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Abuse in childhood and cardiometabolic health in early adulthood: evidence from the Avon Longitudinal Study of Parents and Children

Soares. Childhood abuse and cardiometabolic health

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1 **Abstract**

2 **Background:** Although childhood abuse has been consistently associated with
3 cardiovascular disease in later adulthood, its associations with cardiometabolic health
4 in younger adults are poorly understood. We assessed associations between
5 childhood physical, sexual, and psychological abuse and cardiometabolic outcomes
6 at 18 and 25 years.

7 **Methods and Results:** We used data on 3,223 participants of the Avon Longitudinal
8 Study of Parents and Children (ALSPAC). Exposure to childhood abuse was self-
9 reported retrospectively at 22 years. We used linear regression to assess the
10 associations between childhood abuse and cardiometabolic outcomes at 18 and 25
11 years. At 18 years, physical (β 1.35kg/m², 95%CI 0.66, 2.05), sexual (β 0.57kg/m²,
12 95%CI 0.04, 1.11) and psychological (β 0.47kg/m², 95%CI 0.01, 0.92) abuse were
13 associated with higher BMI. Physical abuse was also associated with lower HDL (β -
14 0.07mmol/L, 95%CI -0.13, -0.01) and higher CRP (31%, 95%CI 1%, 69%), and sexual
15 abuse was associated with higher heart rate (β 1.92bpm, 95%CI 0.26, 3.58). At age
16 25 all three types of abuse were additionally associated with higher insulin, and sexual
17 abuse was associated with lower cholesterol (-0.14mmol/L, 95%CI -0.26, -0.01). The
18 age at which abuse occurred (<11y/11-17y) had little influence on the associations,
19 and when sex differences were evident, associations were stronger in males.

20 **Conclusions:** Childhood abuse is associated with negative cardiometabolic
21 outcomes even by young adulthood. Further follow-up will determine whether
22 associations strengthen across the life course and whether sex differences persist,
23 which is essential for targeting effective screening programs and early interventions in
24 those who suffered abuse in childhood.

25 **Keywords:** Cardiometabolic health, childhood abuse, ALSPAC

1 INTRODUCTION

2 A growing body of evidence demonstrates associations of childhood abuse with
3 a wide range of adverse mental and physical health outcomes,^{1, 2} including poorer
4 cardiometabolic health. A recent review found that childhood abuse was associated
5 with cardiovascular disease (CVD), diabetes and higher blood pressure/hypertension
6 in the majority of studies.³ However, the age at which associations between childhood
7 abuse and poor cardiometabolic health emerge is unclear. Most studies explore the
8 association of childhood abuse with cardiometabolic health later in adulthood. Those
9 that have investigated cardiometabolic outcomes in younger age groups have found
10 inconsistent results.⁴⁻⁹ A systematic review reported a strong association between
11 childhood maltreatment and obesity in adults, but this was not apparent in children
12 and adolescents.¹⁰ Longitudinal studies assessing body mass index (BMI) trajectories
13 show that associations with childhood abuse vary by age and type of abuse, and
14 positive associations emerge later in adulthood.¹¹ Understanding the age at which
15 associations arise are essential for prevention efforts.

16 Women experience a greater burden of sexual abuse, whereas physical abuse
17 is more common in men.² Sex differences in cardiometabolic health also exist, which
18 might be driven by sex hormones, sex-specific molecular mechanisms, including
19 glucose and lipid metabolism, as well as cardiac energy metabolism and cardiac
20 function.¹² Sex differences in the associations between childhood abuse and
21 cardiometabolic health are therefore plausible but evidence is limited, and among the
22 studies that have explored sex differences, no consistent pattern has been found.^{2, 3}

23 Many studies examine a broad range of adversities under the Adverse
24 Childhood Experiences (ACEs) umbrella,^{2, 13} which can include highly heterogeneous
25 exposures (e.g. childhood abuse, neglect and several forms of household

1 dysfunction), often combined into a summary score.¹⁴ But there is limited
2 understanding of how childhood abuse specifically impacts cardiometabolic health.
3 Furthermore, most studies fail to consider the frequency and/or timing of the abuse.

4 We aimed to assess the associations of physical, sexual and psychological
5 abuse in childhood with measures of cardiometabolic health in early adulthood (18
6 years and 25 years) in a contemporary general population cohort, explore whether
7 there are sex differences in these associations, and whether associations differ by the
8 age at which childhood abuse occurred.

9

10 **METHODS**

11 *Data availability*

12 Because of the sensitive nature of the data collected for this study, requests to
13 access the dataset from qualified researchers may be sent to the ALSPAC Executive
14 Committee at <https://proposals.epi.bristol.ac.uk/>.

15

16 *Study Population*

17 The Avon Longitudinal Study of Parents and Children (ALSPAC) is a
18 prospective population-based pregnancy cohort (see www.alspac.bris.ac.uk) that
19 recruited pregnant women living in the Avon area of the United Kingdom who were
20 due to give birth between April 1991 and December 1992.¹⁵ In total, 14,541
21 pregnancies were enrolled and children, mothers and their partners have been
22 followed up repeatedly ever since. Please note that the study website contains details
23 of all the data that is available through a fully searchable data dictionary and variable
24 search tool. For full details of the data from the ALSPAC study, see
25 <http://www.bristol.ac.uk/alspac/researchers/our-data>.

1 The study participant flow is given in Figure 1. Participants were included if they
2 had data on at least one type of abuse and one cardiometabolic outcome. Participants
3 pregnant at the 18- and 25-year clinic assessments were excluded as pregnancy could
4 alter BMI and cardiometabolic health outcomes, resulting in the inclusion of 3,223
5 participants in the study. Ethical approval was obtained from the ALSPAC Law and
6 Ethics Committee and the Local Research Ethics Committee. Consent for biological
7 samples has been collected in accordance with the Human Tissue Act (2004).

8

9 *Abuse in Childhood*

10 Exposure to childhood abuse (before 18 years) was retrospectively self-
11 reported in a questionnaire at ~22 years. The questionnaire used to collect information
12 on abuse was based on the Child Abuse Questionnaire¹⁶ and the Sexual Experiences
13 Survey¹⁷ and includes the three main types of abuse: physical, sexual and
14 psychological abuse; see [http://www.bristol.ac.uk/media-](http://www.bristol.ac.uk/media-library/sites/alspac/documents/questionnaires/YPB-life-at-22-plus.pdf)
15 [library/sites/alspac/documents/questionnaires/YPB-life-at-22-plus.pdf](http://www.bristol.ac.uk/media-library/sites/alspac/documents/questionnaires/YPB-life-at-22-plus.pdf), section H.
16 Participants were asked about experiences occurring in childhood (before 11 years),
17 and during adolescence (11-17 years). Details about the abuse categorisation are
18 available in supplementary material. We assessed abuse in each time period (<11/11-
19 17 years) and also combined both time periods to indicate abuse <18 years, and
20 generated a summary score varying from 0 (no experience of abuse <18 years old) to
21 3 (experience of all abuse types < 18 years old).

