using Rubin's rules to combine estimates across imputed datasets.[34] Due to the high proportion of missing data, we also conducted all analyses using the complete case dataset (online supplemental appendix 10).

RESULTS

Sample characteristics

In both cohorts, there was an even distribution of child sex (LSAC: 51.0% male; ALSPAC: 48.9% male; see table 2). Most children came from Anglo-European families in LSAC (86.3%) or white families in ALSPAC (96.0%). Overall, 44.0% of LSAC children had mothers with high education, whereas 16.2% of ALSPAC children had mothers with high education. ALSPAC children had a higher prevalence (43.7%) of exposure to multiple adversities than LSAC children (22.2%). In both cohorts, children with low/medium education had higher levels of BMI and chronic inflammation than those with high maternal education.

Associations between maternal education, multiple adversities and BMI/GlycA

Compared with children whose mothers had high education, those with low/medium maternal education had higher levels of BMI (figure 2A), after controlling for all baseline confounders. Despite wide confidence intervals, we found small associations between low/medium maternal education and higher GlycA levels (eg, for medium maternal education in LSAC: 1.81%

Table 1 Measurement of exposure, mediator, outcomes and potential confounders

Variable	Measurement details
Exposure	
Maternal education (0–1 year)	Maternal education at 0–1 year was used as a key indicator of socioeconomic resources within the family environment.[16] This was categorised as low, medium and high as most appropriate to each cohort. In LSAC, maternal education in Wave 1 was self-reported by the main caregiver and coded as (1) low: year 12 or below; (2) medium: certificate I/II/III/IV or advanced diploma; (3) high: bachelor's degree or above. In ALSPAC, maternal education was collected from a self-reported questionnaire at 18 weeks of gestation and coded as (1) low: certificate of secondary education, vocational or ordinary level; (2) medium: advanced level, who completed the end of high school exams; (3) high: university degree or above. We also used household occupation as an alternative indicator of family socioeconomic position in sensitivity analyses (see online supplemental appendix 2 for details).
Mediator	
Multiple childhood adversities (2–11 years in LSAC and 1–12 years in ALSPAC)	We examined four modifiable adversities in the family context that had a strong focus on policy intervention: family violence, household member mental illness, household member substance abuse and harsh parenting (see online supplemental appendix 3 for details). These adversities have been consistently examined in the childhood adversity literature,[19] and had repeated assessments available in each cohort. As in O'Connor *et al*,[10] we focused analysis on a composite indicator of multiple childhood adversities (hereafter referred to as 'multiple adversities' for brevity), given evidence suggests that exposure to multiple adversities can have a cumulative health impact beyond their individual effects.[18] First, participants were coded as being exposed to each type of adversity if an event had occurred at any time point in childhood. Then we calculated a cumulative score across childhood (a count of the number of adversities; in the case of children who experienced the same type of adversity at two waves, they were counted as 'two') (see online supplemental appendix 4 for the distribution of each adversity). Second, we dichotomised the total number of adversities as 'less than two' vs 'two or more'.[10] We also considered 'three or more' adversities as an alternative cut-off value to define multiple adversities in sensitivity analyses (online supplemental appendix 5).
Outcomes	
Body mass index (11–12 years in LSAC and 13 years in ALSPAC)	Children's BMI was obtained at 11–12 years in LSAC (n=1871) and at 13 years in ALSPAC (n=6704). Children were weighed to the nearest 50 g using digital bathroom scales and measured to the nearest 0.1 cm using a portable rigid stadiometer by a trained researcher. BMI was calculated using the following formula: BMI=weight (kg)/height $(m)^2$. Continuous BMI values were used for data analysis in the main document. A binary outcome of BMI (overweight and obesity vs those not) was used for sensitivity analysis (online supplemental appendix 6).
GlycA (11–12 years in LSAC and 15.5 years in ALSPAC)	GlycA (mmol/L) was used as an indicator of chronic inflammation,[18] measured in serum samples at 11–12 years in LSAC (n=1180) and plasma samples at 15.5 years in ALSPAC (n=3363), respectively. GlycA is elevated in both acute and chronic inflammatory conditions in childhood and is associated with cardiovascular risk in adulthood. It may capture chronic cumulative inflammation better than other inflammatory biomarkers.[18] As the distribution of GlycA was skewed, log-transformed GlycA values were analysed. High sensitivity C reactive protein (hsCRP) has also been commonly examined in the literature;[18] though with inconsistent evidence as to its association with adversity. We examined hsCRP as an alternative inflammatory outcome for completeness given its widespread use in the literature (online supplemental appendix 7).
Confounders	
Baseline confounders (0–1 year)	We posit three potential confounders at 0–1 year (see online supplemental appendix 1 for rationale) based on Jackson's framework:[43] child's sex (female/male), maternal age at childbirth (continuous) and family ethnic background (Anglo or European/Ethnic minority/Indigenous in LSAC; White/non-white in ALSPAC).

