

Supplementary Table 1. Childhood adversity exposures: collection and categorisation

	Description	Categories	Age ¹	Method
Psychosocial early life adversities				
Maltreatment	Participant asked “As a child do you feel you were mistreated by your parents in any way?”	Yes vs No	43 years	Retrospective report by participants
Low parental concern	Parental concern derived in teacher interviews, in which teachers were asked “to what extent do this child’s parents show interest in his/her progress at school?”	Little interest vs average to very interested	13 years	Teacher questionnaires/school records and maternal interview
Parental psychiatric history	Mother asked if they or partner had a psychiatric illness during the 0-15 yrs of child’s life	Present vs not present	0-15 years	Maternal report
Parental divorce	Experience of parental divorce/separation during the 0-15 yrs of child’s life	Divorced vs not divorced	0-15 years	Maternal report
Mother affectionless control	Parental bonding instrument used to collect retrospective report of participants perception on their parents’ style of attachment and affection – affectionless control defined: mothers care score < 27 & overprotection score >13.5. ²	Affectionless control vs not affectionless control parenting	43 years	Retrospective report by participants
Father affectionless control	Parental bonding instrument used to collect retrospective report of participants perception on their parents’ style of attachment and affection – affectionless control defined: fathers care score < 24 & overprotection score >12.5. ²	Affectionless control vs not affectionless control parenting	43 years	Retrospective report by participants
Parental death	Experience of parental death during the 0-15 yrs of child’s life	Parental death vs no parental death	0-15 years	Reported by parent/ guardian
Maternal separation	Experience of separation from the mother during the 0-6 yrs of child’s life	Separation (permanent, regular, or ≥ 9 weeks) vs no separation (< 3.5 days)	0-6 years	Maternal reports
Socioeconomic adversities				
Low father social class	Fathers occupation according to the UK Registrar General’s Classification	professional & intermediate, skilled nonmanual, skilled manual, partly skilled & unskilled	4 years (or 7/11 if missing)	Maternal report of occupation
Renting a house from a private landlord	Housing tenure	Private landlord owned home vs nonprivate landlord owned home (council, charitable trust, and home owner)	2 years (or 11/15 years if missing)	Maternal/health visitor reports
Maternal education	Maternal educational attainment	Primary only vs other	4 years	Maternal report of education

Footenote:

¹We used adversity measures from the earliest possible visit. If an individual was missing data, we used their measure from the next visit. For example, “4 years (or 7/11 years if missing)” means we used data from the age 4 years visit. If this was missing, we used data from the age 7 years visit. And if this was missing, we used data from the age 11 years visit.

²Caleyachetty R, Hardy R, Cooper R, Richards M, Howe LD, Anderson E, Kuh D, Stafford M. Modeling Exposure to Multiple Childhood Social Risk Factors and Physical Capability and Common Affective Symptoms in Later Life. *J Aging Health*. 2018;30(3):386-407

Supplementary table 2. Demographic, exposure and outcome variables of those included in the current study (Cortisol sample (N=843)) and those not included in the current study.

	Included (N= 843)			Excluded (N=4,519)		
Demographic		N with data		N with data		p-value for difference
Birthweight	Mean (SD)	3.4 (0.5)	843	3.4 (0.6)	4484	0.537
Sex	%					
Female		52.9	843	46.5	4,519	0.001
Maternal education	%					
Primary		56.9		65.2	3,498	<0.001
Other		43.1	843	34.8		
Paternal social class	%					
Professional and intermediate		30.7		24.6	3,830	<0.001
Skilled non-manual		18.5		15.0		
Skilled manual		30.0		34.0		
Partly skilled and unskilled		20.8	843	26.6		
Housing tenure	%					
Private landlord		51.0		44.7	3,853	0.001
Other		49.0	843	55.3		
Exposures						
ELA score	%					
0		47.3	843	41.7	1,253	0.08
1		26.5		30.0		
2		19.5		20.8		
>3		6.8		7.5		
Individual adversities	%					
Maltreatment		3.9	843	7.1	2,197	0.001
Low parental concern for child's education		9.1	843	17.7	2,971	<0.001
Parental psychiatric history		2.3	843	2.1	4,519	0.747
Parental divorce		3.1	843	6.3	4,519	<0.001
Paternal affectionless control		30.3	843	30.3	2,067	0.964
Maternal affectionless control		30.7	843	30.1	2,101	0.751
Parental death		3.7	843	5.9	4,431	0.009
Parental separation		3.8	843	6.4	3,608	0.004
Outcomes						
Morning cortisol (nmol/L)	Median (IQR)	18.61 (11.94)	843	17.96 (11.23)	935	0.317
Evening cortisol (nmol/L)	Median (IQR)	2.36 (1.87)	843	2.43 (2.27)	922	0.007
DS (nmol/L/h)	Mean (SD)	-1.2 (0.69)	843	-1.15 (0.66)	726	0.117
CAR (nmol/L)	Mean (SD)	6.25 (11.97)	843	5.69 (11.19)	719	0.346

