

## Supplementary material

### **Supplement 1: Adversity measures**

*Physical abuse:* Assessed at 7 timepoints (1.6 years, 2.6 years, 3.6 years, 4.9 years, 5.9 years, 6.9 years, 8.7 years), mothers responded to whether their child has been physically hurt by anyone. Exposure to physical abuse at any of the assessment wave was coded 1, otherwise 0.

*Sexual abuse:* Mothers responded to whether their child has been abused by anyone at any time from 1.6 years to age 8.5 years. Assessments were taken at 7 timepoints (1.6 years, 2.6 years, 3.6 years, 4.9 years, 5.9 years, 6.9 years, 8.7 years), with exposure coded 1 and non-exposure coded 0.

*Inconsistent caregiving:* when the participants were aged 1.6 years, 2.6 years, 3.6 years, 4.9 years, 5.9 years, 6.9 years, 8.7 years (7 timepoints), mothers were asked if the main caregiver of their child has changed since time of last assessment. A positive response was coded 1 at each assessment timepoint and taken as an indicator of inconsistent caregiving.

*Family instability:* family instability was measured by questions asking mothers if their child was (a) taken into care (b) separated from the mother > one week (c) separated from the father > one week (d) acquired a new parent. These questions were obtained at 7 timepoints (1.6 years, 2.6 years, 3.6 years, 4.9 years, 5.9 years, 6.9 years, 8.7 years). Exposure to any of these events at any assessment point was coded 1 and taken as an indicator of family instability.

*Caregivers' abuse:* Parental physical or emotional abuse was assessed at 6 timepoints (8 months, 1.9 years, 2.9 years, 3.11 years, 5.1 years, 6.1 years) and respondents were asked (a) you were physically cruel to your children (b) your partner was physically cruel to your children (c) you were emotionally cruel to your children (d) your partner was emotionally cruel to your children. Exposure to any of these questions at any assessment timepoint was coded 1 to indicate exposure to caregivers' abuse, otherwise coded 0 to indicate non-exposure.

Maternal psychopathology: maternal psychopathology was assessed with three different indices: 1. Crown-Crisp Experimental Index (CCEI)<sup>1</sup> which has both anxiety and depression subscales; 2. Edinburgh Postnatal Depression Scale (EPDS)<sup>2</sup>. These two questionnaires were administered at 3 timepoints (8 months, 1.9 years, 2.9 years). The third measure of maternal psychopathology was a question on suicide attempts obtained at 6 timepoints (8 months, 1.9 years, 2.9 years, 3.11 years, 5.1 years, 6.1 years). Following the threshold established in previous ALSPAC studies,<sup>3</sup> participants were coded to be exposed to maternal psychopathology at any assessment point if the mother reports any of (a) CCEI anxiety subscale score greater than 10 (b) CCEI depression subscale score greater than 9 (c) EPDS score greater than 12 (d) suicidal attempt since last assessment time.

Maternal victimization: mothers were asked if their partner was physically or emotionally cruel to them. A positive response to either question was coded 1 and taken as indicator of exposure to maternal victimization. These questions were obtained at 6 timepoints when the participants were aged 8 months, 1.9 years, 2.9 years, 3.11 years, 5.1 years, 6.1 years.

*Parental legal problems:* Mothers were asked if they had been in trouble with the law or if their partner had been in trouble with the law at different 6 timepoints (when the child was aged 8 months, 1.9 years, 2.9 years, 3.11 years, 5.1 years, 6.1 years). A positive response to either of the questions at any timepoint was coded 1 and served as indicator of exposure to parental legal problem.

Parental separation or divorce: mothers were asked if they had either separated or divorced from their partners at any of the 6 timepoints: 8 months, 1.9 years, 2.9 years, 3.11 years, 5.1 years, 6.1 years. A positive response to either question at any assessment timepoint was coded 1 and taken as indicator of exposure to parental separation.

Financial distress: when the participants were aged 8 months, 1.9 years, 2.9 years, 5.1 years, 7.1 years (5 timepoints), mothers were asked on a scale of 1- 4 (1 = not difficult; 2 = slightly

difficult; 3 = fairly difficult; 4 = very difficult), the degree to which they find it difficult to afford (a) food (b) cloth (c) heat (d) rent (e) items for child. In line with the threshold established [in previous study](#),<sup>3</sup> participants were coded 1 if at any timepoint, their mothers reported slight difficulty in affording at least three or more of child's items.

