BJPsych | The British Journal of Psychiatry (2023)
223, 377–381. doi: 10.1192/bjp.2023.33

Paper

# Child maltreatment and telomere length in middle and older age: retrospective cohort study of 141 748 UK Biobank participants

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**Background**

There is evidence that child maltreatment is associated with shorter telomere length in early life.

**Aims**

This study aims to examine if child maltreatment is associated with telomere length in middle- and older-age adults.

**Method**

This was a retrospective cohort study of 141 748 UK Biobank participants aged 37–73 years at recruitment. Leukocyte telomere length was measured with quantitative polymerase chain reaction, and log-transformed and scaled to have unit standard deviation. Child maltreatment was recalled by participants. Linear regression was used to analyse the association.

**Results**

After adjusting for sociodemographic characteristics, participants with three or more types of maltreatment presented with the shortest telomere lengths ($\beta = -0.05$, 95% CI −0.07 to −0.03; $P < 0.0001$), followed by those with two types of maltreatment ($\beta = -0.02$, 95% CI −0.04 to 0.00; $P = 0.02$), referent to those who had none. When adjusted for depression and post-traumatic stress disorder, the telomere lengths of participants with three or more types of maltreatment were still shorter ($\beta = -0.04$, 95% CI −0.07 to −0.02; $P = 0.0008$). The telomere lengths of those with one type of maltreatment were not significantly different from those who had none. When mutually adjusted, physical abuse ($\beta = -0.05$, 95% CI −0.07 to −0.03; $P < 0.0001$) and sexual abuse ($\beta = -0.02$, 95% CI −0.04 to 0.00; $P = 0.02$) were independently associated with shorter telomere length.

**Conclusions**

Our findings showed that child maltreatment is associated with shorter telomere length in middle- and older-aged adults, independent of sociodemographic and mental health factors.

**Keywords**

Epidemiology; post-traumatic stress disorder; trauma; risk assessment; comorbidity.



## Child maltreatment and stress response

Adverse childhood experiences are a major public health issue and affect over 19.4 million children.[1] Exposure to cumulative adverse childhood experiences is also a significant predisposing factor for many psychological conditions in teenagers and adults, contributing to a wide range of health issues, including cardiovascular disease, diabetes, depression and post-traumatic stress disorder (PTSD).[2–4] Among all adverse childhood experiences, child maltreatment is arguably one of the more severe components.[1,4–6] Child maltreatment broadly includes all forms of physical and/or emotional ill treatment, sexual abuse, neglect and negligent treatment of children under the age of 18 years.[5]

The existing evidence confirms that exposure to a single or sequence of chronically traumatic events may activate the biological stress response systems.[7] Long-term exposure to early-life stress was found to trigger stress-reactive networks and stress hormones, including the hypothalamic-pituitary-adrenal axis, central nervous system and endocrine and immunological systems,[1,6,8–10] cortisol and catecholamines, and other stress factors such as oxidants and cytokines.[10] These stress-response mechanisms have been hypothesised to play a significant role in the progression of early adversity to disease,[9] and are often indicated by telomere shortening – a marker for biological ageing.[11]

## Stress and telomere length

Telomeres are nucleo-protein complexes containing tandem $(TTAGGG)_n$ repeats that are required for chromosomal and genetic stability.[1] Mean telomere length acts as an indicator of biological ageing because it shortens with each DNA replication cycle in primary somatic cells, as a result of the end replication problem. It has been reported to predict morbidity and mortality within the diseasome of ageing (including cardiovascular disease, obesity, chronic kidney disease and cancer).[1,9,12,13] Oxidative stress leading to macromolecular damage is one of the factors that can influence telomere attrition, and has been shown to shorten telomeres in somatic cells or cells that do not replicate.[8] In germline and stem cells, telomerase – a ribonucleoprotein complex that adds TTAGGG repeats – assists in actively replenishing telomeric repeats during replication, but it is not active in most somatic cells.[8] Therefore, telomere attrition owing to oxidative stress in somatic cells may serve as a cumulative marker of chronic stress, and provides a link between stress and age-related psychological problems.[8] Several studies have indicated that there is a strong relationship between early-life stress and poor health outcomes associated with shortened telomere length.[4,8]