22 The study data were collected and managed using REDCap electronic data
23 capture tools hosted at University of Bristol.¹⁸

24

25 *Outcomes*

1 Height and weight were measured in research clinics at both 18 and 25 years
2 using standard procedures. Participants fasted overnight or for a minimum of 6 hours.
3 Total cholesterol, plasma triglycerides and high-density lipoprotein (HDL) cholesterol
4 were measured using enzymatic reagents for lipid determination from the standard
5 Lipid Research Clinics Protocol. Low-density lipoprotein (LDL) cholesterol
6 concentrations were calculated using the Friedewald equation.¹⁹ Serum insulin was
7 measured with ELISA (Mercodia, Uppsala, Sweden), which does not cross-react with
8 proinsulin. An automated particle-enhanced immunoturbidimetric assay (Roche UK,
9 Welwyn Garden City, UK) was used to measure plasma glucose and C-reactive
10 protein (CRP).

11

12 *Confounders*

13 We considered household occupational social class, maternal and paternal
14 education, ethnicity, age, and sex as potential confounders. Household occupational
15 social class was assessed at recruitment to the study and defined based on the highest
16 of mothers and their partners' self-reported occupation using the 1991 British Office of
17 Population and Census Statistics (OPCS) classification. Maternal and paternal
18 education were also assessed at recruitment and correspond to the highest
19 educational attainment achieved. Ethnicity was classified as white/non-white, as most
20 participants were of white ethnicity (96%).

21

22 *Statistical Analysis*

23 Data were analysed using Stata 16.1 (Stata Corp., 2016). Positively skewed
24 outcome variables were log-transformed for analyses and back transformed for
25 presentation of results.

1 We investigated each type of abuse separately and assessed associations of
2 childhood abuse with cardiometabolic health considering abuse exposure occurring i.
3 before 11 years, ii. between 11-17 years, and iii. at any age before 18 years. We used
4 linear regression to estimate associations of childhood abuse with measures of
5 cardiometabolic health at 18 and 25 years, unadjusted and adjusted for the potential
6 confounders define above. We used the outcomes in their original units, as well as
7 standardized measures to allow comparability across the different outcomes. We
8 compared the associations for abuse <11 years and between 11-17 years by
9 comparing the point estimates and examining whether 95% confidence intervals
10 (95%CI) overlapped and by using seemingly unrelated estimation to assess the
11 difference between the coefficients. We explored possible sex differences in the
12 associations between childhood abuse and cardiometabolic outcomes in a model
13 including an interaction term between each type of childhood abuse and sex.

14 We also used linear regression to examine the association between a summary
15 score of abuse types that occurred <18 years (ranging from 0-3) and the
16 cardiometabolic outcomes. We assessed whether there was a dose-response
17 relationship (i.e. increase in the outcomes by increase in the score of abuse) by using
18 the score as continuous and a Wald test for linear trend.

19

20 *Sensitivity analysis*

21 Considering that different types of childhood abuse commonly co-occur, we
22 performed sensitivity analysis with the types of abuse mutually adjusted to estimate
23 their independent associations.

24 Mental health can influence the report of childhood abuse, such that individuals
25 with higher psychological distress are more likely to report adverse childhood

1 experiences.²⁰ Therefore, we also performed sensitivity analysis adjusting for
2 depression at the time of childhood abuse reporting. Depression was measured using
3 the Short Mood and Feelings Questionnaire (SMFQ),²¹ a 13-item questionnaire with
4 score ranging between 0–26, in which a greater score represents higher depression.

5 To explore the frequency of childhood abuse occurrence, we recategorized the
6 occurrence of each type of abuse into the following frequency categories: never,
7 rarely/sometimes and often/very often. As each abuse type was assessed by multiple
8 questions, we applied the response indicating the highest frequency per type. More
9 details are presented in supplementary material.

10

11 *Missing data*

12 There was missing data on outcomes and covariates. The highest proportion
13 of missing data was observed for insulin at age 18 (44.7%), followed by total
14 cholesterol, HDL, LDL, triglycerides, glucose and CRP (43.7%) at 18 years
15 (Supplementary Table 1). To increase precision and reduce selection bias, we
16 conducted multivariate multiple imputation using chained equations to impute missing
17 information. Twenty cycles of regression switching were used and estimates of results
18 were averaged across the imputed datasets according to Rubin's rules.²² More details
19 on the imputation models are available in supplementary material.

20 We also performed analysis in those with complete data on child abuse,
21 covariates and outcomes (complete cases) as a sensitivity analysis.

22

23 **RESULTS**

24 Table 1 presents characteristics of the participants included in the analysis (n
25 = 3,223) compared to those excluded from the analysis. Included participants were

1 more likely to be female, white, and to have a higher socioeconomic position.
2 Cardiometabolic health measures were generally more favourable in included
3 participants (lower BMI, SBP, lipids, except for HDL, and glucose), though differences
4 were relatively small in magnitude. The distribution of data after imputation is similar
5 to the observed data (Supplementary Table 1).

6 Approximately 5% reported physical abuse, and it was more likely to have
7 occurred <11 years (Table 2). The report of sexual abuse was higher in females (12%)
8 than in males (3%), and whilst in males the prevalence was similar in both age periods,
9 in females it was higher between 11-17 years. Psychological abuse was also more
10 reported by females (14%) than males (10%), and it was more likely to have occurred
11 between 11-17 years. The co-occurrence between the different types of abuse is
12 presented in Supplementary Figure 1. Nearly 20% experienced at least one type of
13 abuse, and physical and psychological abuse commonly co-occurred, such that 65%
14 of those who reported physical abuse also reported psychological abuse (2.4% of the
15 participants). Frequencies of abuse occurrence are reported in Supplementary Table
16 2.

17 The majority of the associations between childhood abuse and cardiometabolic
18 outcomes at 18 and 25 years was similar regardless of whether abuse occurred <11
19 years or between 11-17 years (Supplementary Tables 3 and 4). The exceptions were
20 for the associations of physical abuse with heart rate at both 18 and 25 years, glucose
21 at 18 years, and BMI at 25 years, where stronger associations were observed for
22 physical abuse that occurred between 11-17 years, and between psychological abuse
23 and both glucose and insulin at 25 years, where stronger associations were observed
24 for psychological abuse that occurred <11 years (Supplementary Tables 3 and 4).

1 Therefore, given the similarity of the results according to the age at which abuse
2 occurred, the main results are reported for abuse experienced at any age <18 years.

3 Most associations were similar in males and females, and main results are
4 therefore presented for both sexes combined. Sex stratified results are presented in
5 supplementary material.

7 *Cardiometabolic health at 18 years*

8 Unadjusted and adjusted associations of childhood abuse with the
9 cardiometabolic outcomes in their original scale are presented in Supplementary
10 Tables 5 and 6, respectively, and adjusted associations with standardised outcomes
11 are presented in Figures 2 – 4. Physical (β 1.35 kg/m², 95%CI 0.66, 2.05), sexual (β
12 0.57 kg/m², 95%CI 0.04, 1.11) and psychological (β 0.47 kg/m², 95%CI 0.01, 0.92)
13 abuse were associated with higher BMI at 18 years, even when adjusting for potential
14 confounders. Physical abuse was also associated with lower HDL (β -0.07 mmol/L,
15 95%CI -0.13, -0.01) and higher CRP (β 31%, 95%CI 1%, 69%), and sexual abuse was
16 also associated with higher heart rate (β 0.57 bpm, 95%CI 0.04, 1.11).

