Environmental Science and Pollution Research (2023) 30:71131–71140
https://doi.org/10.1007/s11356-023-27428-w

RESEARCH ARTICLE

Association between mixed exposure of polycyclic aromatic hydrocarbons and telomere length in general population: NHANES 2001–2002

Daheng Yang[1] · Xiaoqin Chen[1] · Weidong Cao[2] · Cheng Xu[3] · Lin Chang[1] · Guangfeng Long[1]

Received: 13 February 2023 / Accepted: 1 May 2023 / Published online: 10 May 2023

Abstract

Although an association between single polycyclic aromatic hydrocarbons (PAHs) adult exposure and telomere length has been reported, the evidence of mixed PAHs (1-napthol, 2-napthol, 3-fluorene, 2-fluorene, 3-phenanthrene, 1-phenanthrene, 2-phenanthrene, and 1-pyrene) exposure and telomere length in the adult general population is still not clear. A total of 1460 adults over the age of 20 years provided urine information on 8 PAHs and selected covariates from the 2001–2002 National Health and Nutrition Examination Survey (NHANES). Bayesian nuclear machine regression (BKMR) was conducted to analyze these associations of telomere length in multiple PAH-exposed environments. Linear regression is mainly used for correlation analysis of PAHs with selected covariate adjustments. Restricted cubic spline (RCS) is used to estimate the correlation between selected PAHs and telomere length. After adjusting for potential covariates, PAHs mixed exposure was negatively associated with telomere length. The linear regression results showed that 2-napthol and 2-fluorene were negatively correlated with telomere length. Telomere length decreased by 1.0% in the fully adjusted model per increment of one unit in the base-10-logarithm-transformed 2-napthol and 2-fluorene concentrations ($P = 0.030$ and 0.049, respectively). However, the other 6 PAH metabolites were not significantly different. In addition, RCS results showed that 2-napthol has a marginal dose effect relationship with telomere length. Our present study suggested that PAHs are negatively associated with telomere length in the general population of the USA. Considering that the low level of PAHs exposure in the general population can also induce reduced telomere length and potential health risks, future research is needed to explore potential mechanisms.

Keywords Polycyclic aromatic hydrocarbon · Telomere length · BKMR · NHANES

Introduction

Polycyclic aromatic hydrocarbons (PAHs) are chemical substances that naturally exist in gasoline, crude oil, and coal. Breathing is the main exposure route to PAHs among the general population (Shi et al. 2022). In addition, eating food and drinking water containing PAHs are also one of the sources of exposure, and skin contact is also considered another potential exposure route. Previous studies have found that PAHs could increase the risk of lung cancer and cardiovascular disease (Mallah et al. 2022, Wang et al. 2022) and nervous system disorders (Das and Ravi 2022). However, whether PAHs affect the reduced effect of telomere length in epidemiology is currently an unexplored question.

Telomeres are regions at the end of chromosomes that repeat DNA sequences. Telomeres can help maintain genetic integrity and are believed to be closely related to aging and cancers (Barrett et al. 2015, Lansdorp 2022).

Responsible Editor: Lotfi Aleya

Daheng Yang, Xiaoqin Chen, and Weidong Cao contributed equally to the present study and should be regarded as joint first authors.

✉ Guangfeng Long
szwlgfzays@163.com

[1] Department of Clinical Laboratory, Children's Hospital of Nanjing Medical University, 72 Guangzhou Road, Nanjing 210008, People's Republic of China

[2] Nanjing Key Laboratory of Pediatrics, Children's Hospital of Nanjing Medical University, Nanjing, China

[3] School of Public Health, Nanjing Medical University, Nanjing, China

Telomere length (TL) is a complex hereditary trait that is related to cancers and age-related diseases (Srinivas et al. 2020). TL was considered one of the best biomarkers of aging and to estimate the risk for age-related diseases and mortality (Herrmann and Herrmann 2020, Vaiserman and Krasnienkov 2020). Previous evidence has supported that environmental chemicals are associated with telomere length. Astuti et al. observed that the telomere length of smokers is shorter than that of nonsmokers (Astuti et al. 2017). Isaevska et al. reviewed that exposure to ambient air pollution during pregnancy is associated with shortened telomere length (Isaevska et al. 2021). Fernandes et al. summarized that exposure to persistent organic pollutants such as polychlorinated biphenyls, volatile organics benzene and toluene, pesticide mixtures, and heavy metals may affect telomere homeostasis (Fernandes et al. 2021). This evidence suggests that exposure to environmental chemicals may cause telomere length shortening. It is worth mentioning that the real environment is often a mixed exposure situation, and the mixed exposure effect rather than the single environmental chemicals may be more able to reflect the actual exposure situation and health effects. National Institutes of Health recommends paying more attention to the health effects of mixed exposure (Taylor et al. 2016). In recent years, there has been concern about populations exposed to polyfluoroalkyl substances and polybrominated diphenyl ethers mixed exposure (Eick et al. 2021), metal mixture exposure (Cowell et al. 2020), benzene, toluene, ethylbenzene, and xylene mixture (Niu et al. 2022), which may shorten the length of the telomere in epidemiological studies. It was found that the mixed exposure of these environmental chemicals was correlated with telomere length. However, studies on PAHs mixed exposure and single PAHs exposure and telomere length are scarce.

In this study, the National Health and Nutrition Examination Survey (NHANES), a national survey and publicly available database, was used to extract the population for the detection of telomere length and PAHs exposure. After adjusting for bias factors, we analyzed the association between single and combined PAHs and TL. Subsequently, we show the dose–response relationship between PAHs and telomere length through restricted cubic spline (RCS). In addition, sensitivity analysis was conducted to verify the robustness of our results.