ALSPAC, Avon Longitudinal Study of Parents and Children; BMI, body mass index; GlycA, glycoprotein acetyls; LSAC, Longitudinal Study of Australian Children.

higher, 95% CI=0.26% 3.36%), after adjusting for all baseline confounders. Detailed tables of these results are available in online supplemental appendix 11. Overall, the differences in outcomes appeared to be greater when comparing medium and high maternal education groups in LSAC and to be greater when comparing low and high maternal education in ALSPAC.

We also observed a small association between exposure to multiple adversities and higher BMI/GlycA levels (figure 2B), after adjusting for baseline confounders and maternal education. Small associations were found between low/medium maternal education and exposure to multiple adversities (figure 2C), adjusting for baseline confounders. Together, all these findings are consistent with the expected relationships depicted in figure 1.

Extent to which intervening on multiple adversities could reduce socioeconomic inequities in BMI/GlycA

For LSAC children, if we were able to reduce the levels of multiple adversities among children with low/medium maternal education to be the same as those with high maternal education, we could potentially reduce 0.4%–1.8% of maternal education differences in BMI and 0.4%–3.3% in GlycA (table 3). For ALSPAC children, the potential benefit was smaller, with 0%–0.8% reduction in maternal education differences in BMI and 0%–2.3% reduction in GlycA. In both cohorts, we found that reducing multiple adversities to be at the levels of children with high maternal education had a larger benefit in children with medium maternal education than in those with low maternal education.

We found similar results in a range of sensitivity analyses when using household occupation as an alternative exposure (LSAC: managers/professionals; associate professionals; tradespersons/advanced clerical and service workers; intermediate/elementary clerical and service workers; ALSPAC: professionals/managerial and technical; skilled non-manual/skilled manual; partly skilled/unskilled), three or more childhood adversities as an alternative mediator and hsCRP as an alternative outcome. For example, if we used three or more adversities to define multiple childhood adversities, the potential benefits ranged from 0.1% to 6.0% reduction in our outcomes.

DISCUSSION

This study used two early-life longitudinal cohorts to examine the potential benefits of addressing childhood adversity to reduce socioeconomic inequities in children's BMI and inflammation respectively. We estimated small associations linking low/medium maternal education at birth with higher levels of BMI and inflammation in late childhood. There were also small associations linking low/medium maternal education to multiple adversities, and multiple adversities to higher levels of BMI and inflammation. Despite these associations being in the expected directions, causal mediation analyses showed that even if we could offer effective interventions to decrease the levels of

Table 2 Sample characteristics in LSAC and ALSPAC analysed samples

Variable	LSAC (n=1873)				ALSPAC (n=7085)			
	Mean (SD)/ frequency (%)	Maternal education			Mean (SD)/ frequency (%)	Maternal education		
		High	Medium	Low		High	Medium	Low
Exposure								
Maternal education								
High	825 (44.0)	–	–	–	1047 (16.2)	–	–	–
Medium	619 (33.0)	–	–	–	1724 (26.7)	–	–	–
Low	429 (22.9)	–	–	–	3675 (57.0)	–	–	–
Mediator								
Multiple adversities (≥2)								
No	1138 (77.8)	524 (79.6)	374 (75.9)	240 (77.2)	3018 (56.3)	561 (60.0)	819 (56.0)	1601 (56.8)
Yes	324 (22.2)	134 (20.4)	119 (24.1)	71 (22.8)	2341 (43.7)	374 (40.0)	643 (44.0)	1216 (43.2)
Outcome								
Body mass index	19.22 (3.43)	18.68 (2.86)	19.76 (3.90)	19.46 (3.55)	19.81 (3.53)	19.19 (3.01)	19.65 (3.43)	19.98 (3.63)
GlycA*	0.96 (0.91–1.04)	0.96 (0.90–1.03)	0.97 (0.91–1.05)	0.98 (0.91–1.05)	0.17 (0.11–0.25)	0.16 (0.11–0.22)	0.16 (0.11–0.24)	0.18 (0.11–0.26)
Baseline confounders								
Child's sex								
Female	918 (49.0)	411 (49.8)	295 (47.7)	212 (49.4)	3616 (51.1)	544 (52.0)	874 (50.7)	1858 (50.6)
Male	955 (51.0)	414 (50.2)	324 (52.3)	217 (50.6)	3457 (48.9)	503 (48.0)	850 (49.3)	1817 (49.4)
Maternal age at birth	31.98 (4.90)	32.95 (3.97)	31.57 (5.25)	30.72 (5.59)	29.45 (4.57)	32.07 (3.58)	30.43 (4.28)	28.25 (4.51)
Family ethnicity background								
Anglo/European or White	1616 (86.3)	696 (84.4)	551 (89.0)	369 (86.0)	6088 (96.0)	994 (95.9)	1629 (95.3)	3452 (96.3)
Ethnic minority or non-White	220 (11.7)	125 (15.2)	53 (8.6)	42 (9.8)	255 (4.0)	42 (4.1)	80 (4.7)	131 (3.7)
Indigenous	37 (2.0)	4 (0.5)	15 (2.4)	18 (4.2)	–	–	–	–