17 The only evidence for sex differences was observed for the associations
18 between sexual abuse and both BMI and heart rate (p-value for sex interaction=0.052
19 and 0.048, respectively), which was observed in males (BMI: β 2.15 kg/m², 95%CI
20 0.62, 3.68; heart rate: β 8.07 bpm, 95%CI 2.02, 14.12) but not females (BMI: 0.33
21 kg/m², 95%CI -0.26, 0.93; heart rate: β 1.25 bpm, 95%CI -0.43, 2.93) (Supplementary
22 Table 7).

23 When the types of abuse were mutually adjusted, the point estimates usually
24 reduced, and there was evidence of an independent association of physical abuse
25 with BMI (β 1.22 kg/m², 95%CI 0.47, 1.97) and HDL (β -0.07 mmol/L, 95%CI -0.14, -

1 0.01), and of sexual abuse with heart rate (β 1.83 bpm, 95%CI 0.15, 3.52)
2 (Supplementary Table 8). When depression was included in the adjustment
3 (Supplementary Tables 9-11), the point estimates were usually attenuated compared
4 to the main analysis, and the associations of physical abuse with higher BMI (β 1.20
5 kg/m², 95%CI 0.50, 1.90) and lower HDL (β -0.06 mmol/L 95%CI -0.12, 0.00), and
6 between sexual abuse and higher heart rate (β 1.79 bpm, 95%CI 0.11, 3.47) were still
7 evident (Supplementary Table 9). When considering the frequency of abuse
8 occurrence, there was evidence of associations of physical abuse and sexual abuse
9 experienced often/very often with higher BMI (Supplementary Table 12). Point
10 estimates for abuse occurring rarely/sometimes (compared to never) were generally
11 smaller and all confidence intervals crossed the null value. The one exception was the
12 association of physical abuse with lower triglycerides in those reporting abuse
13 occurring rarely/sometimes compared to never.

14 A higher score of childhood abuse was associated with higher BMI and higher
15 heart rate (Table 3). Each additional experience of abuse was associated with, on
16 average, 0.50 kg/m² (95%CI 0.23; 0.76) higher BMI, and those who experienced all
17 types of childhood abuse had a 2.29 kg/m² (95%CI 0.70; 3.88) higher BMI than those
18 who did not experience any type of abuse in childhood. Those who experienced all
19 types of child abuse also had a 5.43 bpm (95%CI 0.41; 10.46) higher heart rate than
20 those who did not experience any type of abuse. No sex differences were observed
21 for the associations between the score of childhood abuse and cardiometabolic
22 outcomes at age 18 (Supplementary Table 14).

23

24 *Cardiometabolic health at 25 years*

1 All associations observed at 18 years were also observed at age 25, except for
2 the association between physical abuse and CRP. Additionally, some further
3 associations emerged at age 25. All types of abuse were also associated with higher
4 insulin; physical abuse was associated with 0.3 SD (95%CI 0.1; 0.4) higher insulin,
5 which corresponds to 26% (95%CI 12; 41) higher than those who did not experience
6 physical abuse, sexual abuse was associated with 13% (95%CI 3, 23) higher insulin,
7 and psychological abuse was associated with 9% (95%CI 0, 19) higher insulin (Figures
8 2 – 4; Supplementary Table 6). Sexual abuse was also associated with lower total
9 cholesterol (β -0.14 mmol/L, 95%CI -0.26, -0.01).

10 The association between sexual abuse and higher heart rate was stronger in
11 males (β 6.45 bpm, 95%CI 2.66; 10.24) than females (β 1.48 bpm, 95%CI 0.10; 2.86,
12 p-value for sex interaction=0.023), and associations of psychological abuse with both
13 higher triglycerides (β 18%, 95%CI 6, 31) and CRP (β 31%, 95%CI 0, 72) were evident
14 only in males, whilst the association with lower total cholesterol (β -0.14 mmol/L,
15 95%CI -0.27, -0.02) was only observed in females (Supplementary Table 7).

16 When the types of abuse were mutually adjusted, there was evidence of
17 independent associations of physical and sexual abuse with BMI and insulin
18 (Supplementary Table 8). Adjustment for depression attenuated the point estimates,
19 and associations of all types of abuse with BMI and of physical and sexual abuse with
20 insulin were still evident (Supplementary Tables 9-11). All of the confidence intervals
21 for abuse occurring rarely/sometimes crossed the null value (Supplementary Table
22 13). Physical and sexual abuse occurring often/very often were associated with higher
23 BMI (β 1.22kg/m², 95%CI 0.32, 2.12, and 1.56 kg/m², 95%CI 0.63, 2.50, respectively).

24 A dose-response relationship was observed between a higher score of
25 childhood abuse and higher BMI, higher insulin, lower total cholesterol and lower HDL

1 (Table 3). For example, each additional experience of abuse was associated with, on
2 average, 10% (95%CI 5; 15) higher insulin, and experiencing all three types of abuse
3 was associated with 49% (95%CI 16; 92) higher insulin concentration than those who
4 did not experience any type of abuse. Sex differences were observed for the
5 associations between the summary score of abuse and both triglycerides and CRP at
6 25 years, with stronger associations observed in males than females (Supplementary
7 Table 14).

8 Associations between child abuse and cardiometabolic outcomes at ages 18
9 and 25 years were similar when including only complete cases, though in the latter
10 confidence intervals were wider due to more imprecision in the estimates
11 (Supplementary Table 15).

12

13 **DISCUSSION**

14 This population-based cohort study aimed to assess the associations between
15 childhood abuse and cardiometabolic outcomes in young adults. Childhood abuse (all
16 types and the score of abuse) was consistently associated with higher BMI at 18 and
17 25 years. At age 25, in addition to associations with BMI, all types of abuse and the
18 score were associated with higher insulin. Additional associations were observed for
19 the specific types of abuse and the abuse score with outcomes at both ages 18 and
20 25 years (e.g., sexual abuse and higher heart rate at ages 18 and 25, and abuse score
21 and lower HDL at 25 years). There was weaker evidence of an association between
22 child abuse and the other cardiometabolic outcomes assessed (e.g. point estimates
23 for physical and sexual abuse in relation to DBP were consistently positive at both 18
24 and 25 years of age, but confidence intervals cross the null). Associations between
25 child abuse and cardiometabolic health outcomes were overall similar if abuse

1 occurred <11 years or between 11-17 years. Few associations differed by sex, and
2 when sex differences were evident, males had stronger associations than females.

3 While our findings are in line with some previous studies that found positive
4 associations between adverse life events and cardiometabolic risk factors such as
5 obesity and blood pressure,^{6, 8} not all studies have noted associations between
6 childhood abuse and cardiometabolic health in young adults.^{5, 7} A cohort study found
7 no evidence for a relationship between child maltreatment and blood pressure or
8 hypertension in young adults,⁷ and a systematic review of 20 studies concluded that
9 there was no evidence of an association between childhood adversity and levels of
10 inflammatory and other CVD immune markers in young people.⁵ It is possible that
11 some associations differ by cardiometabolic outcomes or are inconsistent because of
12 the different ages, settings and methods.