Method

Study population

The NHANES is a research program designed to evaluate the health and nutrition status of adults, adolescents, and children in the USA. We merged laboratory tests, information from questionnaires, and physical examinations using unique survey participant identifiers, and we linked the database of laboratory tests to other NHANES databases. The inclusion criteria were subjects who had PAHs level data and information on telomere length. The exclusion criteria were lacked of PAHs detection data, lacked of telomere length data, and pregnancy. Flow chart of the selection process of the participants is shown in Fig. 1. Finally, 1460 individuals were included in our retrospective study, with 716 males and 744 females. Our present study is a cross-sectional analysis of NHANES data from 2001 to 2002 because telomere length was measured only in 1999–2002. The NCHS Institutional Review Committee approved the NHANES protocol, and signed informed consent forms were obtained.

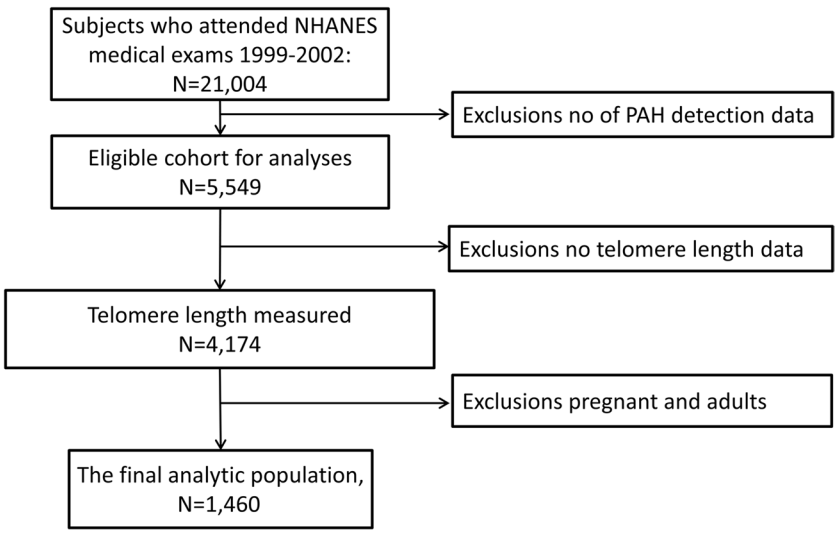

Fig. 1 Eligible participants and those included in the analyses of the associations between urinary polycyclic aromatic hydrocarbon levels and telomere length. NHANES, National Health and Nutrition Examination Survey; PAH, polycyclic aromatic hydrocarbon

Urinary PAHs metabolite measurement

For the detailed detection method of PAHs, information about laboratory procedures is reported on the official website (CDC, https://wwwn.cdc.gov/nchs/data/nhanes/2003-2004/labmethods/l31pah_c_met.pdf). In brief, isotope dilution capillary gas chromatography-tandem mass spectrometry (Thermo Finnigan, Bremen, Germany) was used to measure urinary PAHs metabolites, including enzymatic hydrolysis of glucuronidated/sulfated OH-PAHs metabolites, extraction, derivatization, and analysis. A total of 8 urinary PAHs metabolites (1-napthol, 2-napthol, 3-fluorene, 2-fluorene, 3-phenanthrene, 1-phenanthrene, 2-phenanthrene, and 1-pyrene) were determined from spot urine specimens.

Telomere length measurement

After home interviews, blood samples were collected from subjects at a mobile screening center, and DNA samples from the blood were stored at the CDC's National Center for Environmental Health laboratory. Quantitative polymerase chain reaction (PCR) methods were performed to measure telomere length ratios (T/S ratios) relative to standard reference DNA samples as previously reported (Cawthon 2002). The samples were analyzed on repeated wells to obtain 6 data points for every sample. Control DNA values were used to normalize run-to-run variability. Each DNA sample was analyzed three times over 3 days. All potential outliers were identified and excluded from the calculation for each sample (<2% of the sample).

Covariates

Sociodemographic information, such as age, sex, race/ethnicity, body mass index (BMI), education, serum cotinine, poverty income ratio (PIR), and creatinine, were obtained by the trained staff according to standardized procedures. The above data were acquired through participant interviews, physical examination, and biological sample collection. Race was divided into a total of five categories (Mexican–American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other races). There were also five categories of education level: "less than 9th grade," "9–11th grade," "high school graduate/GED or equivalent," "some college or AA degree," and "college graduate or above." Serum cotinine, a marker of environmental smoking exposure, was regarded as smoking exposure in our present study. We performed log transformation as covariate adjustment. The PIR indicator is used to estimate the ratio of household income to the poverty threshold. We divide the PIR variable into two categories: (a) less than 1 or (b) greater than or equal to 1. BMI is the weight (kilogram) divided by the square of height (meter), and we regarded BMI as a three-category variable (< 25 kg/m^2, 25–30 kg/m^2, and ≥ 30 kg/m^2).