Abbreviations: ELA: early life adversity, DS: diurnal slope, CAR: cortisol awakening response, IQR: interquartile range, SD: standard deviation

Supplementary table 3. Demographic, exposure and outcome variables of those included in the current study (CRP sample (N=1,050)) and those not included in the current study.

	Included (N=1,050)			Excluded (N=4,312)		
Demographic		N with data		N with data		p-value for difference
Birthweight	Mean (SD)	3.4 (0.5)	1,150	3.36 (0.6)	4,177	0.093
Sex	%	-	-	-	-	
Female		50.6	1,150	46.7	4, 212	0.017
Maternal education	%	-	-			
Primary		56.8	-	66.0		
Other		43.2	1,150	34.0	3,191	<0.001
Paternal social class	%	-	-			
Professional and intermediate		30.1	-	24.2		
Skilled non-manual		17.9	-	14.9		
Skilled manual		30.6	-	34.1		
Partly skilled and unskilled		21.4	1,150	26.9	3, 523	<0.001
Housing tenure	%	-	-	-		
Private landlord		49.1	-	44.8		
Other		50.9	1,150	55.2	3, 546	0.010
Exposure variables		-	-			
ELA score	%	-	-			
0		46.3	-	41.1		
1		27.5	-	29.9		
2		19.6	-	21.1		
≥3		6.7	1,150	7.8	946	0.124
Individual adversities	%	-	-			
Maltreatment		4.6	1,150	7.2	1,890	0.004
Low parental concern for child's education		11.0	1,150	17.9	2,664	<0.001
Parental psychiatric history		2.00	1,150	2.1	4, 212	0.775
Parental divorce		3.2	1,150	6.5	4,212	<0.001
Paternal affectionless control		30.4	1,150	30.2	1,760	0.905
Maternal affectionless control		29.4	1,150	30.9	1, 794	0.391
Parental death		3.5	1,150	6.1	4, 124	0.001
Parental separation		4.00	1,150	6.5	3,301	0.002
Outcomes						
CRP	Median (IQR)	2 (2.3)	1,150	2.2 (2.68)	915	0.215

Abbreviations: ELA: early life adversity, DS: diurnal slope, CAR: cortisol awakening response, IQR: interquartile range, SD: standard deviation

Supplementary table 4. Cortisol and CRP outcomes at 60-64 years by individual ELAs.