13 A review and meta-analysis of studies investigating the association of childhood
14 maltreatment with obesity found a stronger association for obesity in adulthood (OR
15 1.38, 95%CI 1.28,1.50), compared to obesity in young people (OR 1.13, 95%CI 0.92,
16 1.39).¹⁰ In the UK 1958 Birth Cohort, there was no evidence of associations of
17 childhood abuse with BMI at the ages of 16, 23 and 33; associations between physical
18 abuse and BMI became apparent at age 45 in males and females and associations
19 with psychological abuse emerged later, at age 50.¹¹ In our study of a more
20 contemporary birth cohort (1991-2), associations between all types of abuse in
21 childhood and BMI were already apparent at age 18 and remained at age 25.
22 Furthermore, there was evidence of associations with additional cardiometabolic
23 health measures at ages 18 and 25. These results were overall robust when the types
24 of childhood abuse were mutually adjusted or adjusted for depression, and positive
25 associations with these cardiometabolic outcomes were also observed for a higher

1 score of childhood abuse. Generational differences in obesity levels, frequency and
2 perception of abuse, and chance may play a role in explaining these different findings
3 in the two UK cohorts.

4 Few studies have explored timing-specific effects of abuse on cardiometabolic
5 health,² although there is evidence of different associations by timing of abuse on other
6 outcomes.²³⁻²⁵ We were able to assess childhood abuse experienced <11 years and
7 between 11-17 years and found that associations with cardiometabolic health were
8 similar. This corroborates previous findings observed for adult cardiometabolic
9 health.²⁶ However, we have assessed broad age categories and we cannot be certain
10 that they do not mask differences that would be apparent if we could examine timing
11 of exposure by narrower age ranges/life course stages (e.g., early childhood, mid-
12 childhood, early adolescence and late adolescence).²³ Though recall bias due to
13 retrospective report of childhood abuse could affect the associations by timing of
14 childhood abuse, we would expect such bias to affect associations with all outcomes
15 in the same direction. However, we showed that some associations were stronger for
16 abuse occurring <11 years (e.g., the association between psychological abuse and
17 insulin at 25 years), and some were stronger if abuse occurred between 11-17 years
18 (e.g., the association between physical abuse and heart rate). Therefore, recall bias
19 is unlikely to explain the differences by timing of childhood abuse. Previous evidence
20 for mental health suggests that abuse/maltreatment experienced in adolescence have
21 stronger negative consequences on mental health than does abuse/maltreatment
22 experienced only in childhood.^{24, 25} Differences by age at abuse in the associations
23 between childhood abuse and cardiometabolic outcomes were still evident when
24 analyses were further adjusted for depression measured using the SMFQ

1 (Supplementary Tables 10 and 11), suggesting that this may not fully explain the age-
2 specific results found.

3 We also examined abuse in frequency categories. Associations between
4 childhood abuse and cardiometabolic outcomes were driven mainly by those
5 experiencing more frequent abuse. It will be valuable to repeat this analysis at older
6 ages to see whether adverse cardiometabolic health emerges at a later age in those
7 exposed less frequently or not.

8 Pathways from abuse in childhood to adverse cardiometabolic health include
9 behavioural, mental health related and biological mechanisms ² - these are not
10 necessarily mutually exclusive. For example, exposure to maltreatment can cause
11 emotional dysregulation, which in turn may result in developing maladaptive coping
12 strategies, including emotional eating,²⁷ and subsequent obesity.²⁸ Childhood abuse
13 may affect cardiometabolic risk through downstream effects on health behaviours
14 (e.g., unhealthy diet or physical inactivity), or direct physiological changes resulting
15 from disruption of regulatory pathways, such as the stress response system.²⁹ Such
16 cascading effects may explain the further emergence of differences in cardiometabolic
17 health at 25 years, as downstream impacts of abuse in childhood on physical health
18 may take time to appear.

19 Although most associations were similar in males and females, there were
20 stronger associations between childhood abuse and some cardiometabolic outcomes
21 – heart rate, total cholesterol, triglycerides and CRP – in males. Previous studies
22 assessing associations between childhood maltreatment/victimisation with
23 inflammation^{30, 31} and CVD have shown stronger associations in females,^{32, 33} others
24 have shown stronger associations with CVD in males,^{34, 35} whilst some have observed
25 little evidence of sex differences³⁶. Further studies of sex differences are needed, as

1 are studies to elucidated sex specific pathways that can in turn inform sex specific
2 CVD prevention and treatment.

3

4 *Strengths and Limitations*

5 This study included a large-scale population cohort with repeated measures of
6 multiple biomarkers of cardiometabolic health. Whilst most studies do not consider the
7 age at which childhood abuse occurred, we were able to do so, and showed no
8 consistent differences by timing at exposure to abuse in the associations with
9 cardiometabolic health.

10 Our study also has several limitations. One limitation is attrition, which is typical
11 of long-term prospective studies and is more common in those from socioeconomically
12 deprived backgrounds.³⁷ To minimize selection bias, we conducted multiple imputation
13 to impute missing confounders and outcome data. The similarity between results from
14 the complete case analysis (Supplementary Table 15) and the analysis of imputed
15 datasets suggest that results are not substantially affected by selection bias.

16 The sample is predominantly white and relatively affluent, and this may limit
17 generalizability. Nevertheless, the prevalence of childhood abuse found in our study
18 lies within the range of estimates reported in the UK, where physical abuse ranged
19 from 3.6% to 32.6%, sexual abuse from 0.7% to 27.8%, and psychological abuse from
20 4.0% to 66.7%.³⁸

21 Abuse was assessed retrospectively by self-report, as is standard in large,
22 population-based studies. However, we used questions that reduce bias by asking
23 about specific acts of violence as opposed to nominal questions about 'abuse'. Even
24 though ALSPAC has information on childhood abuse collected prospectively, these
25 are mainly reported by the parents and do not cover the entire period before 18 years.

1 Furthermore, the prospective information on different types of abuse was assessed at
2 different time points, so that investigating and comparing the associations of different
3 abuse types by age at exposure would not be possible.

4 Retrospective report of abuse can be influenced by concurrent mental health
5 factors,²⁰ and a recent meta-analysis demonstrated poor agreement between
6 prospective and retrospective measures of child abuse, suggesting that these might
7 identify different groups of individuals.³⁹ Whilst prospective measures are generally
8 considered more valid and have better specificity,⁴⁰ retrospective measures may have
9 better sensitivity. The use of retrospective report of abuse might underestimate
10 associations with objectively measured outcomes, such as cardiometabolic health,⁴⁰
11 and therefore if bias due to retrospective reporting is present, it is likely to have
12 underestimated the associations. It is unlikely that levels of cardiometabolic health
13 markers would influence recall or reporting of childhood abuse. However, mental
14 health and CVD might have a bidirectional relationship,⁴¹ and mental health can
15 influence the report of childhood abuse.²⁰ Sensitivity analysis adjusting for depression
16 at the time of childhood abuse reporting show overall similar results, and therefore
17 reverse causality in the associations between childhood abuse and cardiometabolic
18 outcomes is unlikely.