Statistical analysis

The Mann–Whitney *U* test and Fisher's exact test or the chi-squared test were used to compare the differences in continuous and categorical variables. We performed linear regression to evaluate the correlations between each PAHs and TL. Model 1 was adjusted for age, and model 2 was additionally adjusted for race, BMI, PIR, serum cotinine categorical variable, and education levels. Urinary creatinine was adjusted in models 1 and 2. Missing categorical covariates were replaced with extrema. We used the Bayesian kernel machine regression (BKMR) method to calculate the association of PAHs mixture exposure with telomere length (Bobb et al. 2015). In this study, we utilized the BKMR model to estimate the cumulative effect of a mixture of PAHs on TL. We presented posterior means and 95% posterior credible intervals to demonstrate the expected change in TL associated with concurrent changes in all PAHs of the mixture from their median level. Using hierarchical variable selection, we identified the most important PAHs within the mixture and presented conditional-PIPs from the BKMR. We also displayed the difference in TL level for a change in PAHs concentration between the 25th and 75th percentile for each PAHs in the mixture, when other PAHs were fixed at either the 25th, 50th, or 75th percentile levels. PAH-specific exposure-response curves and potential interactions among the PAHs were also presented by estimating the predicted telomere length level for each level of the PAHs of interest, while holding all other PAHs exposure at the median, 25th, or 75th percentile. Due to the lack of PAHs detection data in some subjects, some samples were not detected for PAHs concentrations. When we analyzed the relationship between mixed PAHs exposure (BKMR analysis) and telomere length, we only included all eight PAH-tested subjects. We divided PAHs by creatinine as another indicator of PAHs internal exposure, observed the association between this indicator and telomere length, and took this part of the results as the content of the sensitivity analysis. The results of the associations of single PAHs and telomere length are presented as the average percent difference and 95% confidence interval (CI), as in a previous study (Huang et al. 2019). Briefly, we first computed the interquartile range (IQR) of PAHs. Then, the percent difference (%) was equal to (IQR ^ beta-1)∗100% (Xu et al. 2021). We used the *BKMR* packages in R software (version 3.5.0) in the present analyses. We conducted other analyses by using Stata version 14.0 (StataCorp). We considered a two-sided value of *P* less than 0.05 to be statistically significant.

Result

Baseline information of the study population

Of the 1460 subjects included in the study, the TL length was 105.1 ± 26.7 (Table 1). The telomere length of the three age groups, 20–39, 40–59, and above 60, was 117.9 ± 26.8, 104.4 ± 22.7, and 91.0 ± 23.3 mean T/S ratio, respectively, showing a gradual decrease ($P<0.001$). The telomere lengths of men and women were 102.6 ± 25.4 and 107.6 ± 27.7, respectively. The telomere length of women was higher than that of men ($P<0.001$). There were differences in telomere length among different ethnic groups, education levels, and BMI classifications ($P=0.033$, 0.008, and 0.003, respectively), while no difference was observed in telomere length between different subjects of cotinine and PIR classification ($P=0.375$ and 0.289, respectively).

The distribution of eight PAHs is shown in Table S1. We used Pearson's correlation analysis to study all 8 pairs of PAHs in the population ($N=1460$) to determine the interaction between PAHs and PAHs in the PAHs mixture, as shown in Fig. S1. Notably, moderate correlation coefficients were shown between 3-fluorene and 2-fluorene (Pearson's correlation coefficient $R^2 = 0.77$), 2-fluorene and 2-phenanthrene ($R^2 = 0.60$), and 1-phenanthrene and 2-phenanthrene ($R^2 = 0.54$), all of which were statistically significant (Fig. S1).

We determined the association of mixed PAHs and telomere length by performing the BKMR model. Figure 2 presents the entire association between the PAHs mixtures and telomere length. The most common PAH mixtures were associated with a decreased telomere length, suggesting a negative association between mixed PAHs and telomere length. Figure 3 shows the change trend of the exposure

Table 1 Demographic and clinical characteristics of the study population from NHANES 2001 to 2002

Covariate	Participants (numbers)	Telomere length (T/S ratio × 100)	*P* value
Total	1,460	105.1 ± 26.7	
Age (years)			<0.001
20–39	521	117.9 ± 26.8	
40–59	497	104.4 ± 22.7	
< 60	442	91.0 ± 23.3	
Gender			< 0.001
Male	716	102.6 ± 25.4	
Female	744	107.6 ± 27.7	
Race/ethnicity			0.033
Non-Hispanic White	304	104.7 ± 20.4	
Non-Hispanic Black	59	106.0 ± 23.6	
Mexican American	798	104.2 ± 29.1	
Other race — including multi-racial	255	108.4 ± 26.7	
Other Hispanic	44	105.9 ± 23.4	
Education level			0.008
Less than 9th grade	193	99.4 ± 21.6	
9–11th grade	227	103.2 ± 26.6	
High school grad/GED or equivalent	343	106.2 ± 29.5	
Some college or AA degree	380	106.4 ± 26.7	
College graduate or above	315	107.3 ± 26.0	
BMI (kg/m^2)			0.003
<25	443	109.2 ± 29.8	
25–30	519	104.5 ± 25.6	
>30	433	102.6 ± 24.0	
Serum cotinine (ng/mL)			0.375
<LOD	313	102.9 ± 26.3	
LOD-10	783	105.7 ± 26.5	
>10	352	105.9 ± 27.6	
PIR			0.289
<1	222	108.8 ± 30.5	
≥1	1,158	104.6 ± 25.9	