There is some evidence of an association between child maltreatment and telomere length, but studies are subject to limited sample sizes and inconsistent child maltreatment measures. Some previous studies have found that children exposed to more stress have a shorter telomere length even at a young age, with evidence of a dose-dependent association between childhood stress and telomere length.[1,14–16] Most of the existing studies on adverse early experiences are small, with one meta-analysis including only 30 773 participants in total, with the large majority having telomere length measured as children, adolescents and younger adults.[1] To our knowledge, only one study has investigated the association between adverse early experiences and telomere shortening in older people,[16] but they did not include being abused or neglected in childhood as adverse events. Hence, it is currently unknown



https://doi.org/10.1192/bjp.2023.33 Published online by Cambridge University Press

whether maltreatment in childhood is associated with telomere length in middle-age and older adults. This study aimed to use data on UK Biobank participants to study whether and to what extent child maltreatment is associated with telomere length in middle and older age.

## Method

### Study design and participants

This is a retrospective cohort study. Between 2007 and 2010, the UK Biobank recruited 502 488 participants from the general population. The participants attended one of 22 assessment centres across England, Scotland and Wales, where they completed an online questionnaire and underwent a personal interview. The information collected at baseline included household data (postcode, rented/owned accommodation, number of people in household), sociodemographic information (age, gender, highest educational level, employment status, car ownership and ethnic group) and lifestyle information (tobacco and alcohol consumption, and completion of the standard Physical Activity Questionnaire). Postcode was used to derive Townsend area deprivation indices for the participants, which is a composite area-based measure derived from unemployment, car ownership, household overcrowding and owner occupation, with higher scores indicating higher levels of deprivation.[17,18]

### Child maltreatment and mental health

Participants were invited to complete an online mental health questionnaire.[19] Overall, 157 348 (31.3%) participants completed the questionnaire, but 5308 were excluded for incomplete data, resulting in 152 040 usable responses. The online questionnaire measured current symptoms of depression and PTSD, using two well-established tools: the Patient Health Questionnaire-9 (PHQ-9) and Post-Traumatic Stress Disorder Check List – Civilian Short Version (PCL-S). Specifically, the PHQ-9 measures depression severity via the frequency of nine items, ranging from 0 (not at all) to 3 (nearly every day). All items are summed to provide a total score of depression severity, with higher scores indicating more severe symptoms. Previous work has demonstrated the validity and reliability of the use of this scale in the UK Biobank.[20] The PCL-S consists of five items that map onto the DSM-IV criteria.[21]

The mental health questionnaire also included an assessment of child maltreatment with the Childhood Trauma Screener,[4] a shortened version of the Childhood Trauma Questionnaire (CTQ). It consists of one five-point Likert scale item for each of five types of child maltreatment (physical abuse, physical neglect, emotional abuse, emotional neglect and sexual abuse), and has been validated against the CTQ with good overall ($r = 0.88$) and satisfactory type-specific ($r = 0.55$–$0.87$) correlations.[4] The CTQ is a widely used instrument for measuring child maltreatment and has been validated against actual records of abuse and neglect, and threshold values on the Likert scale derived from the validation study[22] were used to define the presence or absence of each type of child maltreatment. In this study, the primary exposure variable was the number of types of child maltreatment (range 0–5), as it reflects the dimensions of maltreatment.

### Telomere length

Detailed information on measurement of telomere length in the UK Biobank has been provided elsewhere.[23] Briefly, DNA was extracted from peripheral blood leukocytes. Telomere length was assayed with quantitative polymerase chain reaction. The assay results were presented as a relative ratio of the telomere repeat copy number (T) to a single-copy gene (S). The calculated T/S ratios were then adjusted for technical variation, log-transformed and *Z*-standardised so that they approximated to a normal distribution with mean of 0 and s.d. of 1.