Neighbourhood stress: when the participants were aged 1.9 years and 2.9 years, mothers were asked to indicate on a scale of 0-2 (0 = no problem; 1 = minor; 2 = serious problem) the following problems in their homes (a) noise from other homes (b) noise from the street (c) rubbish dumped (d) vandalism (e) burglaries (f) mugging (g) disturbance from the youths. A total score 8 and above (corresponding to 95th percentile) was coded 1 and served as indicator of exposure to neighbourhood stress.

## **Supplement 2: Deviations from pre-registration**

We specified the research questions and statistical analyses (e.g. latent class analysis, latent regression, multivariate regression and zero-order correlational analysis) in a pre-registered document. However, the analytic strategies we employed in this study deviated from the pre-registration in [four](#) major ways. First, [on the excellent recommendations of the reviewers, we dropped latent class regression for Kruskal-Wallis test. The latter is a better and clearer statistical approach for testing our second research question: Are there group differences in cognitive performance among the different adversity subgroups.](#) Second, aside the main statistical analyses specified in the pre-registration, we performed an additional structured life-course modelling approach (SLCMA) to account for the effects of timing of adversity exposure. This additional analysis enabled a clearer understanding of the theoretical importance of timing of adversity exposure and addressed the question of whether sensitive periods or accumulation model best explained the observed association between childhood adversity and cognitive functioning. [Third](#), contrary to the pre-registered strategy of summing

the adversity exposure across all assessment timepoints for each adversity type, we binarized adversity exposure (exposed = 1; not exposed = 0) in line with previous ASLAPAC studies.<sup>3,4,5</sup> This binarized format is more statistically compatible with latent class analysis as the continuous variable format of the cumulative approach specified in our pre-registration would have saturated the model and made it more difficult to interpret. Lastly, we specified in the pre-registration that all available sample would be used in the analyses. This is relatively vague and would have involved 4 different subsamples i.e. participants who had data on adversity measures between 8 months to 8.7 years, as well as different samples of respondents who completed each of stop signal task, n-back task and emotion recognition task at age 24. Rather, our final analytic sample consisted of 2,965 participants whose mothers responded to a set of adversity measures at 8 months (the first timepoint) and who at age 24, completed all three cognitive tasks used in the study.

<b>Table S1</b>		
Exploratory latent class analysis involving 1-8 class models to determine the optimal class solution		
	BIC	Entropy
Model 1	29661.23	NAN
Model 2	27487.36	0.7887366
Model 3	27391.71	0.7550159
Model 4	27346.83	0.8235624
<b>Model 5</b>	<b>27304.43</b>	<b>0.822617</b>
Model 6	27356.97	0.8527311
Model 7	27414.43	0.8473717
Model 8	27471.22	0.8645015

BIC = Bayesian information criterion. Note: A combination of fit indices were used to determine the optimal class model with the class solution with lowest BIC value and relatively higher entropy score preferred.

Figure S1: shows the fit indices of the exploratory latent class analysis for model 1- model 8. Panel A = BIC scores. Panel B. Entropy scores. Class 5 solution was preferred because it yielded lowest BIC value with relatively high entropy score.