BMI, body mass index; *PIR*, income-to-poverty ratio; *LOD*, limit of detection

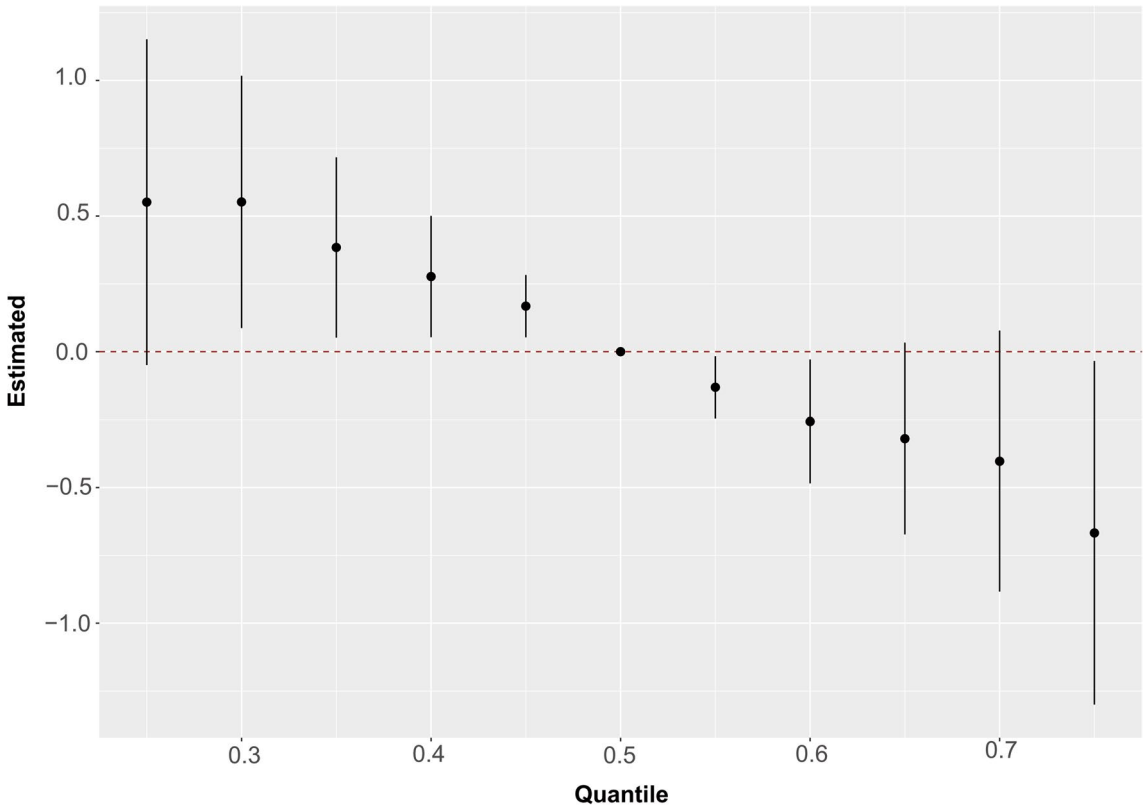

Fig. 2 Joint effect (95% CI) of polycyclic aromatic hydrocarbon mixtures (1-napthol, 2-napthol, 3-fluorene, 2-fluorene, 3-phenanthrene, 1-phenanthrene, 2-phenanthrene, 1-pyrene) on telomere length by the BKMR model when all polycyclic aromatic hydrocarbons at particular percentiles were compared to all chemicals at their 50th percentile. The results were adjusted for age, race, sex, education level, serum cotinine, poverty income ratio, body mass index, and creatinine

reaction function of all 8 PAHs based on the potential nonlinear and nonadditive effects among the eight PAHs. The other seven PAHs were fixed at their intermediate levels, and the 2-napthol exposure level levels with telomere length decreased within a certain concentration range. The other 7 PAHs were not associated with telomere length. Table S2 lists each PAHs in the urinary samples and the posterior inclusion probability (PIP) from the BKMR model of telomere length. Among the eight PAHs, 2-napthol had the highest PIP of 0.2346. The PIPs of 2-napthol and 2-fluorene were higher than 0.2, suggesting a significant correlation with telomere length.

Due to the nonnormal distribution of each PAHs variable, we performed log transformation of PAHs variables and conducted linear regression analysis to evaluate the association between each PAHs and telomere length, as listed in Table 2. In model 1, each increment of one unit in the base-10-logarithm-transformed 2-napthol and 2-fluorene caused decreases of 1.0% (95% CI, −1.0, −0.8, P = 0.018) and 1.0% (95% CI, −1.0, −0.4, P = 0.030) in telomere length, respectively. In the fully adjusted model, 2-napthol and 2-fluorene exposure were associated with 1.0% reduced telomere length (P = 0.030 and 0.049). Multivariate analysis of the other PAHs suggested no significant associations.

We performed RCS to visualize the relationship between PAHs and telomere length (Fig. 4). With increasing concentrations of 2-napthol and 2-fluorene, the length of both substances decreased gradually, although there was no significant difference (2-napthol, P nonlinearity = 0.808, P total= 0.092; 2-fluorene, P nonlinearity = 0.460, P total= 0.541).

In the sensitivity analyses, we used PAHs divided by creatinine as an exposure indicator; rather than creatinine as a covariate in the statistical analysis, we observed no significant differences in the percentage change (Table S3).

Discussion

Through a large sample of the general population, this study found that PAHs combined exposure was negatively correlated with telomere length, in which 2-napthol and 2-fluorene contributed more, and 2-napthol and 2-fluorene single exposure were both negatively associated with telomere length. Moreover, 2-napthol and 2-fluorene also showed a marginal dose effect relationship with telomere length.