19 We acknowledge that multiple tests have been carried out, which might have
20 increased the risk of type 1 error. Only 12 results would 'survive' formally correcting
21 for multiple testing ($p < 7.58 \times 10^{-4}$) (Supplementary Table 16). Yet we do not consider
22 each exposure-outcome investigated completely independent and we did not use p-
23 value thresholds to guide our conclusions. We have interpreted our results with
24 caution, based on patterns of results, the magnitude of estimates and their CIs, rather
25 than statistical significance.⁴²

1

2 *Conclusion*

3 Our findings suggest downstream effects of childhood abuse on
4 cardiometabolic risk factors in early adulthood, suggesting that young people who
5 have experienced abuse may benefit from early screening for cardiometabolic health.

6 Further follow-up with similar cohorts using repeated measures of biomarkers
7 of cardiometabolic health will be valuable in drawing life course trajectories to
8 determine whether these further diverge or otherwise, and whether sex differences
9 are observed. Future research into the mechanisms by which early life abuse affects
10 cardiometabolic health may inform secondary prevention efforts.

11

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5

6 **Contributors**

7 AZ, ALGS, SH and AF designed the study, interpreted the data and drafted the
8 manuscript. ALGS and AZ analysed the data. All authors contributed to revising the
9 manuscript critically for important intellectual content. All authors approved the version
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13

14 **Competing interests**

15 None declared.

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Table 1. Characteristics of participants included in the analysis (N = 3,223) and excluded from the analysis due to missing childhood abuse data (N = 11,460)

Characteristics	Participants included in analysis, N (%) or mean (SD)	Participants excluded from analysis, N (%) or mean (SD)	<i>P</i> value
Gender			< 0.001
Female	2,143 (66.5)	5,051 (44.1)	
Male	1,080 (33.5)	6,409 (55.9)	
Ethnicity, <i>n</i> (%)			<0.001
White	2,818 (96.4)	8,492 (94.5)	
Non-White	105 (3.6)	495 (5.5)	
Maternal education, <i>n</i> (%)			< 0.001
CSE	285 (8.7)	2,212 (23.8)	
Vocational	209 (7.1)	1,001 (10.8)	
O level	1,000 (33.9)	3,235 (34.8)	
A level	849 (28.7)	1,903 (20.5)	
University degree	638 (21.6)	938 (10.1)	
Paternal education, <i>n</i> (%)			< 0.001
CSE	436 (15.0)	2,636 (29.7)	
Vocational	181 (6.3)	815 (9.2)	
O level	610 (21.0)	1,890 (21.3)	
A level	853 (29.4)	2,209 (24.9)	
University degree	820 (28.3)	1,317 (14.9)	
Social Class, <i>n</i> (%)			< 0.001
I	144 (5.2)	206 (2.5)	
II	804 (29.3)	1,644 (20.4)	

III (non-manual)	770 (28.0)	1,857 (23.0)	
III (manual)	658 (24.0)	2,549 (31.6)	
IV	308 (11.2)	1,368 (16.9)	
V	62 (2.3)	451 (5.6)	
18-year outcomes			
BMI, kg/m ²	22.6 (4.1)	23.2 (4.4)	<0.001
Heart Rate, bpm	70.1 (10.6)	69.3 (11.2)	0.030
SBP, mmHg	115.7 (11.5)	117.9 (11.5)	<0.001
DBP, mmHg	64.7 (7.6)	64.5 (7.4)	0.414
Total cholesterol, mmol/L	3.8 (0.7)	3.7 (0.7)	0.032
HDL, mmol/L	1.3 (0.3)	1.2 (0.3)	<0.001
LDL, mmol/L	2.1 (0.6)	2.1 (0.6)	0.559
Triglycerides, mg/dL ^a	0.8 (0.4)	0.9 (0.4)	0.034
Glucose, mmol/L ^a	5.0 (0.6)	5.1 (0.6)	0.233
Insulin, mg/dL ^a	8.1 (7.8)	8.7 (8.6)	0.028
CRP, mg/l ^a	1.5 (4.0)	1.7 (6.0)	0.268
25-year outcomes			
BMI kg/m ²	24.7 (5.0)	25.3 (5.2)	0.001
Heart Rate, bpm	70.1 (10.6)	69.3 (11.2)	0.030
SBP, mmHg	115.5 (11.2)	117 (11.7)	<0.001
DBP, mmHg	67.1 (7.9)	66.7 (8.0)	0.127
Total cholesterol, mmol/L	4.4 (0.8)	4.5 (0.9)	0.001
HDL, mmol/L	1.6 (0.4)	1.5 (0.4)	0.020
LDL, mmol/L	2.4 (0.7)	2.5 (0.8)	<0.001
Triglycerides, mg/dL ^a	0.9 (0.5)	1.0 (0.7)	<0.001
Glucose, mmol/L ^a	5.3 (0.6)	5.4 (0.8)	<0.001
Insulin, mg/dL ^a	9.6 (9.2)	10.0 (10.0)	0.258

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CRP, mg/l ^a	2.2 (5.3)	2.4 (8.6)	0.443
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BMI: body mass index, Cholesterol: total cholesterol, CRP: C-reactive protein, DBP: diastolic blood pressure;

HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; SBP: systolic blood pressure

^a Median (inter-quartile range); P-values are for comparison of log transformed values.

Social occupation: I: Professional occupation, II: Managerial and technical occupations, III: Skilled occupation, IV:

Partly-skilled occupation, V: unskilled occupations

Table 2. Prevalence of childhood abuse according to sex (N = 3,223)

	< 11 years	11-17 years	< 18 years
	% (95%CI)	% (95%CI)	% (95%CI)
Males (n = 1,080)			
Physical abuse	4.8 (3.4, 6.1)	0.5 (0.0, 1.0)	5.0 (3.6, 6.3)
Sexual abuse	2.0 (1.1, 3.0)	1.9 (1.0, 2.8)	3.4 (2.3, 4.6)
Psychological abuse	0.8 (0.2, 1.4)	10.2 (8.3, 12)	10.2 (8.4, 12.1)
Females (n = 2,143)			
Physical abuse	5.1 (4.1, 6.0)	0.7 (0.3, 1.0)	5.1 (4.1, 6.1)
Sexual abuse	5.1 (4.1, 6.0)	8.9 (7.7, 10.2)	12.0 (10.6, 13.4)
Psychological abuse	1.0 (0.6, 1.4)	13.6 (12.1, 15.1)	13.7 (12.2, 15.2)

Table 3. Adjusted association between score of child abuse and cardiometabolic outcomes at 18 and 25 years (N = 3,223)