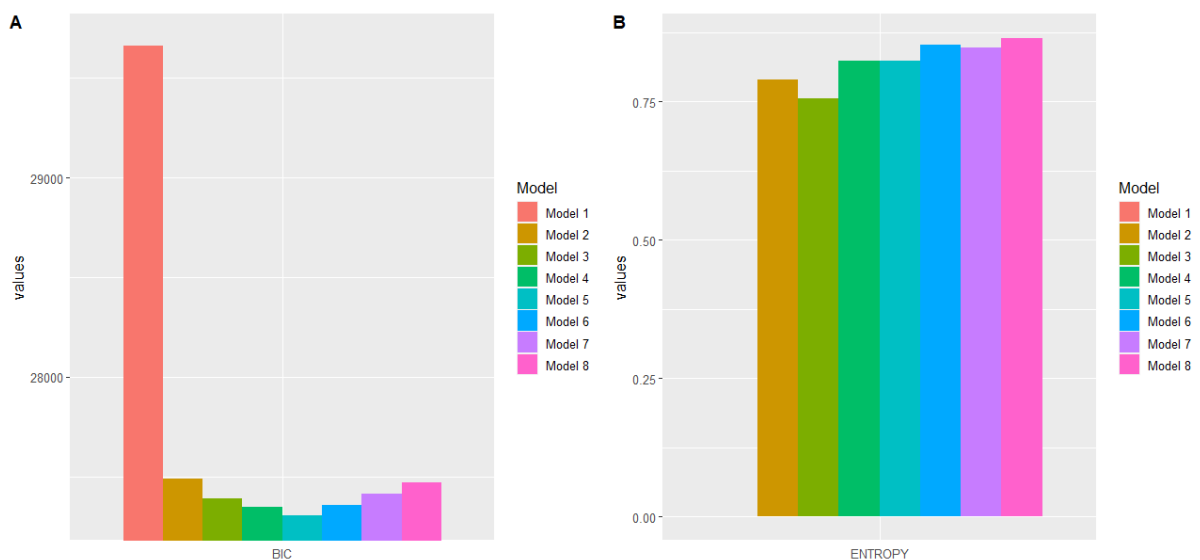




Table S2

Number and (percentage) of exposure to childhood adversity across childhood and at different assessment timepoints in the study sample.

	Childhood (8months – 8.7 years)	8 months	1.3 – 1.9 years	2-6 - 2.9 years	3.6 – 3.11 years	4.9 years	5.1 – 5.9 years	6.1 – 7.1 years	8.7 years
Physical abuse	470 (15.9%)	-	72 (2.4%)	93 (3.1%)	96 (3.2%)	137 (4.6%)	96 (3.2%)	80 (2.7%)	116 (3.9%)
Sexual abuse	29 (.9%)	-	0 (0%)	1 (.03%)	5 (.17%)	7 (.2%)	13 (.4%)	8 (.2%)	5 (.1%)
Inconsistent caregiving	736 (24.8%)	-	236 (8%)	235 (7.9%)	213 (7.2%)	203 (6.8%)	110 (3.7%)	79 (2.7%)	70 (2.4%)
Family instability	1487 (50.2%)	-	368 (12.4%)	649 (21.9%)	609 (20.5%)	433 (14.6%)	372 (12.5%)	286 (9.6%)	293 (9.8%)
Caregivers abuse	426 (14.4%)	78 (2.6%)	93 (3.1%)	94 (3.2%)	120 (4%)	-	173 (5.8%)	192 (6.5%)	-
Maternal psychopathology	661 (22.3%)	229 (7.7%)	310 (10.5%)	431 (14.5%)	8 (.2%)	-	9 (.3%)	12 (.4%)	-
Maternal victimization	721 (24.3%)	205 (6.9%)	226 (7.6%)	315 (10.6%)	236 (8%)	-	283 (9.5%)	245 (8.3%)	-
Parental legal problems	248 (8.4%)	24 (.81%)	47 (1.6%)	60 (2%)	83 (2.8%)	-	76 (2.6%)	55 (1.9%)	-
Parental separation/divorce	497 (16.8%)	82 (2.8%)	116 (3.9%)	168 (5.7%)	156 (5.3%)	-	190 (6.4%)	178 (6%)	-
Financial distress	676 (22.8%)	316 (10.7%)	300 (10.1%)	318 (10.7)	-	-	199 (6.7%)	149 (5%)	-
Neighbourhood stress	527 (17.8%)	361 (12.2%)	353 (11.9%)	-	-	-	-	-	-

Note: Exposed = 1; Not exposed = 2. Values in the table represent the proportion of participants exposed to different adversity types across childhood and at different assessment timepoints. Participants are coded to be exposed to adversity across childhood (8 months – 8.7 years) if exposure at any of the assessment timepoints was reported.





Table S3

Pearson correlations between the adversity variables in the study sample.