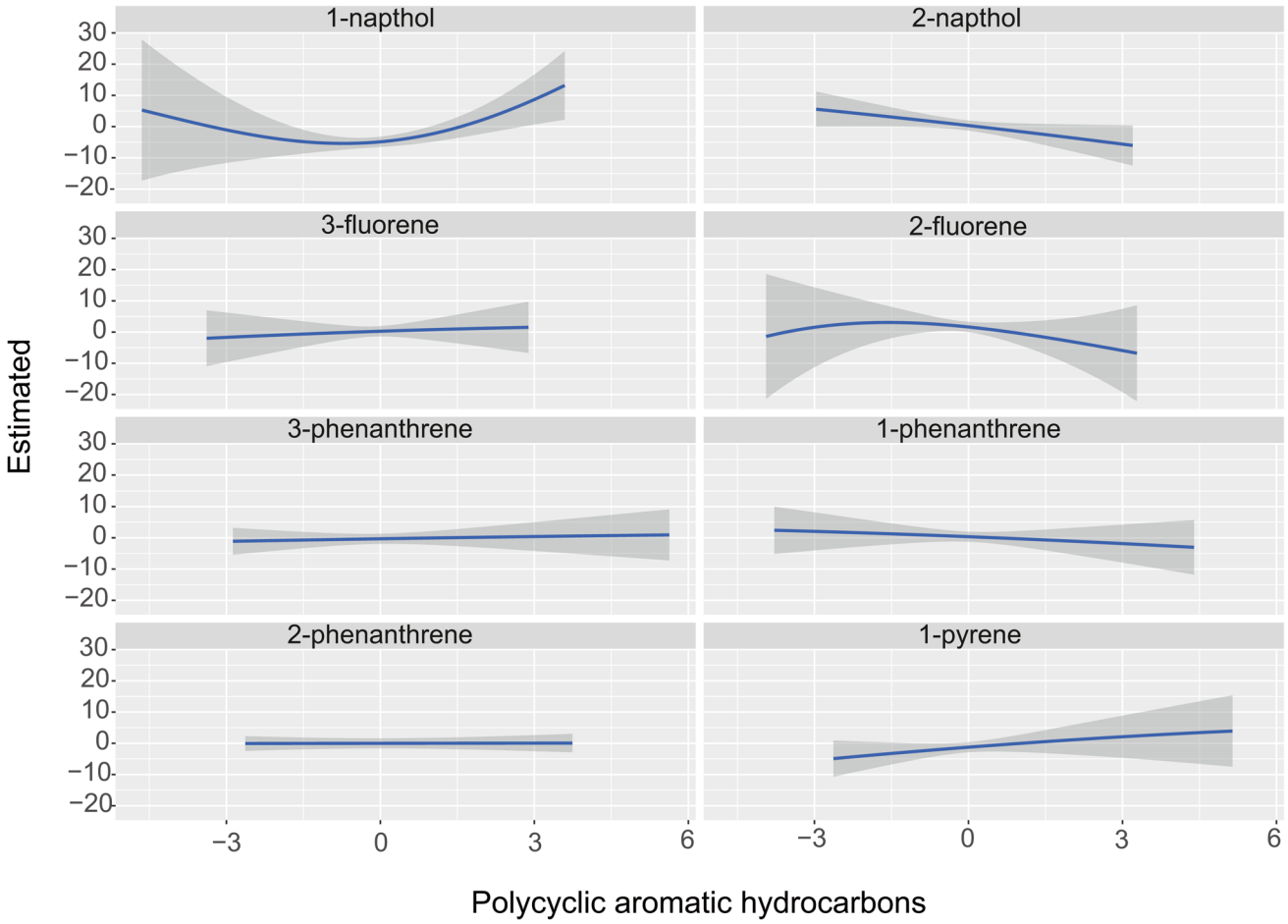

Fig. 3 Univariate exposure response function (95% CI) between the polycyclic aromatic hydrocarbon concentration and telomere length, while the concentration of other chemicals was fixed at the median. The vertical axis can be interpreted as the relationship between polycyclic aromatic hydrocarbons and telomere length. The results were assessed using the BKMR model, which was adjusted for age, race, sex, education level, serum cotinine, poverty income ratio, body mass index, and creatinine in the study population

A previous review summarized that occupational exposure to PAHs can cause a decrease in telomere length (Zhang et al. 2013). Subsequently, other researchers verified the above conclusions through the following larger sample of occupational population. Zhang et al. measured urine biomarkers of PAHs exposure in 692 coke oven plant workers. They observed that the median concentration of 1-hydroxypyrene was 0.09 ng/ml and was associated

Table 2 Adjusted difference changes and 95% confidence intervals in the lymphocyte telomere length per 1 increment in the log-transformed value of polycyclic aromatic hydrocarbons in US adults (2001–2002)

	Model 1			Model 2		
PAHs	%	95% CI	*P*	%	95% CI	*P*
1-Napthol	4.61	−0.99, 20.89	0.574	15.35	−0.98, 27.52	0.405
2-Napthol	−1.00	−1.00, −0.76	0.018	−1.00	−1.00, −0.58	0.03
3-Fluorene	−0.95	−1.00, 0.20	0.065	−0.97	−1.00, 0.71	0.087
2-Fluorene	−0.99	−1.00, −0.39	0.030	−1.00	−1.00, −0.04	0.049
3-Phenanthrene	−0.40	−0.96, 8.16	0.714	−0.37	−0.96, 10.37	0.76
1-Phenanthrene	−0.85	−1.00, 5.62	0.326	−0.87	−1.00, 5.79	0.313
2-Phenanthrene	−0.50	0.94, 3.07	0.513	−0.39	−0.93, 4.49	0.664
1-Pyrene	−0.57	−0.95, 2.83	0.488	−0.28	−0.93, 6.64	0.787

PAHs, polycyclic aromatic hydrocarbons; *CI*, confidence intervals. Model 1, age. Model 2, model 1 plus gender, race, education levels, BMI category, PIR category, and serum cotinine