		Cortisol sample				CRP sample					
		CAR (nmol/L)	DS (nmol/L/h)	Evening cortisol (nmol/L)	Morning cortisol (nmol/L)	CRP (mg/L)					
		All (N=843)				All (N= 1,050)		Female (N=582)		Male (N=568)	
Adversity	Sample size (N)	Mean (SD)	Mean (SD)	Median (IQR)	Mean (SD)	Sample size (N)	Median (IQR)	Sample size (N)	Median (IQR)	Sample size (N)	Median (IQR)
Maltreatment											
No maltreatment	810	6.25 (12.0)	-1.21 (0.69)	2.36 (1.86)	20.24 (9.67)	1,097	2.01 (2.23)	549	2.16 (2.44)	548	1.92 (2.18)
Maltreatment	33	6.21 (11.25)	-0.96 (0.48)	2.34 (2.08)	16.99 (7.11)	53	1.89 (3.32)	33	1.98 (2.84)	20	1.07 (2.74)
p-value	-	0.985	0.039	0.546	0.057	-	0.71		0.825		0.280
Parental concern for child's education											
High parental concern for child's education	766	6.1 (11.87)	-1.21 (0.69)	2.35 (1.87)	20.31 (9.58)	1,024	1.97 (2.23)	520	2.09 (2.5)	504	1.9 (2.38)
Low parental concern for child's	77	7.75 (12.94)	-1.07 (0.67)	2.5 (1.94)	18.07 (9.6)	126	2.57 (2.6)	62	2.71 (2.72)	64	2.43 (2.46)
p-value	-	0.247	0.078	0.552	0.051	-	0.041		0.070		0.275
Parental psychiatric history											
No parental psychiatric history	824	6.17 (11.94)	-1.2 (0.69)	2.36 (1.87)	20.14 (9.64)	1,127	2.0 (2.3)	572	2.14 (2.49)	555	1.92 (2.22)
Parental psychiatric history	19	9.66 (13.04)	-1.1 (0.54)	2.83 (3.94)	18.86 (7.34)	23	1.78 (2.43)	10	2.62 (2.08)	13	1.68 (1.03)
p-value	-	0.209	0.526	0.040	0.567	-	0.491		0.936		0.349
Parental divorce											
No parental divorce	817	6.27 (12.1)	-1.2 (0.69)	2.37 (1.86)	20.11 (9.63)	1113	2 (2.27)	561	2.15 (2.43)	552	1.91 (2.26)
Parental divorce	26	5.59 (6.77)	-1.26 (0.6)	2.19 (1.75)	19.97 (8.76)	37	1.76 (2.56)	21	1.83 (5.0)	16	1.72 (1.08)
p-value	-	0.774	0.676	0.027	0.939	-	0.900		0.769		0.543
Paternal control											
Normal control	588	6.09 (11.97)	-1.23 (0.68)	2.37 (1.87)	20.53 (9.58)	800	2.0 (2.15)	408	2.1 (2.37)	392	1.92 (2.5)
Paternal affectionless control	255	6.62 (11.98)	-1.13 (0.69)	2.34 (1.86)	19.15 (9.59)	350	2.0 (2.56)	174	2.19 (2.83)	176	1.9 (2.44)
p-value	-	0.557	0.035	0.971	0.056	-	0.428		0.494		0.636
Maternal control											
Normal control	584	6.08 (11.48)	-1.21 (0.67)	2.38 (1.94)	20.32 (9.47)	812	2.0 (2.17)	401	2.04 (2.2)	411	1.94 (2.58)
Maternal affectionless control	259	6.63 (13.03)	-1.17 (0.71)	2.34 (1.82)	19.64 (9.87)	338	2.0 (2.6)	181	2.3 (2.83)	157	1.88 (2.15)

p-value	-	0.539	0.431	0.820	0.347	-	0.341		0.410		0.696
Parental death											
No parental death	812	6.09 (11.78)	-1.21 (0.67)	2.38 (1.87)	20.16 (9.47)	1,110	2.04 (2.3)	560	2.16 (2.48)	550	1.96 (2.25)
Parental death	31	10.47 (15.88)	-1.05 (0.99)	2.12 (2.42)	18.86(12.51)	40	1.82 (1.85)	22	2.05 (2.32)	18	1.28 (1.05)
p-value	-	0.045	0.203	0.717	0.461	-	0.241		0.662		0.021
Parental separation											
No parental separation	811	6.19 (11.94)	-1.21 (0.69)	2.36 (1.86)	20.16 (9.62)	1,104	2.0 (2.24)	559	2.12 (2.43)	545	1.9 (2.21)
No Parental separation	32	7.79 (12.82)	-1.08 (0.69)	2.57 (2.24)	18.73 (9.08)	46	2.41 (2.57)	23	2.4 (4.39)	23	2.41 (2.88)
p-value	-	0.459	0.329	0.561	0.407	-	0.419		0.570		0.56

Abbreviations: ELA: early life adversity, CRP: c-reactive protein, CAR: cortisol awakening response, DS: diurnal slop

Supplementary table 5. Associations between individual ELAs and cortisol outcomes at 60-64 years: Estimated using general linear regression