*Median and IQR are shown for GlycA.
ALSPAC, Avon Longitudinal Study of Parents and Children; GlycA, glycoprotein acetyls; LSAC, Longitudinal Study of Australian Children.

multiple adversities among children with low/medium maternal education to be like that of their peers with high maternal education, maternal education differences in BMI and inflammation would only reduce minimally.

In both cohorts, we found social gradients in children's BMI and chronic inflammation, consistent with previous findings.[15 35] The social determinants of health framework highlight that multiple nested levels of exposures and environments shape a child's health and lead to subsequent health inequities.[36] Low maternal education is a key socioeconomic indicator signalling fewer social and economic resources in the family and likely limited access to healthy foods causing overweight in both mothers and children.[37] Psychosocial and environmental pathways (eg, low social support, financial stress, neighbourhood poverty) may also link low maternal education to childhood BMI and inflammation,[35 38] which in turn lead to greater chronic disease risk later in life.

Our causal mediation analysis suggests that, in both Australian and UK settings, the potential benefits of addressing multiple adversities to reduce socioeconomic inequities are minimal, with the mediator only explaining up to 3.3% of the total effect of maternal education on children's BMI and inflammation. This contrasts to a recent finding from the UK Millennium Cohort Study (MCS),[16] which estimated that multiple adversities explained 19% of the total effect of maternal education on adolescents' overweight and obesity. However, considerable differences between the MCS and the present study regarding measurement of socioeconomic inequities and adversities may explain this discrepancy. The MCS used the relative index of inequality (RII) as the measure of total inequities, whereas we compared maternal education categories to quantify total inequities. Mediation analysis to decompose the RII is difficult to interpret, as it refers to shifting the mediator between its state at hypothetical extremes of the socioeconomic scale, which would be impossible in practice.[39] Further differences include the types and timeframe of adversities considered as well as the definition of the adversity intervention target, all of which could further influence the differences in findings between the present study and the MCS.

We found that, in both cohorts, the potential benefits of decreasing levels of multiple adversities appeared to be more prominent in children with medium maternal education (LSAC: certificate I/II/III/IV or advanced diploma; ALSPAC: advanced level) than in those with low maternal education (LSAC: year 12 or below; ALSPAC: certificate of secondary education, vocational or ordinary level). This could be due to the higher levels of multiple adversities seen among children with medium maternal education. Previous research suggested that some adversities (eg, family violence) occur in all communities and not all were patterned socioeconomically.[40] Our findings suggest that interventions targeting adversity should not only target those most vulnerable (eg, low maternal education), but also consider families at risk of adversity across the social gradient.