Variables	1	2	3	4	5	6	7	8	9	10	11
1. Physical abuse	-										
2. Sexual abuse	.14 ***	-									
3. Inconsistent caregiving	.09***	.02	-								
4. Family instability	.12***	.07***	.12***	-							
5. Caregivers abuse	.23***	.14***	.09***	.17***	-						
6. Maternal psychopathology	.16***	.09***	.04*	.12***	.24***	-					
7. Maternal victimization	.16***	.10***	.10***	.21***	.44***	.23***	-				
8. Parental legal problems	.16***	.13***	.06***	.14***	.23***	.15***	.24***	-			
9. Parental separation/divorce	.11***	.13***	.05**	.29***	.26***	.18***	.42***	.30***	-		
10. Financial distress	.10***	.09***	.00	.12***	.19***	.24***	.21***	.20***	.30***	-	
11. Neighbourhood stress	.14***	.08***	.00	.10***	.15***	.16***	.16***	-.16***	.14***	.26***	-

Note: n = 2965; \*\*\* = significant at p&lt;0.001; \*\* = significant at p&lt;0.01; \* = significant at p&lt;0.05.

Table S4					
An estimated class-conditional response probability for 5 adversity classes.					
Adversity types	Class 1 (Low adversity)	Class 2 (Dysfunctional family)	Class 3 (Parental deprivation)	Class 4 (Family Poverty)	Class 5 (Global adversity)
Physical abuse	8.99	37.86	17.27	17.91	68.06
Sexual abuse	0.14	0.82	1.27	1.20	17.42
Inconsistent caregiving	21.92	39.15	30.94	8.67	49.01
Family instability	39.89	59.28	91.78	57.66	95.61
Caregivers' abuse	1.47	53.14	33.10	14.36	85.14
Maternal psychopathology	10.78	47.68	34.19	52.39	69.37
Maternal victimization	6.86	61.72	76.90	28.84	89.87
Parental legal problems	2.90	8.90	22.29	12.04	71.89
Parental separation/divorce	3.38	0.00	100	31.41	89.73
Financial distress	10.26	21.92	38.11	97.02	84.71
Neighbourhood stress	9.86	25.04	17.55	60.14	65.28
Note: Values (%) represent the percentage probability that participants in each adversity classes respond to being exposed to the different adversity measures.					

Table S5									
Descriptive statistics of cognitive outcomes of the different adversity subgroups									
Adversity subgroups (N)	SSRT			N-back			Emotion Total		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Class 1 - Low adversity (2123)	0.034	0.991	-4.760, 3.620	0.030	0.974	-7.310, 0.868	0.005	0.978	-4.770, 2.780
Class 2 - Dysfunctional family (284)	0.008	0.969	-3.450, 2.000	0.071	0.839	-6.070, 0.868	0.064	1.022	-4.770, 2.000
Class 3 - Parental deprivation (286)	-0.083	1.035	-3.390, 3.090	-0.118	1.157	-7.180, 0.868	-0.011	1.021	-4.120, 2.520
Class 4 - Family Poverty (180)	-0.237	1.073	-4.230, 2.040	-0.166	1.145	-6.530, 0.868	-0.105	1.132	-3.730, 2.390
Class 5 - Global adversity (92)	-0.099	0.962	-3.220, 1.700	-0.221	1.123	-5.710, 0.868	-0.072	1.065	-5.300, 1.740

Note: N = Sample size of each adversity subgroup; SSRT = stop signal reaction time; SD = standard deviation. Cognitive outcomes are in standardized unit.

Table S6

Result of zero-order correlation examining association between binarized (ever exposed vs never exposed) score of each childhood adversity measure and cognitive outcomes

	SSRT	N-back correct	Emotion Total	Happy	Surprise	Fear	Sad	Anger	Disgust
Physical abuse	-0.03	0.00	0.02	-0.02	0.00	0.04*	0.03	0.01	0.00
Sexual abuse	-0.05**	-0.04*	-0.06**	-0.02	-0.06***	-0.03	-0.02	-0.04*	-0.03
Inconsistent caregiving	0.01	0.05**	0.07***	0.02	0.02	0.05**	0.04*	0.06**	0.02
Family instability	-0.05**	-0.01	0.01	0.02	0.01	0.00	0.01	0.02	-0.02
Caregivers abuse	-0.02	-0.01	0.01	-0.01	-0.02	-0.01	0.03	0.01	0.03
Maternal psychopathology	-0.03	-0.02	0.00	0.01	-0.01	0.01	0.01	0.01	-0.02
Maternal victimization	-0.02	-0.04*	-0.02	0.00	-0.02	-0.02	-0.01	-0.02	-0.01
Parental legal problems	-0.02	-0.03	-0.03	-0.01	0.00	-0.04*	0.00	0.00	-0.02
Parental separation/divorce	-0.03	-0.06***	-0.02	0.01	-0.01	-0.03	0.00	-0.02	0.01
Financial distress	-0.07***	-0.06**	-0.03	0.02	0.01	-0.03	-0.05**	-0.01	-0.02
Neighbourhood stress	-0.05**	-0.03	0.00	-0.02	0.02	0.00	0.00	0.00	0.00