	CAR (nmol/L) s% (95% CI)	DS (nmol/L/h) s% (95% CI)	Evening cortisol (nmol/L) s% (95% CI)	Morning cortisol (nmol/L) s% (95% CI)
Model 1				
Adversity				
Maltreatment	0.82 (-11.4, 13.04)	6.9 (-0.36, 14.16)	-8.06 (-30.62, 14.5)	-22.06 (-43.19, -0.93)
Low parental concern for child's education	5.3 (-2.92, 13.5)	4.29 (-0.59, 9.17)	4.7 (-10.44, 19.89)	-18.64 (-32.83, -4.45)
Parental psychiatric history	10.74 (-5.21, 26.7)	4.98 (-4.51, 14.48)	32.04 (2.64, 61.44)	-2.48 (-30.16, 25.2)
Parental divorce	2.04 (-11.7, 15.77)	-1.59 (-9.77, 6.59)	-30.35 (-55.64, -5.06)	-0.74 (-24.56, 23.08)
Paternal affectionless control	1.01 (-4.14, 6.17)	2.65 (-0.42, 5.71)	-0.46 (-9.98, 9.06)	-6.8 (-15.72, 2.13)
Maternal affectionless control	0.47 (-4.67, 5.61)	0.51 (-2.54, 3.57)	-1.15 (-10.63, 8.33)	-3.85 (-12.75, 5.04)
Parental death	9.36 (-3.21, 21.93)	2.05 (-5.44, 9.54)	5.09 (-18.14, 28.32)	-25.91 (-47.65, -4.16)
Parental separation	4.91 (-7.49, 17.31)	3.4 (-3.98, 10.77)	7.64 (-15.25, 30.53)	-14.75 (-36.23, 6.72)
Model 2				
Adversity				
Maltreatment	1.62 (-10.64, 13.89)	6.97 (-0.35, 14.28)	-7.98 (-30.67, 14.72)	-21.54 (-42.79, -0.29)
Low parental concern for child's education	4.55 (-3.82, 12.92)	4.48 (-0.52, 9.47)	4.97 (-10.52, 20.47)	-16.93 (-31.43, -2.42)
Parental psychiatric history	10.27 (-5.68, 26.22)	5.1 (-4.46, 14.62)	32.33 (2.9, 61.8)	-2.27 (-30.00, 25.46)
Parental divorce	2.26 (-11.5, 16.02)	-1.3 (-9.53, 6.93)	-32.59 (-57.97, -7.21)	-0.96 (-24.88, 22.94)
Paternal affectionless control	0.82 (-4.33, 5.97)	2.59 (-0.48, 5.67)	-0.45 (-9.98, 9.08)	-6.43 (-15.36, 2.51)
Maternal affectionless control	0.18 (-4.96, 5.31)	0.47 (-2.6, 3.54)	-1.13 (-10.63, 8.37)	-3.94 (-12.85, 4.97)
Parental death	9.17 (-3.4, 21.75)	1.97 (-5.55, 9.5)	6.21 (-17.1, 29.52)	-24.64 (-46.45, -2.83)
Parental separation	4.36 (-8.1, 16.82)	3.48 (-3.97, 10.92)	8.99 (-14.07, 32.06)	-14.5 (-36.13, 7.13)

Footnote:

Model 1. Adjusted for age and sex

Model 2: Adjusted for age, sex, birthweight, paternal social class, maternal education, and housing tenure

All outcomes have been log transformed and multiplied by 100, so interpretation of the coefficient is on a % scale

Abbreviations: ELA: early life adversity, CI: confidence interval, DS: diurnal slope, CAR: cortisol awakening response

Supplementary Table 6. Sensitivity Analyses: Associations between ELA score and cortisol outcomes at 60-64 years in the secondary cortisol sample (N= 627): Estimated using general linear regression