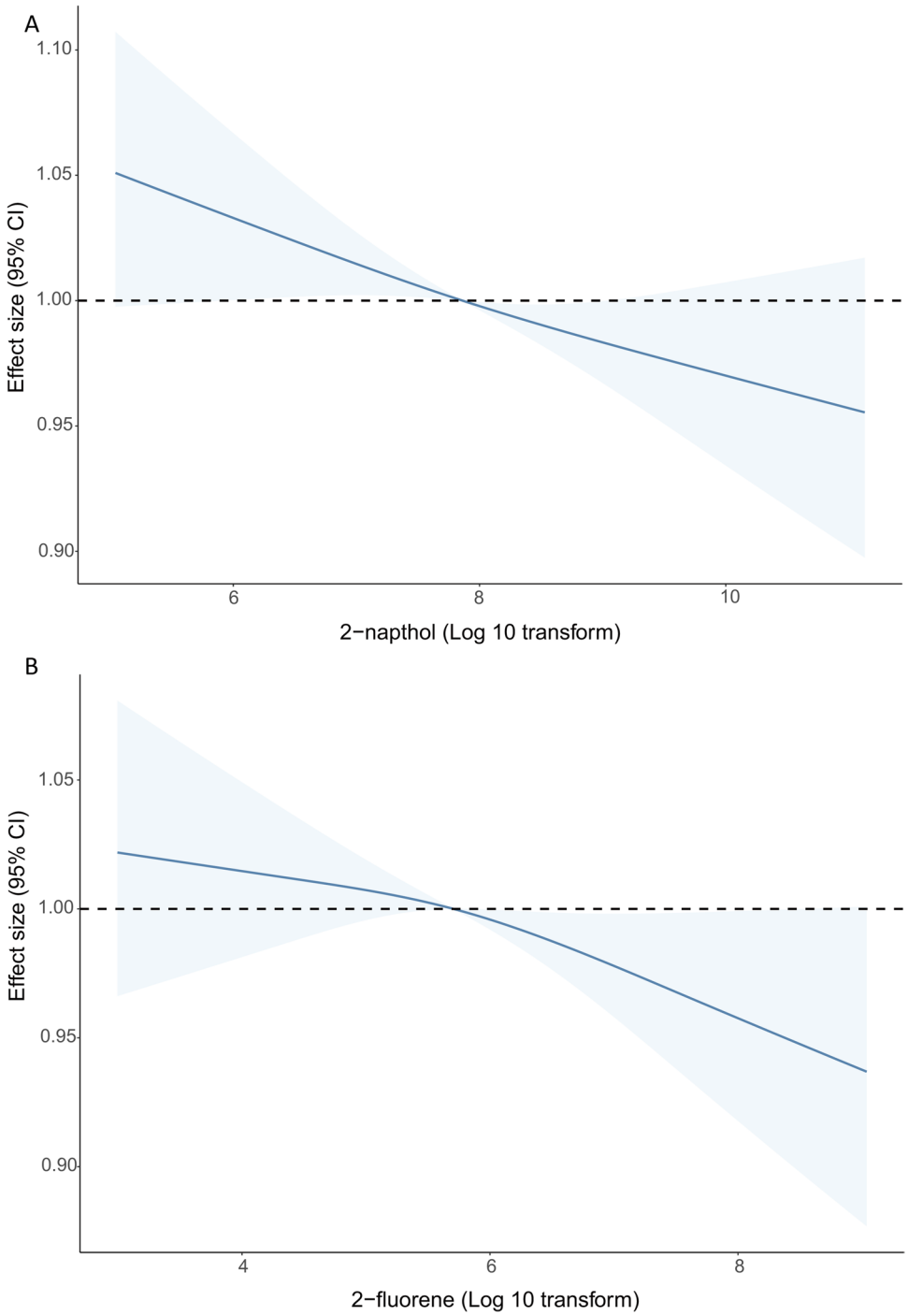

Fig. 4 The nonlinear relations between exposure to polycyclic aromatic hydrocarbons (A: 2-napthol; B: 2-fluorene) and telomere length among participants. The solid lines represent estimates of the effects, and the dashed line represents the 95% CI. The model was adjusted for age, race, sex, education level, serum cotinine, poverty income ratio, body mass index, and creatinine

with shortened telomere length (Zhang et al. 2021). Duan et al. detected four urine PAHs in 544 coke oven workers and found that the median values of 1-hydroxypyrene, 2-hydroxynaphthalene, and 3-hydroxyphenanthrene were 83.80, 84.97, and 18.20 pg/μg creatinine, respectively. The above three PAHs metabolites are related to the shortening of telomere length (Duan et al. 2020). Another study suggested that the median 1-hydroxypyrene in 1243 coke-oven workers was 3.29 μg/mmol creatinine. It had significant dose–response relationships with increased telomere length decline (Fu et al. 2018). This evidence suggests that the concentration of PAHs in the occupationally exposed population is related to the shortening of telomere length. However, in reality, the general population is exposed to lower PAHs than the occupational exposure population. Does the low dose of PAH in the general population also cause the shortened effect of telomere length?

Previous reports on PAHs and telomere length in the general population showed that PAHs exposure was also associated with decreased cell telomere length. PAHs metabolism was detected in 191 people, and the median level of 2 + 3-phenanthrene was 1.09 μg/mmol creatinine. Additionally, 2 + 3-phenanthrene was observed to be the most important component of PAH-induced telomere length reduction (Hou et al. 2020). Adli et al. found an inverse association between urinary 1-hydroxipayrene and telomere length in 200 children. The urinary 1-hydroxipayrene medain concentration was 375.5 μg/L (Adli et al. 2021). Nie et al. found that the median values of maternal urinary 2-hydroxynaphthalene, 2-hydroxyfluorene, 9-hydroxyphenanthrene, and 2-hydroxyphenanthrene were 2.937, 0.114, 0.025, and 0.145 ng/mL, respectively, in 247 nonsmoking pregnant women. These four PAH metabolites were associated with decreased trends for cord blood telomere length (Nie et al. 2019). The median levels of 1-hydroxypyrene and 1-hydroxynapthalene were 0.021 and 0.123 μg/g creatinine, respectively, in 444 male urine samples. They were observed to be associated with shortened telomere length in semen (Ling et al. 2016). The results of the above nonoccupational exposure populations are similar to our study. We found that the median 2-napthol and 2-fluorone concentrations were 218.0 μg/g creatinine and 25.0 μg/g creatinine, respectively, which can cause telomere length reduction. However, these two PAH metabolites have not been reported in previous studies. In addition, we also conducted a mixed exposure study. The results showed that PAHs mixed exposure in the general population was related to the reduction of telomere length, while previous mixed exposure methods indicated that the correlation between PAHs and telomere length was null (Shi et al. 2022). The possible reason is that the study included 73 subjects aged from 60 to 69, and their sample size was not as large as our study. They used 3 days of exposure time, and the damaging health effects of PAHs may need to last for a long time. If the exposure time is increased, the observation results may be changed.