### Statistical analyses

Multivariable linear regression was used to study the association between frequency and types of maltreatment and telomere length. We first examined the association between maltreatment frequency and telomere length by using the number of types of maltreatment (0, 1, 2 or ≥3) and the presence or absence (yes/no) of each of the five types of maltreatment (physical abuse, emotional abuse, sexual abuse, physical neglect and emotional neglect), which were mutually adjusted. For each of the outcomes, we adjusted for age, gender, ethnicity, level of deprivation and educational attainment, as these are likely to have affected the exposure to and recall of child maltreatment, as well as telomere length.

Three additional analyses were undertaken. First, the models were then re-run, adjusting for symptoms of depression and PTSD. These were not included in the main analysis because they could be mediators. Second, the frequency of maltreatment was categorised as rarely, sometimes or often/very, to examine the dose–response relationship. Third, moderator analyses were conducted on the main model to investigate whether the association between child maltreatment and telomere length varied by age (<60 *v.* ≥60 years), gender (male versus female), frequency of being able to confide (none versus any), frequency of social visits with family and friends (none versus any), alcohol drinking (<14 *v.* ≥14 units/week), depression (yes versus no) and PTSD (yes versus no). These moderators were analysed separately to avoid dimensionality problems, and were selected because there is prior evidence showing that the effect of trauma on health could differ by these variables.[24,25]

### Ethics approval

The UK Biobank received ethics approval from the Northwest Multi-Centre Research Ethics Committee (reference number 11/NW/03820). All participants gave written informed consent before enrolment in the study, which was conducted in accordance with the principles of the Declaration of Helsinki. Direct dissemination of the results to participants is not possible/applicable.

## Results

Of the 153 623 UK Biobank participants who completed the mental health questionnaire, 8595 (5.6%) and 3280 (2.1%) were excluded because of no valid telomere length or covariate data, respectively. Therefore, the sample size was 141 748 (Supplementary Fig. 1 available at https://doi.org/10.1192/bjp.2023.33).

Table 1 shows the participant characteristics broken down by child maltreatment frequency. Both any type of child maltreatment and multiple types of child maltreatment were more commonly reported by women, Black and South Asian participants, those who lived in more deprived areas, those who did not have a university degree and those who reported more severe symptoms of depression and PTSD. There was no association between child maltreatment and telomere length in univariate analysis (Table 1).

After adjusting for sociodemographic characteristics, participants with three or more types of maltreatment presented with the shortest telomere lengths ($\beta = -0.05$, 95% CI −0.07 to −0.03; $P < 0.0001$), followed by those with two types of maltreatment ($\beta = -0.02$, 95% CI −0.04 to 0.00; $P = 0.02$), referent to those who had none (Fig. 1). The telomere lengths of those who had one



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**Table 1** Participant characteristics