	CAR (nmol/L)		DS (nmol/L/h)		Evening cortisol (nmol/L)		Morning cortisol (nmol/L)	
	s% (95% CI)	p-value for trend	s% (95% CI)	p- value for trend	s% (95% CI)	p- value for trend	s% (95% CI)	p-value for trend
Model 1								
ELA Score (Reference group= 0)								
1	6.15 (-0.6, 12.89)		2.04 (-1.97, 6.06)		-3.21 (-15.21, 8.8)		-9.8 (-21.53, 1.93)	
2	6.91 (-0.45, 14.27)		0.18 (-4.2, 4.56)		-5.42 (-18.52, 7.68)		-4.92 (-17.72, 7.88)	
≥ 3	8.71 (-2.8, 20.21)	0.024	6.89 (0.04, 13.74)	0.176	8.55 (-11.94, 29.03)	0.947	-28.9 (-48.92, -8.89)	0.018
Model 2								
ELA Score (Reference group= 0)								
1	6.15 (-0.59, 12.9)		2.1 (-1.93, 6.13)		-3.12 (-15.18, 8.95)		-9.87(-21.61, 1.87)	
2	6.71 (-0.65, 14.07)		0.27 (-4.13, 4.66)		-5.26 (-18.42, 7.9)		-4.63 (-17.45, 8.18)	
≥ 3	8.99 (-2.6, 20.58)	0.025	7.19 (0.26, 14.11)	0.159	8.85 (-11.87, 29.58)	0.967	-28.78 (-48.96, -8.61)	0.021

Footnote:

Model 1. Adjusted for age and sex

Model 2: Adjusted for age, sex, birthweight, paternal social class, maternal education, and housing tenure

All outcomes have been log transformed and multiplied by 100, so interpretation of the coefficient is on a % scale

Abbreviations: ELA: early life adversity, CI: confidence interval, DS: diurnal slope, CAR: cortisol awakening response

Supplementary table 7. Associations between ELA score and CRP (mg/L) at 60-64 years: Estimated using tobit models

	CRP (mg/L)	
	s% (95% CI)	p-value for trend
Model 1		
ELA Score (Reference group=0)		
1	2.28 (-9.41, 14.51)	
2	3.5 (-10.15, 17.14)	
≥ 3	14.09 (-6.84, 35.03)	0.243
Model 2		
ELA Score (Reference group=0)		
1	2.83 (-9.29, 14.94)	
2	1.04 (-12.53, 14.6)	
≥3	8.8 (-12.13, 29.73)	0.520

Footnote:

Model 1. Adjusted for age and sex

Model 2: Adjusted for age, sex, birthweight, paternal social class, maternal education, and housing tenure

CRP has been log transformed and multiplied by 100, so interpretation of the coefficient is on a % scale

Abbreviations: ELA: early life adversity, CI: confidence interval, CRP: c-reactive protein

Supplementary table 8. Associations between individual ELAs and CRP at 60-64 years: Estimated using tobit models