There are few studies on the mechanism by which PAHs induce alterations in telomere length. A previous study indicated that PAHs cause telomere length reduction in germ cells. Benzo[a]pyrene (B[a]P), a ubiquitous pollutant of PAHs and an active metabolite of benzo[a]pyrene (B[a]P), could induce shortened telomeres in mouse spermatocyte-derived cells via activation of the DNA damage response pathway (Ling et al. 2018). The rats were administered benzo[a]pyrene (B[a]P; 0, 1, 5, and 10 mg/kg) for 4 weeks and found to have shorter STL in germ cells in a dose-dependent manner (Ling et al. 2016). In addition, some epidemiological evidence found oxidative stress (Bortey-Sam et al. 2017, Lu et al. 2016, Xie et al. 2019), PAHs-DNA adducts (Pavanello et al. 2020), and inflammatory reactions (Lee et al. 2017, Miri et al. 2019), which may also be the potential mechanism of PAH-induced telomere length shortening. Due to the unavoidable unknown bias in epidemiological studies, these findings still need more mechanistic studies to be confirmed.

This paper has the following advantages. First, the general population has a large sample size. Second, PAHs combined exposure was studied. Third, this study expressed PAHs exposure by dividing PAHs by creatinine and using creatinine as a covariate in the statistical model. Both results found that PAHs were correlated with telomere length, suggesting that our results were robust. The disadvantage lies in that, first, due to data access restrictions, we could not obtain genetic factor information, and genetics may have affected telomere length as a bias factor, although we corrected other factors that affected telomere length as much as possible in this study.

Conclusion

This study found that PAHs combined exposure is associated with telomere length reduction in the general population of the USA, in which 2-napthol and 2-fluorone may be important PAH components associated with telomere length reduction.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11356-023-27428-w.

Author contribution DHY and CL conceived the study; DHY acquired the data; CL and WDC carried out the statistical analysis; DHY, CL, CX, XQC, and GFL interpreted the findings; and DHY drafted the manuscript. DHY and CX had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. CX and GFL provided input in the analysis; all authors critically reviewed the manuscript. XQC and GFL revised the manuscript for final submission. All authors read and approved the final manuscript.

Availability of data and materials The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval Approval from the ethical board for this study was not required because of the public nature of all the data.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

References

Adli A, Hosseini SM, Lari Najafi M, Behmanesh M, Ghezi E, Rasti M, Kazemi AA, Rad A, Falanji F, Mohammadzadeh M, Miri M, Dadvand P (2021) Polycyclic aromatic hydrocarbons exposures and telomere length: a cross-sectional study on preschool children. Environ Res 195:110757

Astuti Y, Wardhana A, Watkins J, Wulaningsih W, Network PR (2017) Cigarette smoking and telomere length: a systematic review of 84 studies and meta-analysis. Environ Res 158:480–489

Barrett JH, Iles MM, Dunning AM, Pooley KA (2015) Telomere length and common disease: study design and analytical challenges. Hum Genet 134:679–689

Bobb JF, Valeri L, Claus Henn B, Christiani DC, Wright RO, Mazumdar M, Godleski JJ, Coull BA (2015) Bayesian kernel machine regression for estimating the health effects of multi-pollutant mixtures. Biostatistics 16:493–508

Bortey-Sam N, Ikenaka Y, Akoto O, Nakayama SMM, Asante KA, Baidoo E, Obirikorang C, Saengtienchai A, Isoda N, Nimako C, Mizukawa H, Ishizuka M (2017) Oxidative stress and respiratory symptoms due to human exposure to polycyclic aromatic hydrocarbons (PAHs) in Kumasi, Ghana. Environ Pollut 228:311–320

Cawthon RM (2002) Telomere measurement by quantitative PCR. Nucleic Acids Res 30:e47

Cowell W, Colicino E, Tanner E, Amarasiriwardena C, Andra SS, Bollati V, Kannan S, Ganguri H, Gennings C, Wright RO, Wright RJ (2020) Prenatal toxic metal mixture exposure and newborn telomere length: modification by maternal antioxidant intake. Environ Res 190:110009

Das DN, Ravi N (2022) Influences of polycyclic aromatic hydrocarbon on the epigenome toxicity and its applicability in human health risk assessment. Environ Res 213:113677

Duan X, Zhang D, Wang S, Feng X, Wang T, Wang P, Ding M, Zhang H, Liu B, Wei W, Acquaye RM, Yao W, Cui L, Zhou X, Wang W, Yang Y (2020) Effects of polycyclic aromatic hydrocarbon exposure and miRNA variations on peripheral blood leukocyte DNA telomere length: a cross-sectional study in Henan Province, China. Sci Total Environ 703:135600

Eick SM, Goin DE, Cushing L, DeMicco E, Park JS, Wang Y, Smith S, Padula AM, Woodruff TJ, Morello-Frosch R (2021) Mixture effects of prenatal exposure to per- and polyfluoroalkyl substances and polybrominated diphenyl ethers on maternal and newborn telomere length. Environ Health 20:76

Fernandes SG, Dsouza R, Khattar E (2021) External environmental agents influence telomere length and telomerase activity by modulating internal cellular processes: implications in human aging. Environ Toxicol Pharmacol 85:103633

Fu W, Chen Z, Bai Y, Wu X, Li G, Chen W, Wang G, Wang S, Li X, He M, Zhang X, Wu T, Guo H (2018) The interaction effects of polycyclic aromatic hydrocarbons exposure and TERT- CLPTM1L variants on longitudinal telomere length shortening: a prospective cohort study. Environ Pollut 242:2100–2110

Herrmann W, Herrmann M (2020) The importance of telomere shortening for atherosclerosis and mortality. J Cardiovasc Dev Dis 7