Note: \*\*\* = significant at  $p < 0.001$ ; \*\* = significant at  $p < 0.01$ ; \* = significant at  $p < 0.05$ ; SSRT = stop signal reaction time.

Figure S2A

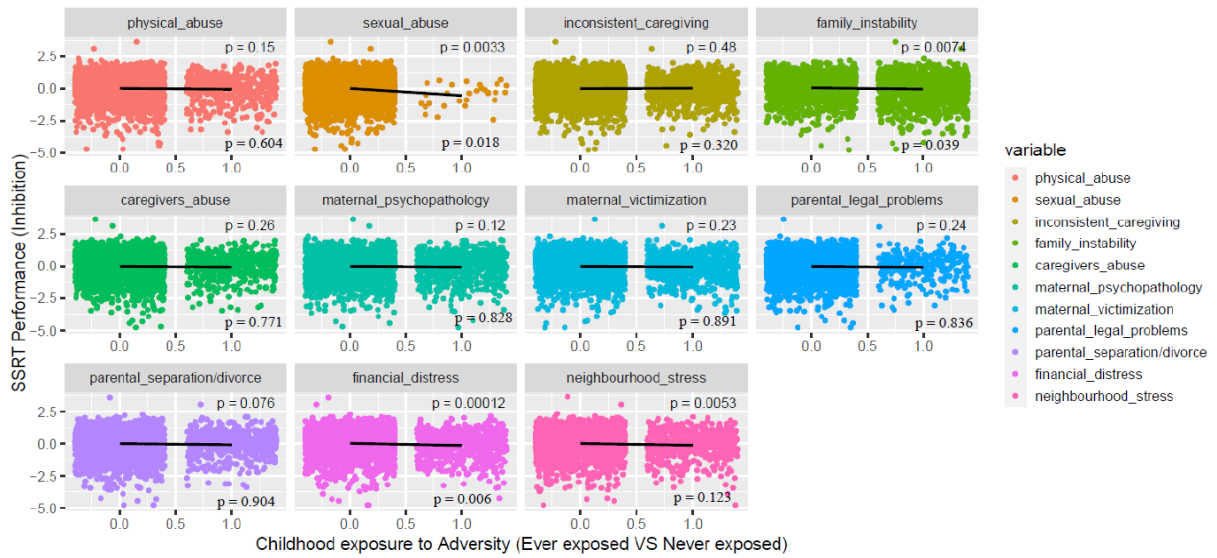


Figure S2B

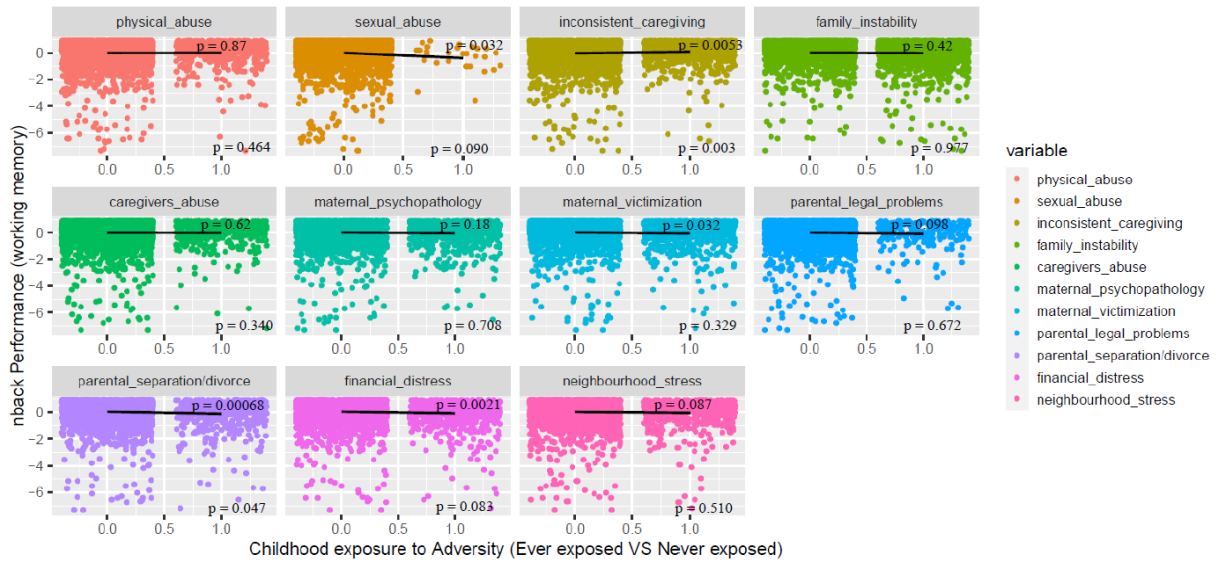
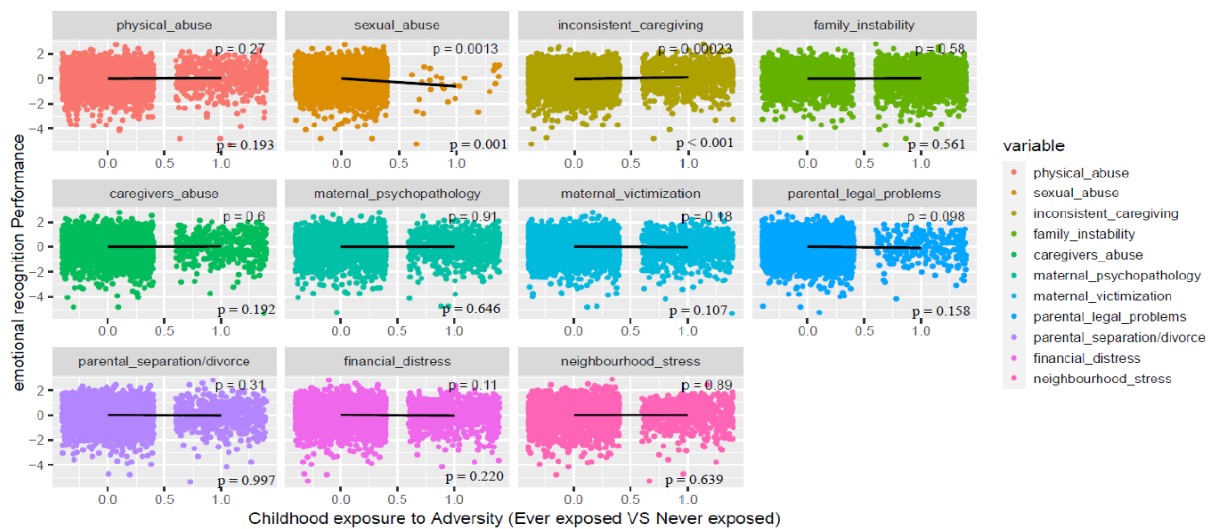


Figure S2C



Figures S2 A-C shows the association between different childhood adversity measures and cognitive performance in (a) inhibition (b) working memory (c) emotion recognition. PLEASE NOTE: the p-values above the regression lines are the zero-order correlation p values while the p-values below the regression lines are the multivariate regression p-values.

### **Supplement 3: Sensitivity analyses and results**

Given the substantial reduction in our study sample size (N=2,965) from the initial ALSPAC [enrolment](#) number (N~14,541), we conducted a latent class sensitivity analysis to see how our latent class result compares with the result from the larger sample of participants. There were two conditions for inclusion in our final analytic sample; First, participants mothers have provided data on adversity measures when participants were 8 months old (this is the first timepoint relevant adversity measures were obtained). Second, participants must have completed three cognitive tasks used in our study at age 24. This second condition resulted in the elimination of several participants from the latent class analysis. In the sensitivity analysis, we used a larger sample of 11,309 participants whose mothers provided relevant adversity data starting at 8 months old.