	CRP (mg/L)			
	All	Females	Males	Males-Females
	s% (95%CI)	s% (95%CI)	s% (95%CI)	s% (95% CI)
Model 1				
Adversity				
Maltreatment	-4.77 (-28.97, 19.42)	4.95 (-26.09, 35.98)	-20.33 (-59.18, 18.51)	24.95 (-24.79, 74.7)
Low parental concern for child's education	16.23 (0.03, 32.42)	21.28 (-1.91, 44.47)	11.39 (-11.27, 34.06)	10.12 (-22.26, 42.5)
Parental psychiatric history	-10.02 (-46.21, 26.18)	6.66 (-48.62, 61.95)	-22.57 (-70.44, 25.3)	28.67 (-44.29, 101.63)
Parental divorce	-0.18 (-28.92, 28.56)	7.46 (-31.02, 45.93)	-10.31 (-53.67, 33.06)	17.14 (-40.78, 75.06)
Paternal affectionless control	4.66 (-6.34, 15.67)	6.12 (-9.55, 21.79)	3.32 (-12.17, 18.81)	2.79 (-19.23, 24.8)
Maternal affectionless control	5.28 (-5.85, 16.4)	6.8 (-8.69, 22.29)	3.59 (12.43, 19.61)	3.14 (-19.13, 25.41)
Parental death	-17.52 (-45.14, 10.11)	8.62 (-28.99, 46.23)	-49.15 (-89.85, -8.45)	57.84 (2.42, 113.26)
Parental separation	8.56 (-17.3, 34.4)	9.8 (-27.02, 46.62)	7.63 (-28.8, 44.06)	2.69 (-49.00, 54.4)
Model 2				
Adversity				
Maltreatment	-5.95 (-29.96, 18.05)	3.28 (-27.35, 33.9)	-21.41 (60.19, 17.37)	22.92 (-26.36, 72.21)
Low parental concern for child's education	10.23 (-6.21, 26.67)	13.16 (-10.02, 36.34)	7.47 (-15.8, 30.74)	11.69 (-20.4, 43.78)
Parental psychiatric history	-10.45 (-46.42, 25.35)	-3.1 (-57.58, 51.38)	-18.75 (-66.65, 29.14)	16.92 (-55.65, 89.5)
Parental divorce	-6.41 (-35.96, 22.14)	-3.22 (-41.15, 34.71)	-14.6 (-57.92, 28.73)	17.66 (-39.68, 75.0)
Paternal affectionless control	3.92 (-6.96, 14.81)	4.32 (-11.05, 19.7)	3.37 (-12.06, 18.81)	1.1 (-20.7, 22.92)
Maternal affectionless control	4.22 (-6.8, 15.23)	3.75 (-11.45, 18.96)	4.0 (-12.0, 20.0)	0.36 (-21.72, 22.44)
Parental death	-20.13 (-47.46, 7.19)	2.66 (-34.12, 39.43)	-50.15 (-90.81, -9.5)	54.19 (-0.67, 109.05)
Parental separation	4.04 (-21.72, 29.81)	1.72 (-34.53, 37.96)	6.94 (-29.62, 43.5)	0.23 (-50.9, 51.35)

Footnote:

Model 1. Adjusted for age (and sex if not stratified by sex)

Model 2: Adjusted for age, birthweight, paternal social class, maternal education, and housing tenure (and sex if not stratified by sex)

All outcomes have been log transformed and multiplied by 100, so interpretation of the coefficient is on a % scale

Abbreviations: ELA: early life adversity, CI: confidence interval, CRP: c-reactive protein

*males-females: difference in effect sizes between males and females from a model with sex-by-adversity interaction terms

Supplementary table 9. Associations between ELA score and cortisol outcomes at 60-64 years (N= 1,462) using FIML estimation.

	CAR (nmol/L %)		DS (nmol/L %)		Evening cortisol (nmol/L %)		Morning cortisol (nmol/L %)	
	s% (95% CI)	p-value for trend	s% (95% CI)	p-value for trend	s% (95% CI)	p-value for trend	s% (95% CI)	p-value for trend
Model 2								
ELA Score (Reference group= 0)								
1	2.3 (-2.44, 7.03)		2.32 (-0.74, 5.38)		0.52 (-9.48, 10.52)		-7.8 (-16.3, 0.68)	
2	1.46 (-3.85, 6.78)		1.95 (-1.48, 5.38)		1.73 (-9.48, 12.95)		-5.15 (-14.68, 4.37)	
≥ 3	2.53 (-5.5, 10.57)	0.418	7.88 (2.71, 13.05)	0.007	0.23 (-16.72, 17.17)	0.831	-25.91 (-40.27, -11.55)	0.002
Model 3								
ELA score (Reference group = 0)								
1	2.13 (-2.61, 6.88)		2.37 (-0.7, 5.44)		1.05 (-8.95, 11.06)		-7.58 (-16.12, 0.96)	
2	1.35 (-3.9, 6.65)		2.02 (-1.41, 5.46)		1.93 (-9.25, 13.11)		-5.01 (-14.57, 4.54)	
≥ 3	2.31 (-5.72, 10.34)	0.457	7.96 (2.77, 13.15)	0.006	0.36 (-16.58, 17.3)	0.798	-25.04 (-39.47, -10.61)	0.004

Footnote:

Model 1. Adjusted for age and sex

Model 2: Adjusted for age, sex, birthweight, paternal social class, maternal education, and housing tenure

All outcomes have been log transformed and multiplied by 100, so interpretation of the coefficient is on a % scale

Abbreviations: ELA: early life adversity, CI: confidence interval, DS: diurnal slope, CAR: cortisol awakening response