| | Number of maltreatment types | | | | |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | ≥3 | *P*-value |
| Total *n* | 94 932 | 28 682 | 10 755 | 7379 | |
| Age, years, mean (s.d.) | 56.11 (7.71) | 55.78 (7.73) | 55.23 (7.79) | 54.12 (7.71) | <0.0001 |
| Male | 42 809 (45.1) | 12 880 (44.9) | 4238 (39.4) | 2349 (31.8) | <0.0001 |
| Ethnicity | | | | | <0.0001 |
| White | 93 090 (98.1) | 27 705 (96.6) | 10 251 (95.3) | 6818 (92.4) | |
| South Asian | 600 (0.6) | 295 (1.0) | 130 (1.2) | 109 (1.5) | |
| Black | 395 (0.4) | 210 (0.7) | 137 (1.3) | 193 (2.6) | |
| Chinese | 129 (0.1) | 101 (0.4) | 49 (0.5) | 41 (0.6) | |
| Mixed | 336 (0.4) | 186 (0.6) | 92 (0.9) | 120 (1.6) | |
| Any other | 382 (0.4) | 185 (0.6) | 96 (0.9) | 98 (1.3) | |
| Deprivation index, mean (s.d.) | −1.90 (2.72) | −1.56 (2.88) | −1.29 (3.02) | −0.80 (3.25) | <0.0001 |
| College or University degree | 44 577 (47.0) | 12 915 (45.0) | 4585 (42.6) | 2972 (40.3) | <0.0001 |
| PHQ-9, mean (s.d.) | 2.20 (3.05) | 3.23 (3.86) | 4.22 (4.65) | 5.45 (5.70) | <0.0001 |
| PCL-S, mean (s.d.) | 1.23 (2.19) | 2.02 (2.92) | 2.97 (3.56) | 4.38 (4.39) | <0.0001 |
| Log(T/S ratio), *z*-score, mean (s.d.) | 0.05 (0.99) | 0.06 (1.00) | 0.06 (1.00) | 0.07 (0.98) | 0.16 |

Numbers presented are mean (s.d.) unless otherwise specified. PHQ-9, Patient Health Questionnaire-9; PCL-S, Post-Traumatic Stress Disorder Check List – Civilian Short Version; T/S, relative ratio of the telomere repeat copy number to a single-copy gene.

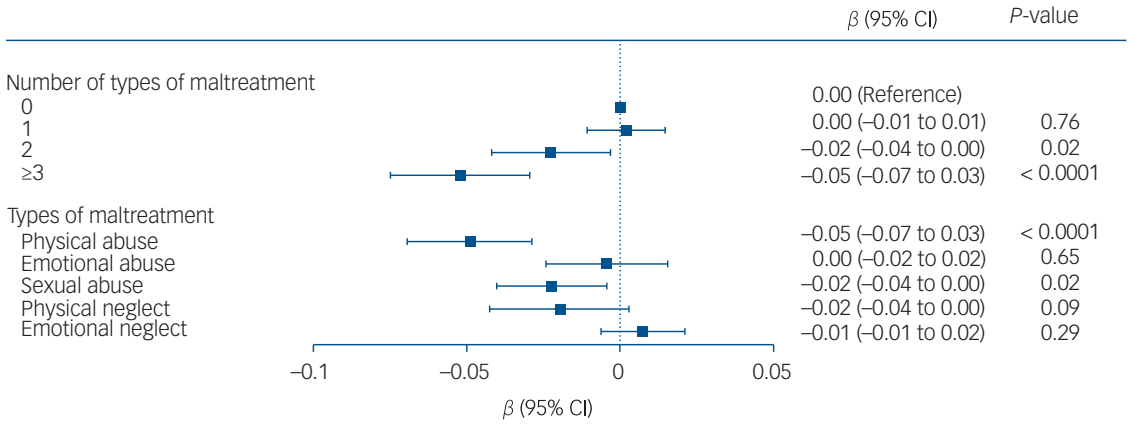


**Fig. 1** Association between maltreatment frequency and telomere length. Adjusted for age, gender, ethnicity, level of deprivation and education attainment.

type of maltreatment were not significantly different from those who had none. When mutually adjusted, physical abuse ($\beta = -0.05$, 95% CI −0.07 to −0.03; $P < 0.0001$) and sexual abuse ($\beta = -0.02$, 95% CI −0.04 to 0.00; $P = 0.02$) were independently associated with shorter telomere length. When adjusted for depression and PTSD, the telomere lengths of participants with three or more types of maltreatment were still significantly shorter ($\beta = -0.04$, 95% CI −0.07 to −0.02; $P = 0.0008$), and the association with physical abuse remained significant ($\beta = -0.05$, 95% CI −0.07 to −0.03; $P < 0.0001$). (Supplementary Figure 2). Dose–response relationships were observed by frequency of physical and sexual abuse (Table 2).