	Score of childhood abuse				p-value*
	1 type of abuse	2 types of abuse	3 types of abuse	Continuous	
	β (95%CI)	β (95%CI)	β (95%CI)	β (95%CI)	
18-year outcomes					
BMI, kg/m ²	0.34 (-0.07, 0.75)	1.44 (0.46, 2.42)	2.29 (0.70, 3.88)	0.50 (0.23, 0.76)	<0.001
Heart rate, bpm	0.43 (-0.84, 1.69)	1.19 (-1.16, 3.54)	5.43 (0.41, 10.46)	0.84 (0.04, 1.64)	0.041
SBP, mmHg	0.20 (-1.03, 1.43)	0.07 (-1.88, 2.02)	0.64 (-3.71, 4.99)	0.10 (-0.73, 0.94)	0.804
DBP, mmHg	0.26 (-0.62, 1.13)	1.25 (-0.24, 2.74)	1.41 (-1.77, 4.58)	0.34 (-0.24, 0.93)	0.246
Cholesterol, mmol/L	-0.01 (-0.10, 0.09)	-0.10 (-0.28, 0.07)	-0.10 (-0.39, 0.19)	-0.02 (-0.08, 0.03)	0.403
HDL, mmol/L	-0.01 (-0.05, 0.02)	-0.10 (-0.19, 0.0)	-0.06 (-0.19, 0.07)	-0.01 (-0.04, 0.01)	0.234
LDL, mmol/L	0.02 (-0.06, 0.09)	-0.07 (-0.22, 0.08)	-0.01 (-0.28, 0.26)	0.00 (-0.06, 0.05)	0.845
Triglycerides, mmol/L ^a	0.98 (0.93, 1.03)	1.04 (0.95, 1.15)	0.93 (0.79, 1.09)	0.98 (0.96, 1.01)	0.202
Glucose, mmol/L ^a	1.00 (0.99, 1.01)	1.01 (0.99, 1.03)	1.00 (0.96, 1.04)	1.00 (0.99, 1.01)	0.928
Insulin, mg/dL ^a	0.99 (0.93, 1.06)	1.22 (1.07, 1.40)	0.97 (0.77, 1.22)	0.99 (0.95, 1.04)	0.815
CRP, mg/l ^a	1.06 (0.93, 1.22)	1.04 (0.80, 1.34)	1.48 (0.79, 2.79)	1.11 (1.00, 1.22)	0.051
25-year outcomes					

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BMI, kg/m ²	0.56 (0.06, 1.06)	1.44 (0.46, 2.42)	2.75 (0.80, 4.71)	0.71 (0.39, 1.03)	<0.001
Heart rate, bpm	0.50 (-0.77, 1.77)	1.19 (-1.16, 3.54)	4.64 (-0.38, 9.66)	0.77 (-0.07, 1.61)	0.070
SBP, mmHg	0.16 (-0.99, 1.32)	0.07 (-1.88, 2.02)	0.54 (-3.65, 4.74)	0.11 (-0.55, 0.77)	0.741
DBP, mmHg	0.40 (-0.47, 1.27)	1.25 (-0.24, 2.74)	1.56 (-1.84, 4.95)	0.52 (0.00, 1.05)	0.052
Cholesterol, mmol/L	-0.06 (-0.16, 0.04)	-0.10 (-0.28, 0.07)	-0.40 (-0.75, -0.05)	-0.07 (-0.13, -0.01)	0.017
HDL, mmol/L	-0.03 (-0.07, 0.01)	-0.10 (-0.19, 0.00)	-0.13 (-0.31, 0.06)	-0.04 (-0.07, -0.01)	0.010
LDL, mmol/L	-0.05 (-0.12, 0.03)	-0.07 (-0.22, 0.08)	-0.21 (-0.50, 0.09)	-0.05 (-0.1, 0.00)	0.060
Triglycerides, mmol/L ^a	1.02 (0.97, 1.08)	1.04 (0.95, 1.15)	0.94 (0.79, 1.12)	1.01 (0.98, 1.05)	0.460
Glucose, mmol/L ^a	1.00 (0.99, 1.01)	1.01 (0.99, 1.03)	1.03 (0.99, 1.07)	1.00 (1.00, 1.01)	0.205
Insulin, mg/dL ^a	1.06 (0.99, 1.14)	1.22 (1.07, 1.40)	1.49 (1.16, 1.92)	1.10 (1.05, 1.15)	<0.001
CRP, mg/l ^a	0.99 (0.85, 1.16)	1.04 (0.80, 1.34)	1.22 (0.71, 2.10)	1.02 (0.94, 1.11)	0.659

Adjusted for age, sex, ethnicity, maternal education, paternal education, and parental social class

BMI: body mass index, Cholesterol: total cholesterol, CRP: C-reactive protein, DBP: diastolic blood pressure; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; SBP: systolic blood pressure

*p-value for linear trend

^a Logged outcome variables were back transformed (exponentiated) and are interpreted as the percentage change in those who experienced abuse compared to those who did not experience that abuse, or per additional abuse type experienced on the abuse score.

In the associations for the score of abuse, 0 (no experience of abuse) is the reference category.

Figure Titles

Figure 1. Study flow

Figure 2. Adjusted associations of physical abuse with cardiometabolic health outcomes at 18 and 25 years (N = 3,223). Point estimates are mean differences of standardized outcome values in individuals who reported physical abuse compared to those who did not.

Figure 3. Adjusted associations of sexual abuse with cardiometabolic health outcomes at 18 and 25 years (N = 3,223). Point estimates are mean differences of standardized outcome values in individuals who reported sexual abuse compared to those who did not.

Figure 4. Adjusted associations of psychological abuse score with cardiometabolic health outcomes at 18 and 25 years (N = 3,223). Point estimates are mean differences of standardized outcome values in individuals who reported psychological abuse compared to those who did not.