Strengths and limitations

A key strength of this study is the replication of analyses in population-based longitudinal data in two large independent samples, enhancing confidence in our findings. We also conducted a series of sensitivity analyses considering different

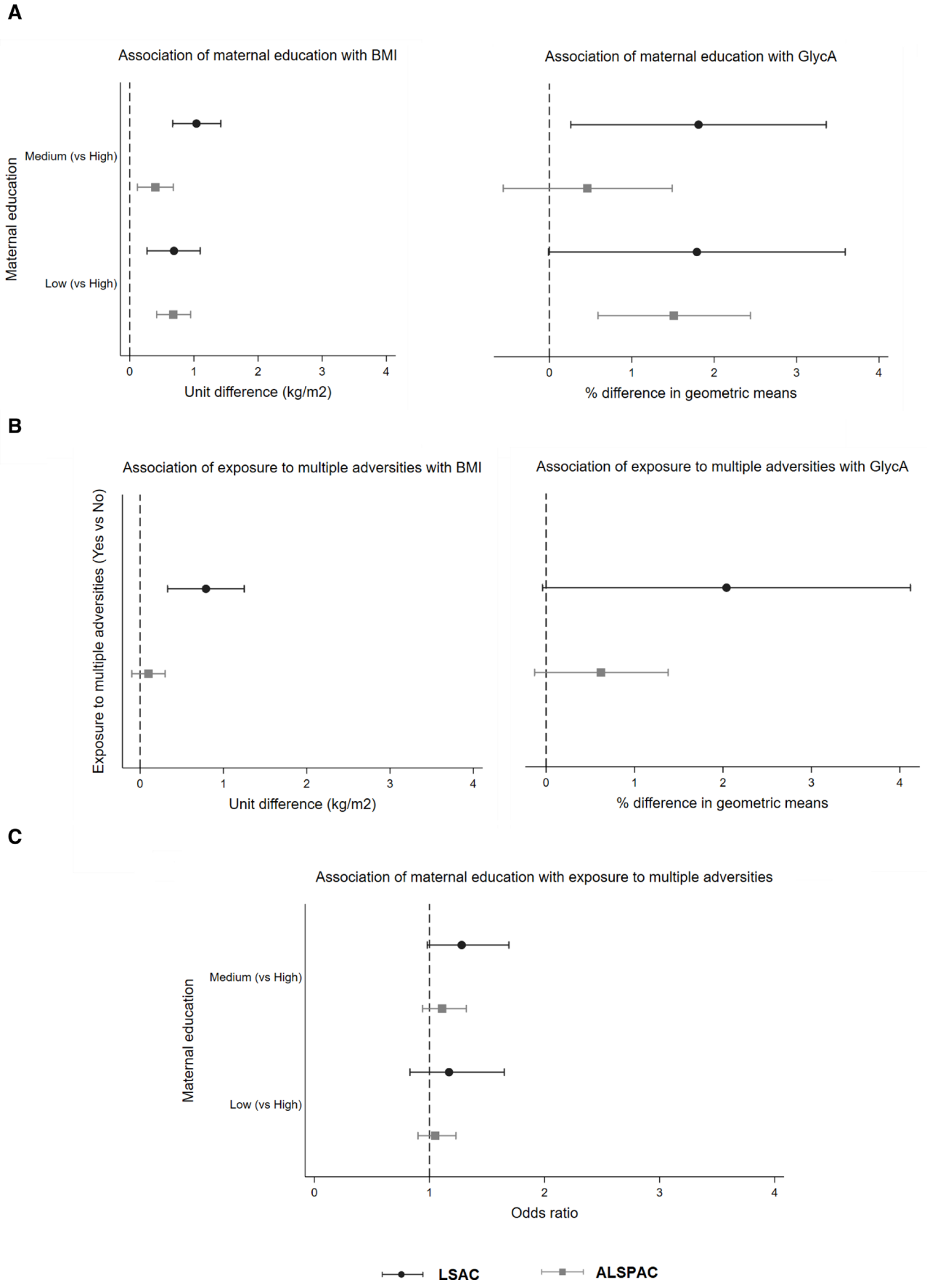

Figure 2 Associations between maternal education, exposure to multiple adversities and body mass index (BMI)/GlycA in Longitudinal Study of Australian Children (LSAC) and Avon Longitudinal Study of Parents and Children (ALSPAC). All figures are adjusted for child's sex, maternal age at birth and family ethnicity background. Maternal education was additionally adjusted for in figure 2B. 95% CIs are shown. GlycA, glycoprotein acetyls.