As we did in the main analysis, we first carried out an exploratory analysis involving class 1 to 8 models to determine which of them best explains the adversity data. Similar to findings reported in our primary analysis, class 5 model offered the optimal class solution given that it yielded better estimates (BIC = 114989; entropy = 0.7367487) compared to other rival class models. An inspection of this class model showed that class 1 consisted of 54.07% of the population. We referred to this class 1 (Figure S3, top left) as “low adversity” because members in this class have very low probability of being exposed to any of the 11 adversity measures with less than 19% probability of exposure in all adversity measures except family instability (38%). Class 2 (Figure S3, top centre) is made up of 14.77% of all participants. We

referred to this class as “parental deprivation” because members in this class reported 98% probability of being exposed to parental divorce or separation and 90% probability of exposure to family instability. Together, these two measures reflect questions designed to measure the extent to which a developing child has been deprived of parental time and availability. Class 3 (Figure S3, top right) is named “dysfunctional family” because members (12.5%) have medium to high probability of exposure to one or more adversity measures characterized by dysfunctional family rearing. Specifically, members in this class reported relatively high probability of exposure to family instability (61%), caregivers’ abuse (51%), maternal psychopathology (44%), maternal victimization (64%) and inconsistent caregiving (34%). Class 4 (Figure S3, bottom left) consists of 9.51% of the population. We called this class “*family poverty*” because participants responded high to financial distress (81%) and neighbourhood disadvantage (52%). These two adversity measures are designed to capture various degrees of socioeconomic disparities and financial deprivation. Lastly, Class 5 (Figure S3, bottom right) is referred to as “*global adversity*” because members in this class (9.15%) have very high probability of being exposed to all the adversity measures in our study. Probability of exposure to adversity measures in this class range from 17% (sexual abuse) to 95% (family instability). Taken together, these findings from our sensitivity analysis are robust and consistent with the results reported in our primary analysis.

#### **Supplement 4: Proportion of variance explained by the independent adversity types.**

As shown in Table S6, the correlation coefficients between the adversity types and cognitive outcomes are between 0.04 and 0.07 for both the positive and negative correlations. This implies that the proportion of variance in cognitive performance explained by any independent adversity predictors is less than 5%. Examining this in detail, financial distress (4.95%), sexual abuse (2.91%), family instability (2.42%) and neighbourhood stress (2.62%) all explained some proportion of variances in poorer performance in inhibition. In working memory, sexual

abuse (1.54%), maternal victimization (1.54%), parental separation or divorce (3.88%) and financial distress (3.2%) independently accounted for a modest variability in poorer working memory ability. In the emotion recognition task, sexual abuse accounted for 3.48% of variance in poorer performance in total emotion recognition, surprise (3.84%) and anger (1.5%). Elsewhere in the emotion recognition task, parental legal problems (2%) and financial distress (2.34%) explained some proportion of variances in poorer recognition of fearful and sad emotions respectively. All correlations for inconsistent caregiving were positive and accounted for some proportion of variances in cognitive abilities including, 2.62% in working memory performance, 4.55% in total emotion recognition, 2.84% in fear, 1.33% in sad and 3.14% anger. Correlation between physical abuse and recognition of fearful emotion was also positive and explained 1.36% of variability in performance in recognition of fearful emotions.