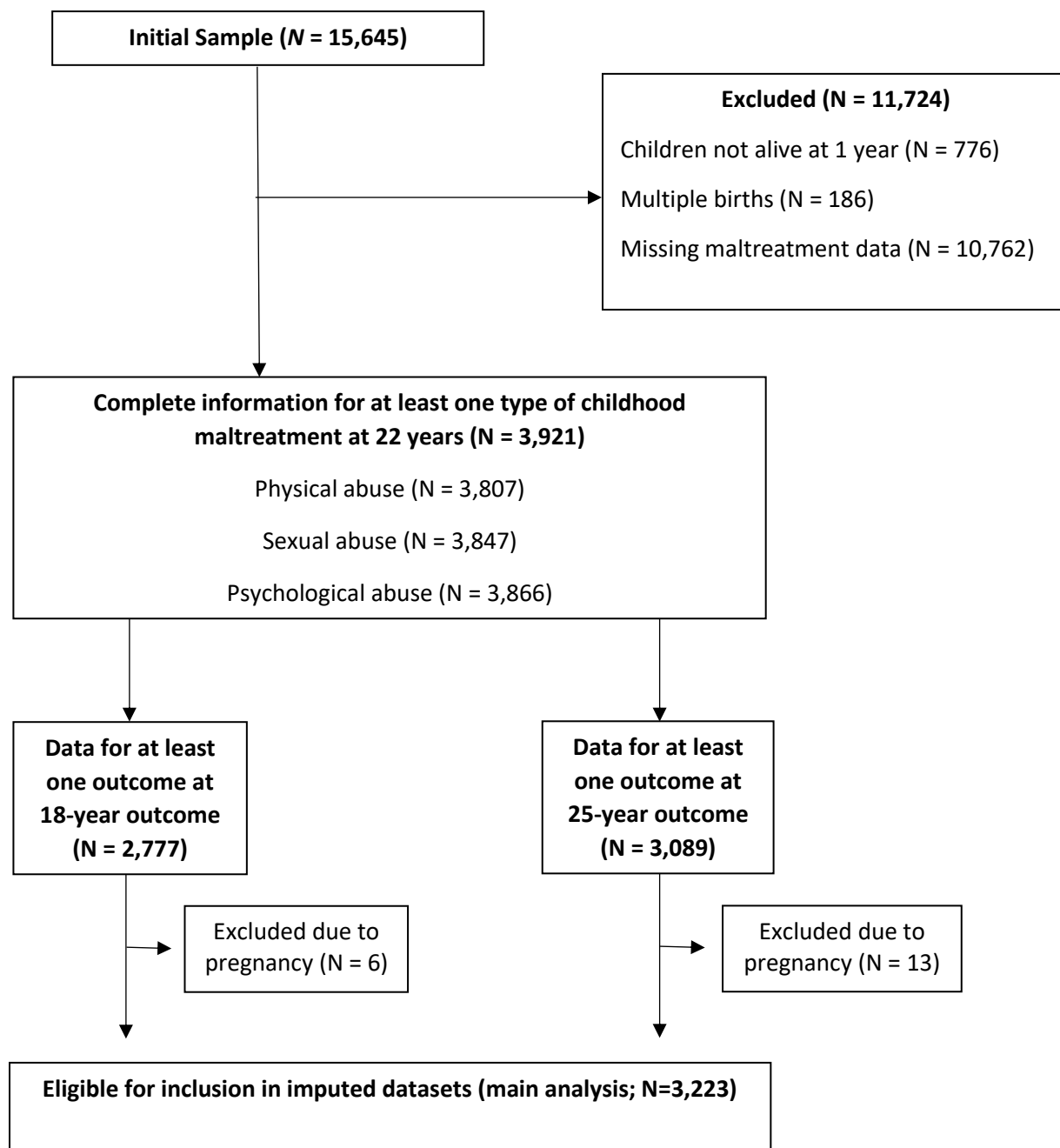


Figure 1. Study flow.

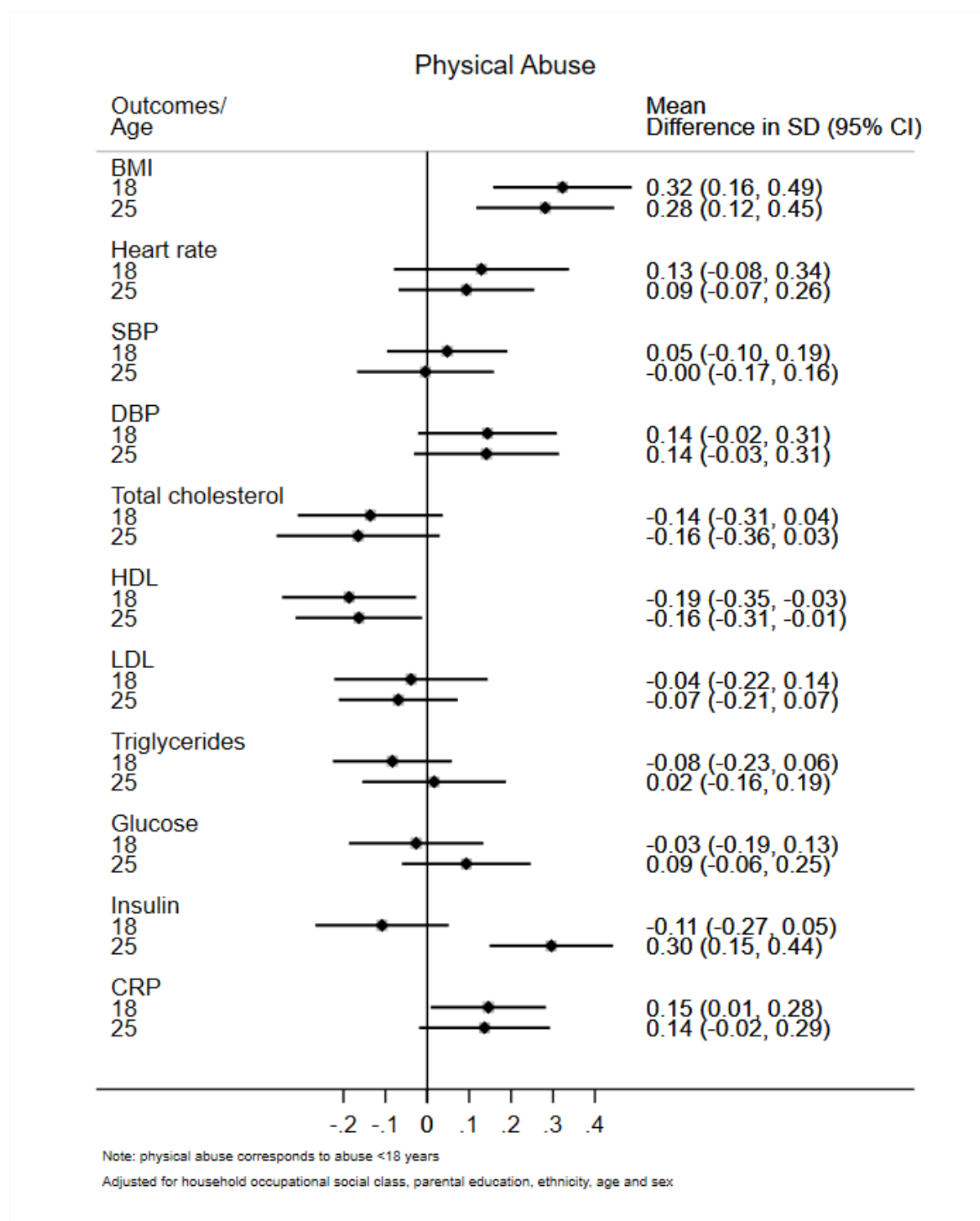


Figure 2. Adjusted associations of physical abuse with cardiometabolic health outcomes at 18 and 25 years (N = 3,223). Point estimates are mean differences of standardized outcome values in individuals who reported physical abuse compared to those who did not.