Table 3 Estimated total, direct effect and indirect effects in causal mediation analyses of the role of multiple adversities in the path from maternal education to BMI and inflammation, along with 95% CI (imputed results)

Group comparison	Cohort	Outcome*	Total effect	Direct effect	Indirect effect	Proportion mediated (%)
Low versus high maternal education	LSAC	BMI	0.64 (0.55 to 0.74)	0.64 (0.55 to 0.73)	0.0029 (0.0020 to 0.0038)	0.4
		Log-transformed GlycA	1.64 (1.62 to 1.65)	1.63 (1.61 to 1.65)	0.0073 (0.0072 to 0.0073)	0.4
	ALSPAC	BMI	0.70 (0.66 to 0.74)	0.70 (0.66 to 0.74)	−0.00068 (−0.00070 to −0.00065)	0
		Log-transformed GlycA	1.54 (1.53 to 1.54)	1.54 (1.54 to 1.55)	−0.0087 (−0.0086 to −0.0086)	0
Medium versus high maternal education	LSAC	BMI	1.03 (0.95 to 1.10)	1.01 (0.94 to 1.08)	0.0181 (0.0171 to 0.0191)	1.8
		Log-transformed GlycA	1.69 (1.68 to 1.71)	1.64 (1.63 to 1.65)	0.0560 (0.0559 to 0.0561)	3.3
	ALSPAC	BMI	0.39 (0.35 to 0.43)	0.39 (0.35 to 0.43)	0.0030 (0.0030 to 0.0031)	0.8
		Log-transformed GlycA	0.40 (0.40 to 0.41)	0.39 (0.39 to 0.40)	0.00938 (0.00937 to 0.00939)	2.3

All estimates are adjusted for baseline confounders at 0–1 year: child's sex, maternal age at birth and family ethnicity background.
*Estimates are expressed as unit (kg/m^2) difference in means for BMI and percentage (%) difference in geometric means for GlycA between exposure groups.
ALSPAC, Avon Longitudinal Study of Parents and Children; BMI, body mass index; GlycA, glycoprotein acetyls; LSAC, Longitudinal Study of Australian Children.

indicators of exposure (household occupation), mediator (three or more adversities) and outcome (hsCRP), all of which showed similar results, again enhancing confidence in the robustness of our findings.

Nevertheless, there are several limitations. First, there has been gradual attrition of LSAC and ALSPAC samples over time, which is ubiquitous in longitudinal cohorts.[16] While we used multiple imputation to reduce the potential for selection bias arising from missing data, it is possible that biases remain. Second, it is important to note that socioeconomic disadvantage is multidimensional. In this study, we measured maternal education as an important aspect of socioeconomic resources because it often precedes income and occupation in the life course and is more stable.[16] However, it may underestimate the influence of socioeconomic conditions as a whole. It would be worthwhile to consider other aspects (eg, geographic location, health conditions) of childhood disadvantage in future.[36] In addition, we used a blunt indicator of three-group maternal education (low/medium/high), which may hinder us from observing a clear social gradient in children's exposure to multiple adversities. Third, we used a crude measure of multiple adversities to answer our research question, providing an important proof of concept. We only focused on four family adversities, thus not capturing other adversities (eg, bullying victimisation) that occur outside the family environment. In addition, the hypothetical intervention that would be capable of achieving a reduction from 'two or more' to 'less than two' adversities remains undetermined (ie, what the intervention actually is and how it is delivered to achieve that reduction from 'two or more' to 'less than two' adversities is not specified). Measurement errors may also exist for parent-report data on adversities. Finally, we cannot fully exclude the possibility of residual confounding (eg, gestational age). In our causal mediation analysis, we assumed no unmeasured confounding (eg, exposure–mediator, exposure–outcome or mediator–outcome). All findings should be interpreted considering these assumptions.

Implications for future research and practice

In the context of increasing burden of NCDs in Australia and the UK,[23 24] it is crucial to prevent and reduce NCD risk factors at an earlier age. In the present study, we captured the exposure, mediator and outcome at critical developmental periods: maternal education at birth when children's health is potentially influenced from the start of life, childhood adversity at 1–12 years when children are most vulnerable to experience multiple adversities, and BMI/inflammation in late childhood or adolescence during which maladaptive lifestyles may be established to exacerbate NCD risk factors in the absence of interventions on adversity. We found that addressing childhood adversity would have small benefits to reduce socioeconomic inequities in childhood BMI and inflammation. While the magnitude of the effect was small, it is plausible that small reductions in inequities in childhood BMI/GlycA may accumulate and translate to substantial health benefits by adulthood, especially when considered at the population level.[41]

Our findings suggest that childhood adversity is an intervention target that warrants attention as part of NCD prevention. Further, it is hard to ignore the underlying inequities associated with the burden of childhood adversity across levels of maternal education. This is a salient reminder that supporting maternal education and investing in girls' education remain important opportunities for achieving intergenerational health equity. Previous literature suggested that increases in maternal education even after the child was born were associated with improvement in children's developmental outcomes.[42] Our findings also suggest that the potential benefits of addressing childhood adversity were even smaller in the UK compared with Australia. Further research should seek to examine whether this holds in other UK and Australian cohorts and investigate potential factors that may account for these differences.