Hou J, Yin W, Li P, Hu C, Xu T, Cheng J, Li T, Wang L, Yu Z, Yuan J (2020) Joint effect of polycyclic aromatic hydrocarbons and phthalates exposure on telomere length and lung function. J Hazard Mater 386:121663

Huang H, Wang Q, He X, Wu Y, Xu C (2019) Association between polyfluoroalkyl chemical concentrations and leucocyte telomere length in US adults. Sci Total Environ 653:547–553

Isaevska E, Moccia C, Asta F, Cibella F, Gagliardi L, Ronfani L, Rusconi F, Stazi MA, Richiardi L (2021) Exposure to ambient air pollution in the first 1000 days of life and alterations in the DNA methylome and telomere length in children: a systematic review. Environ Res 193:110504

Lansdorp PM (2022) Telomeres, aging, and cancer: the big picture. Blood 139:813–821

Lee EY, Lin J, Noth EM, Hammond SK, Nadeau KC, Eisen EA, Balmes JR (2017) Traffic-related air pollution and telomere length in children and adolescents living in Fresno, CA: a pilot study. J Occup Environ Med 59:446–452

Ling X, Zhang G, Chen Q, Yang H, Sun L, Zhou N, Wang Z, Zou P, Wang X, Cui Z, Liu J, Ao L, Cao J (2016) Shorter sperm telomere length in association with exposure to polycyclic aromatic hydrocarbons: results from the MARHCS cohort study in Chongqing, China and in vivo animal experiments. Environ Int 95:79–85

Ling X, Yang W, Zou P, Zhang G, Wang Z, Zhang X, Chen H, Peng K, Han F, Liu J, Cao J, Ao L (2018) TERT regulates telomere-related senescence and apoptosis through DNA damage response in male germ cells exposed to BPDE in vitro and to B[a]P in vivo. Environ Pollut 235:836–849

Lu SY, Li YX, Zhang JQ, Zhang T, Liu GH, Huang MZ, Li X, Ruan JJ, Kannan K, Qiu RL (2016) Associations between polycyclic aromatic hydrocarbon (PAH) exposure and oxidative stress in people living near e-waste recycling facilities in China. Environ Int 94:161–169

Mallah MA, Changxing L, Mallah MA, Noreen S, Liu Y, Saeed M, Xi H, Ahmed B, Feng F, Mirjat AA, Wang W, Jabar A, Naveed M, Li JH, Zhang Q (2022) Polycyclic aromatic hydrocarbon and its effects on human health: an overeview. Chemosphere 296:133948

Miri M, Nazarzadeh M, Alahabadi A, Ehrampoush MH, Rad A, Lotfi MH, Sheikhha MH, Sakhvidi MJZ, Nawrot TS, Dadvand P (2019) Air pollution and telomere length in adults: a systematic review and meta-analysis of observational studies. Environ Pollut 244:636–647

Nie J, Li J, Cheng L, Deng Y, Li Y, Yan Z, Duan L, Niu Q, Tang D (2019) Prenatal polycyclic aromatic hydrocarbons metabolites, cord blood telomere length, and neonatal neurobehavioral development. Environ Res 174:105–113

Niu Z, Wen X, Wang M, Tian L, Mu L (2022) Personal exposure to benzene, toluene, ethylbenzene, and xylenes (BTEXs) mixture and telomere length: a cross-sectional study of the general US adult population. Environ Res 209:112810

Pavanello S, Campisi M, Mastrangelo G, Hoxha M, Bollati V (2020) The effects of everyday-life exposure to polycyclic aromatic hydrocarbons on biological age indicators. Environ Health 19:128

Shi W, Gao X, Cao Y, Chen Y, Cui Q, Deng F, Yang B, Lin EZ, Fang J, Li T, Tang S, Godri Pollitt KJ, Shi X (2022) Personal airborne chemical exposure and epigenetic ageing biomarkers in healthy Chinese elderly individuals: evidence from mixture approaches. Environ Int 170:107614

Srinivas N, Rachakonda S, Kumar R (2020) Telomeres and telomere length: a general overview. Cancers (Basel) 12

Taylor KW, Joubert BR, Braun JM, Dilworth C, Gennings C, Hauser R, Heindel JJ, Rider CV, Webster TF, Carlin DJ (2016) Statistical approaches for assessing health effects of environmental chemical mixtures in epidemiology: lessons from an innovative workshop. Environ Health Perspect 124:A227–A229

Vaiserman A, Krasnienkov D (2020) Telomere length as a marker of biological age: state-of-the-art, open issues, and future perspectives. Front Genet 11:630186

Wang F, Wang Y, Wang Y, Jia T, Chang L, Ding J, Zhou L (2022) Urinary polycyclic aromatic hydrocarbon metabolites were associated with hypertension in US adults: data from NHANES 2009-2016. Environ Sci Pollut Res Int 29:80491–80501

Xie Y, Lin T, Yang M, Zhang Z, Deng N, Tang M, Xiao Y, Guo H, Deng Q (2019) Co-exposure to polycyclic aromatic hydrocarbons and metals, four common polymorphisms in microRNA genes,

and their gene-environment interactions: influences on oxidative damage levels in Chinese coke oven workers. Environ Int 132:105055

Xu C, Liu Q, Liang J, Weng Z, Xu J, Jiang Z, Gu A (2021) Urinary biomarkers of polycyclic aromatic hydrocarbons and their associations with liver function in adolescents. Environ Pollut 278:116842

Zhang X, Lin S, Funk WE, Hou L (2013) Environmental and occupational exposure to chemicals and telomere length in human studies. Occup Environ Med 70:743–749

Zhang B, Liu L, Guo L, Guo S, Zhao X, Liu G, Li Q, Jiang L, Pan B, Nie J, Yang J (2021) Telomere length mediates the association between polycyclic aromatic hydrocarbons exposure and abnormal glucose level among Chinese coke oven plant workers. Chemosphere 266:129111