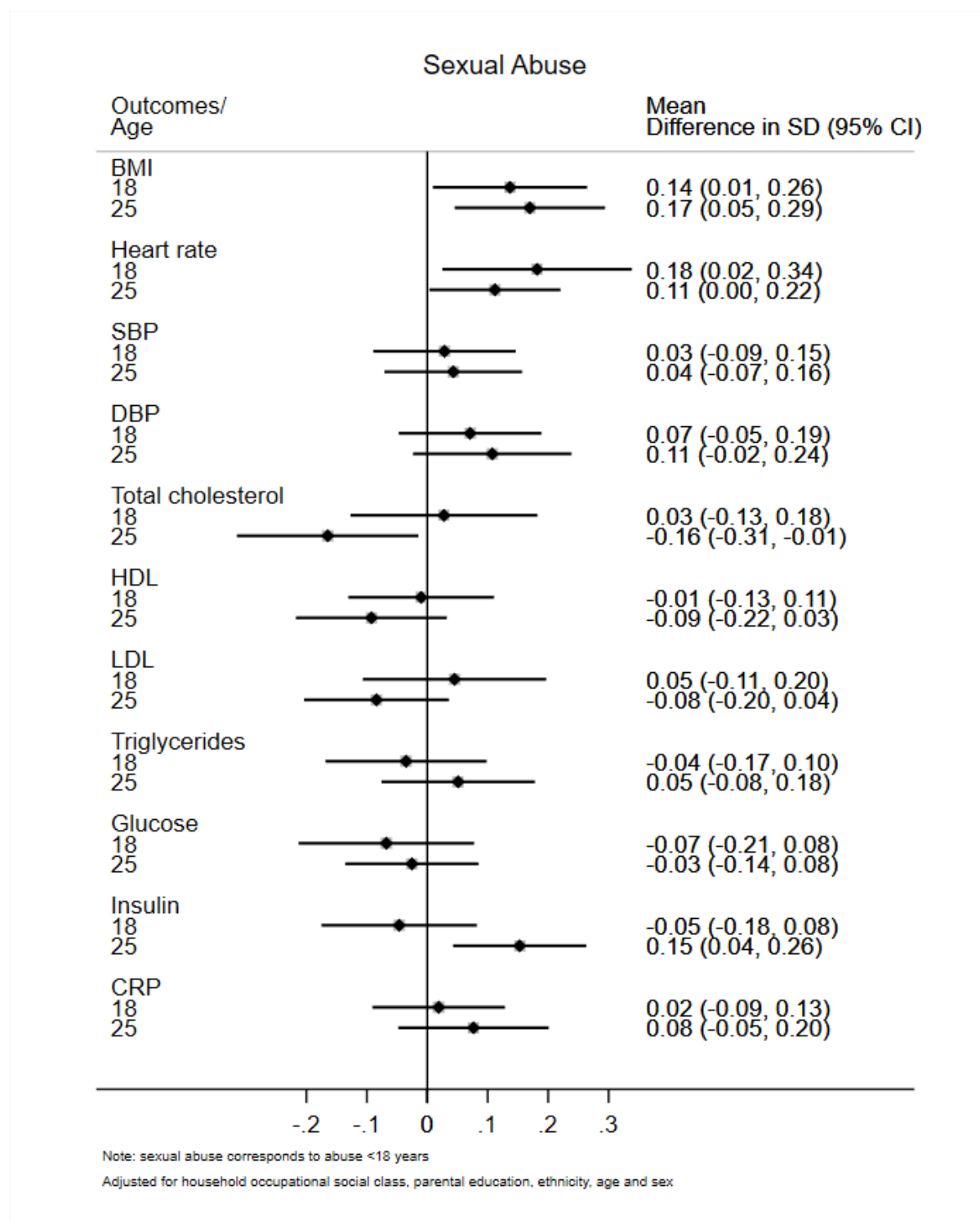


Figure 3. Adjusted associations of sexual abuse with cardiometabolic health outcomes at 18 and 25 years (N = 3,223). Point estimates are mean differences of standardized outcome values in individuals who reported sexual abuse compared to those who did not.

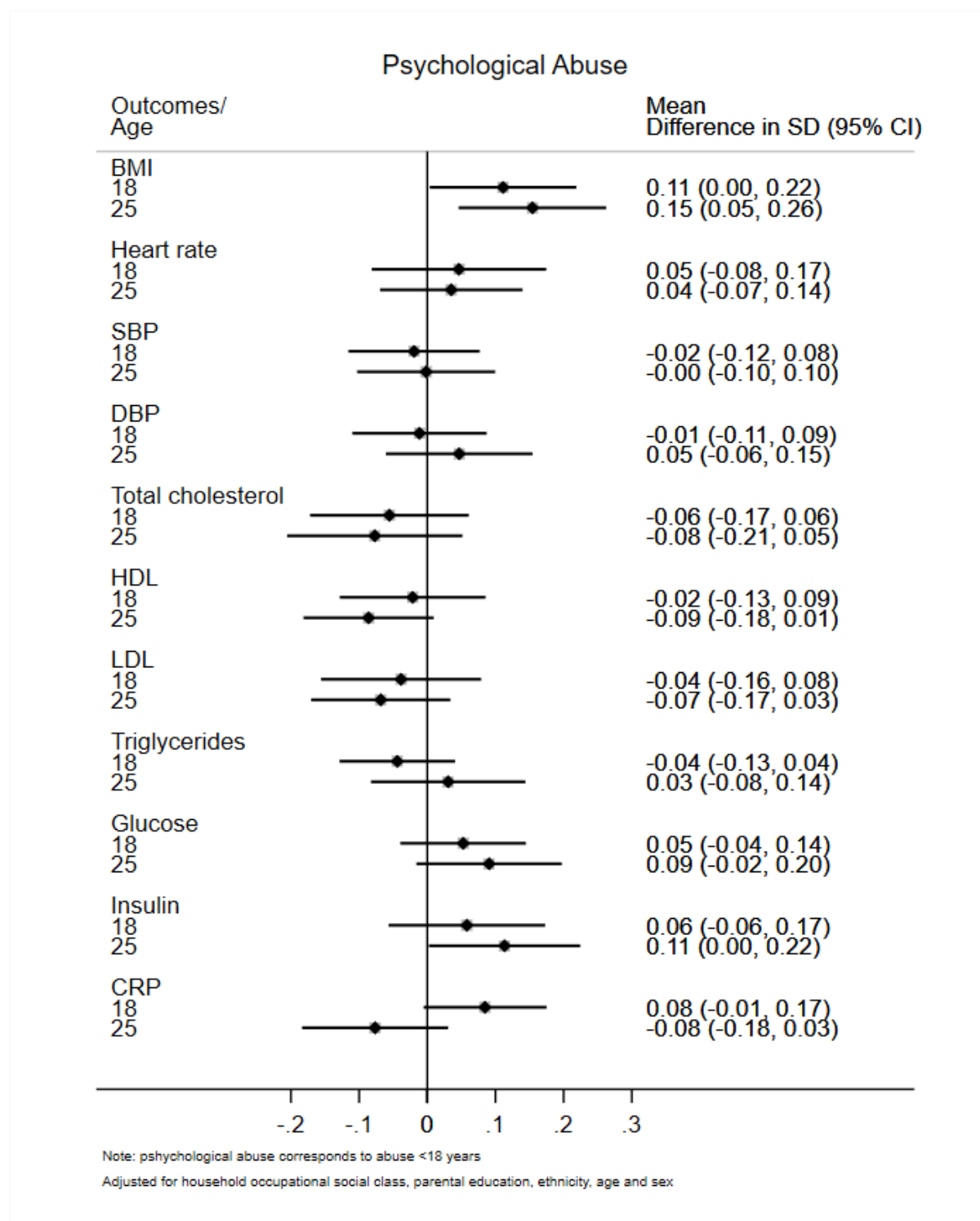


Figure 4. Adjusted associations of psychological abuse score with cardiometabolic health outcomes at 18 and 25 years (N = 3,223). Point estimates are mean differences of standardized outcome values in individuals who reported psychological abuse compared to those who did not.