CONCLUSION

We found small associations between maternal education at birth and BMI and chronic inflammation respectively in late childhood, confirming previous findings. Using causal mediation analysis, we estimated that decreasing the levels of multiple adversities among children with low/medium maternal education to be at the levels of their peers with high maternal education would have small benefits for reducing socioeconomic inequities in BMI and inflammation. Attention to childhood adversity without addressing more upstream socioeconomic conditions (eg, low education and occupation status) may produce few gains. There is a need for policy and practice to help those affected by childhood adversity, but also to consider the underlying poor socioeconomic conditions that drive inequitable health outcomes.

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Acknowledgements This paper uses unit record data from Growing Up in Australia, the Longitudinal Study of Australian Children (LSAC; DOI: 10.26193/F2YRL5) and Avon Longitudinal Study of Parents and Children (ALSPAC). LSAC is conducted by the Australian Government Department of Social Services (DSS). ALSPAC is managed by the ALSPAC Executive Committee. We are extremely grateful to all the families who took part in the LSAC and ALSPAC studies, as well as the study teams, which include interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, administrative workers and nurses. The findings and views reported in this paper are those of the authors and should not be attributed to the Australian Government DSS, any of DSS' contractors or partners, or ALSPAC funders. The Changing Children's Chances investigator team oversees this program of work, and includes SG, MOC, Prof Katrina Williams, SW, HB, NP, MMB, Francisco Azpitarte Raposeiras, Dr Alicia McCoy and Dr Timothy Gilley.

Contributors NP conceptualised and designed the study, drafted the initial manuscript, critically reviewed the manuscript for important intellectual content and obtained funding. MOC, SGr, MMB, DPB and RL conceptualised the study, drafted the initial manuscript and critically reviewed the manuscript for important intellectual content. SGu and DG conceptualised the study, conducted analysis, drafted the initial manuscript and critically reviewed the manuscript for important intellectual content. SGo obtained funding, conceptualised and designed the study, and critically reviewed the manuscript for important intellectual content. SW, HB, GR, MJ and KL conceptualised the study and critically reviewed the manuscript for important intellectual content. NP is responsible for the overall content as the guarantor. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding The UK Medical Research Council (MRC) and Wellcome (Grant ref: 217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. This publication is the work of the authors and NP and RL will serve as guarantors for the contents of this paper. A comprehensive list of grants funding is available on the ALSPAC website (http://www.bristol.ac.uk/Alspac/external/documents/grant-acknowledgements.pdf). This research was specifically funded by the National Institute of Health (NIH) (Grant ref: DK077659), Wellcome Trust and MRC (Grant ref: 07467/Z/05/Z). Access to ALSPAC data was supported by a University College London Global Engagement Award. This work was also supported by Australian Research Council Discovery Grant (grant number DP160101735) and was supported by the Victorian Government's Operational Infrastructure Support Program. MOC is supported by the Melbourne Children's LifeCourse initiative, funded by a Royal Children's Hospital Foundation Grant (2018-984). MMB is supported by Australian Research Council Discovery Early Career Award (DE190101326) and Australian National Health and Medical Research Council (NHMRC) Investigator Grant Emerging Leadership Level 2 (ID 2009572). SGo is supported by an NHMRC Practitioner Fellowship (APP1155290). HB is supported by an RMIT University VC Senior Research Fellowship. NP was supported by a NHMRC Career Development Fellowship (APP1123677). DB is supported by an NHMRC Investigator Grant (APP1175744). RL and DG's time on this study was supported by a UK Economic and Social Research Council grant (Grant ref: ES/P010229/1).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved. The LSAC (ID 13-04) and CheckPoint (ID 14-26) methodologies were approved by the Australian Institute of Family Studies Human Research Ethics Review Board, and the CheckPoint additionally by The Royal Children's Hospital Melbourne Human Research Ethics Committee (ID 33225D). Ethical approval for the study was obtained from the Royal Children's Hospital Human Research Ethics Committee (ID 2019.170). 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 are available upon reasonable request.

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