Table 3 shows the moderation analysis results. The associations between child maltreatment and telomere length were generally consistent across subgroups except for age, where the association was weaker in older people ($\beta_{interaction} = 0.01$, 95% CI 0.00–0.03; $P = 0.04$).

## Discussion

Our study demonstrates that child maltreatment was associated with telomere length in middle and older-aged adults. The associations were strongest for physical and sexual abuse, and there was also evidence of dose–response relationships for these two types of abuse. Depression and PTSD appeared to partially explain the association. These findings echoes previous studies in physical[26] and mental[27] health outcomes.

### Strengths and weaknesses

One of the strengths of using UK Biobank data was a large sample size ($N = 141\,748$) of middle- and older-age adults, providing sufficient power to detect differences, even by subgroup. Additionally, we were able to explore the association of both the frequency and types of maltreatment with telomere length, and therefore demonstrate a dose–response relationship for both physical and sexual abuse. Some limitations and considerations should be acknowledged. We hypothesised that the number of types of maltreatment would indicate cumulative association regardless of the combination, but we did not find such evidence in this study. There were a small number of cases in each of the combinations of the maltreatment types. There could be residual confounding in this study, such as the fact that we did not adjust for antidepressant use. Child maltreatment was recalled by participants rather than having it recorded prospectively, a common disadvantage of the long-term outcomes of childhood exposures. This could have led to recall bias if attribution of childhood events is associated with mental



https://doi.org/10.1192/bjp.2023.33 Published online by Cambridge University Press

**Table 2** Association between child maltreatment frequency and telomere length

| | Rarely true | | Sometimes true | | Often/very often true | |
|---|---|---|---|---|---|---|
| | β (95% CI) | *P*-value | β (95% CI) | *P*-value | β (95% CI) | *P*-value |
| Physical abuse | −0.02 (−0.04 to 0.00) | 0.01 | −0.05 (−0.07 to −0.03) | <0.0001 | −0.08 (−0.12 to −0.03) | 0.0004 |
| Emotional abuse | −0.01 (−0.03 to 0.01) | 0.24 | −0.03 (−0.05 to −0.01) | 0.008 | −0.02 (−0.05 to 0.01) | 0.29 |
| Sexual abuse | −0.01 (−0.03 to 0.01) | 0.40 | −0.04 (−0.07 to −0.02) | 0.002 | −0.07 (−0.12 to −0.02) | 0.006 |
| Physical neglect | −0.03 (−0.09 to 0.04) | 0.44 | 0.00 (−0.04 to 0.05) | 0.85 | 0.03 (−0.01 to 0.06) | 0.10 |
| Emotional neglect | −0.01 (−0.06 to 0.04) | 0.75 | 0.02 (−0.03 to 0.06) | 0.40 | 0.02 (−0.02 to 0.06) | 0.37 |

Adjusted for age, gender, ethnicity, level of deprivation and education attainment.

**Table 3** Moderation analysis for the association between child maltreatment and telomere length

| | $\beta_{interaction}$ (95% CI) | *P*-value |
|---|---|---|
| Age ≥60 years | 0.01 (0.00–0.03) | 0.04 |
| Male | 0.01 (0.00–0.02) | 0.09 |
| Frequency of being able to confide | 0.01 (−0.01 to 0.02) | 0.35 |
| Frequency of social visits with family and friends | 0.03 (−0.08 to 0.14) | 0.64 |
| Alcohol drinking | 0.01 (0.00–0.02) | 0.19 |
| Depression | −0.01 (−0.02 to 0.01) | 0.28 |
| Post-traumatic stress disorder | −0.01 (−0.02 to 0.00) | 0.18 |

Adjusted for age, gender, ethnicity, level of deprivation and education attainment.

health problems. Another limitation was that child maltreatment information was limited to type and frequency, and the temporality of the exposure was not measured. Finally, the potential mechanism between child maltreatment and telomere length was not examined, which warrants future study.