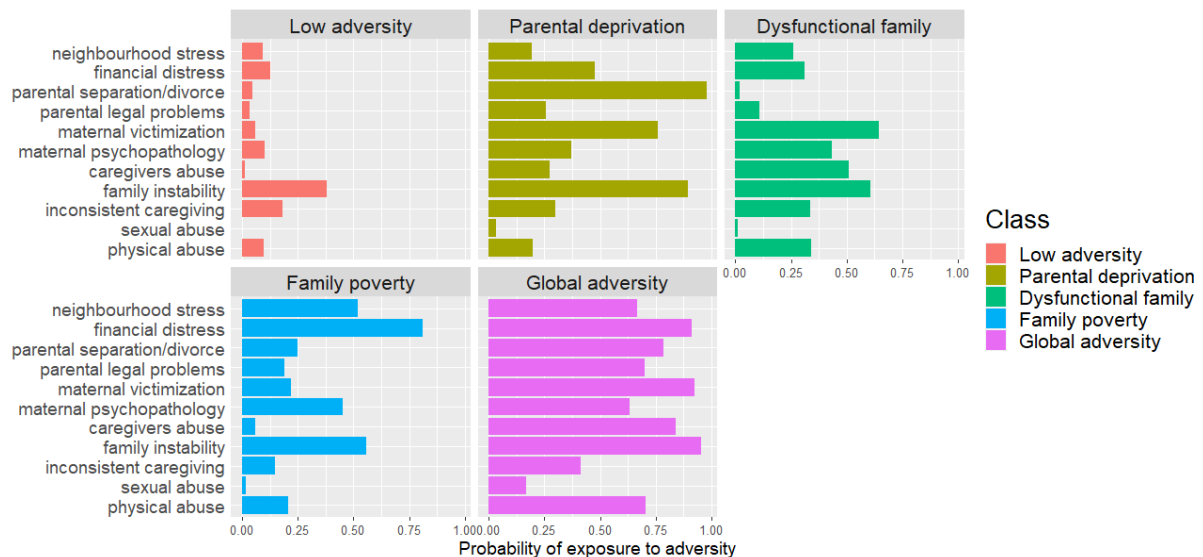


Figure S3: Latent class sensitivity analysis showing the five adversity classes and the corresponding class-conditional response probability for all the adversity measures. The sensitivity results from the unrestricted sample are consistent with findings reported in the primary analysis.



## Supplement 5: Additional limitations of the study

It should also be noted that some of the adversity measures used in the current study are not perfect. For example, the mental health measures that formed the composite for maternal psychopathology were obtained at varied timepoints i.e., 3 timepoints for maternal depression and anxiety but 6 timepoints for maternal suicide attempts. This variation may have had a potential subtle implication on the findings e.g., the reduced prevalence of maternal psychopathology reported after age 3 may be attributable to lack of maternal data on CCEI anxiety, CCEI depression and EPDS depression at the 3 later timepoints i.e., at 3.11 years, 5.1 years, 6.1 years. This could also have had additional implication on the observed timing effect of maternal psychopathology on cognitive functioning in our SCLMA analysis. Moreso, as maternal psychopathology is a broad mental health term, this study may have benefitted from maternal psychopathology measure that incorporated additional data on externalizing and psychotic disorders.

Another potential limitation of the study is the role of confounders. Different antenatal adversity e.g., antenatal depression and antenatal anxiety or risk birth outcomes e.g., preterm birth and low birthweight have been known to have independent effects on life outcomes as are other adversity types e.g., maternal substance use, paternal psychopathology and house crowding. As we did not control for these potential confounders, we urge readers to keep in mind of their possible contributions to the effects observed in our study.

Additionally, some of the analyses conducted in this study may have been underpowered. For example, only 29 participants (0.9% of the total sample) reported exposure to sexual abuse from 1.6 years to 8.7 years. This low prevalence rate in this adversity type may have affected some effects reported in our study. We also note some huge variations in the size of latent class membership: low

adversity (2123) VS Global adversity (92). This varied class membership may equally have affected the result reported in latent class regression.

## References

1. Crown, S., & Crisp, A.H. (1979). Manual of the crown-crisp experiential index. London: Hodder and Stoughton.
2. Cox, J.L., Holden, J.M., & Sagovsky, R. (1987). Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry*, 150, 782–786.
3. Dunn, E. C., Crawford, K. M., Soare, T. W., Button, K. S., Raffeld, M. R., Smith, A. D., ... Munafò, M. R. (2018). Exposure to childhood adversity and deficits in emotion recognition: Results from a large, population-based sample. *Journal of Child Psychology and Psychiatry*, 59(8), 845-854. doi:10.1111/jcpp.12881
4. Dunn, E. C., Soare, T. W., Zhu, Y., Simpkin, A. J., Suderman, M. J., Klengel, T., ... Relton, C. L. (2019). Sensitive periods for the effect of childhood adversity on DNA methylation: Results from a prospective, longitudinal study. *Biological Psychiatry*, 85(10), 838-849. doi:10.1016/j.biopsych.2018.12.023
5. Dunn, E. C., Busso, D. S., Raffeld, M. R., Smoller, J. W., Nelson, C. A., Doyle, A. E., & Luk, G. (2016). Does developmental timing of exposure to child maltreatment predict memory performance in adulthood? Results from a large, population-based sample. *Child Abuse & Neglect*, 51, 181-191. doi:10.1016/j.chiabu.2015.10.014