## Comparison with existing literature

In this study, we found associations between childhood maltreatment and telomere length in middle- and older-aged adults, which meaningfully extends the literature. Although previous studies reported similar findings in children, young adults, middle-aged women and older adults,[1,14,15,28] the sample sizes were small and often not sampled from the general population.[1] In the Nurses' Health Study II,[15] presence of abuse was associated with shorter telomere length but no graded association by severity was observed. This was in contrast to our findings, where both number of types and frequency of maltreatment had dose–response associations with telomere length.

Interestingly, the association between maltreatment and telomere length was slightly weaker in older individuals, which is in contrast to a previous study which found that child maltreatment is directly correlated with the rate of telomere attrition.[29] However, we should note that our findings might be subject to survival bias, as people who had experienced maltreatment could die earlier and might not be included in the UK Biobank,[30] or it could reflect exposome differences.[12]

Although it is not entirely clear how child maltreatment could accelerate telomere shortening, psychological stress is a potential mechanism.[31] It has been consistently shown that child maltreatment sometimes leads to a traumatic stress response, which could alter the individual's long-term response to stress.[32] Cumulative chronic stress could induce higher oxidative stress levels,[33] which accelerates telomere attrition,[34] and lower telomerase activity,[35] which inhibits telomere maintenance.[31] These ultimately manifest as a measurable difference in telomere length in later life.

## Implications

It is still under debate whether telomere length is a causal agent for clinical diseases.[36] Telomere length remains a modest marker of biological ageing, with significant interindividual variability.[37] Although genetically predicted shorter telomere length has been associated with higher risk of cardiovascular disease,[38] cardiovascular disease is not a common complication of dyskeratosis congenita,[39] which is a genetic disorder resulting in critically short telomere length. Regardless of the biological role of telomeres, the association we found in this study indicates that individuals suffering maltreatment in childhood are likely to suffer from shorter telomere length, possibly as an indicator of biological ageing. This may explain why victims of child maltreatment experience a multitude of mortality and morbidity risks[26,27,40,41] – the elevation in risk is simply a reflection of the individual's 'true' biological age.[42,43] If this hypothesis is correct, interventions that could reduce the telomere shortening process (e.g. by reducing chronic perceived stress[32]) among victims of maltreatment might be effective in preventing multiple conditions.

To conclude, our findings indicate that child maltreatment is associated with shorter telomere length in middle- and older-aged adults, independent of sociodemographic and mental health factors.

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First received 7 Sep 2022, final revision 22 Feb 2023, accepted 22 Feb 2023

## Supplementary material

To view supplementary material for this article, please visit http://doi.org/10.1192/bjp.2023.33

## Data availability

The data that support the findings of this study can be requested from the UK Biobank (https://www.ukbiobank.ac.uk/).

## Acknowledgements

We are grateful to all UK Biobank participants. This study was conducted under the UK Biobank project 7155.

## Author contributions

Z.Z. wrote the first draft of the paper and analysed the data. C.K.M.L., K.L.C., R.S.Y.C., J.P.P., H.M. and P.G.S. interpreted the data and critically revised the manuscript. P.I. conceptualised this study, interpreted the data and critically revised the manuscript. F.K.H. conceptualised this study, analysed the data, and critically revised the manuscript. All authors approved the final submitted manuscript.



https://doi.org/10.1192/bjp.2023.33 Published online by Cambridge University Press

## Funding

This study was funded by the Glasgow Children's Hospital Charity (project number GCHC/SPG/2021/05) to F.K.H. and by the Hong Kong Research Grants Council (project number PolyU 15602419) and The Hong Kong Polytechnic University (project code 1-ZE1R) to K.L.C.

## Declaration of interest

None.

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https://doi.org/10.1192/bjp.2023.33 Published online by Cambridge University Press