

A scoping review of maternal adverse childhood experiences and offspring epigenetic aging

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Systematic Review

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Abstract

Background

Adverse Childhood Experiences (ACEs) are traumatic events before age 18. They are prevalent and can be transmitted across generations. Recent studies suggest that parental ACEs are associated with offspring epigenetic aging. This scoping review aims to synthesize evidence on the association between maternal ACEs and offspring epigenetic aging.

Methods

Four English-language databases were searched for studies published from 1995 to 2026 on maternal ACEs and offspring epigenetic aging. Two independent reviewers screened titles, abstracts, and full texts. Content analysis was used to synthesize the findings of the included studies.

Results

Four studies were included. Maternal ACEs were associated with offspring epigenetic age acceleration, but the association was highly conditional, depending on the epigenetic clock, offspring age, sex, and maternal race. Positive findings were most consistent for the Horvath clock in childhood and the Bohlin clock in male newborns. Sex and race were key moderators; prenatal restless sleep acted as a “second hit”.

Conclusion

Evidence suggests maternal ACEs may accelerate offspring epigenetic aging, yet the field is nascent with high heterogeneity. Large, prospective, diverse cohort studies with standardized clocks are needed.

Introduction

Adverse Childhood Experiences (ACEs) refer to potentially traumatic events occurring before the age of 18, typically encompassing ten domains, including abuse (emotional, physical, sexual), neglect (emotional, physical neglect), and household dysfunction (domestic violence, parental separation or divorce, incarceration of a family member, mental illness, and substance abuse, among others). Since Felitti[1] and colleagues[2] first systematically proposed the dose-response relationship between ACEs and multiple disease risks in adulthood during the 1990s, subsequent research has consistently confirmed that ACEs are significant risk factors for cancer, cardiovascular disease, metabolic disorders, and neurodegenerative diseases. According to data from the U.S. Centers for Disease Control and Prevention,[3] 61% of U.S. adults reported experiencing at least one ACE, and one in six reported experiencing four or more types of ACEs. A recent systematic review concluded that adverse childhood experiences accelerate biological aging.[4] Other studies have shown that maternal ACEs are also associated with low birth weight[5] and developmental delays[6] in offspring. It is now well established that maternal ACEs influence child behavioral health outcomes through both direct[7] and indirect[8] pathways[9], with maternal mental health being the most frequently examined mediating factor.[10, 11]

Epigenetics provides an important mechanistic framework for understanding these processes. Epigenetic changes, particularly DNA methylation (DNAm), are thought to play a central role in the intergenerational transmission of stress and trauma. Epigenetic changes refer to environmentally sensitive modifications to DNA that alter gene expression without changing the underlying nucleotide sequence.[12] Epigenetic age is a measure of biological age that reflects the impact of environmental factors on cellular and molecular functions over time, thereby influencing potential disease risk.[13, 14] To date, various methods—collectively referred to as “epigenetic clocks”—have been developed to estimate an individual's epigenetic age based on DNA methylation patterns.[15, 16] Depending on the clock model, epigenetic age is estimated from the methylation levels of dozens to hundreds of CpG (cytosine-phosphate-guanine) sites across the genome.[17] Epigenetic age typically correlates with chronological age, and the first-generation clocks developed by Horvath⁴⁰ and Hannum[14] et al., respectively, were designed for this purpose. Subsequent clocks, including PhenoAge,[18] GrimAge,[19] and DunedinPoAm,[20] aim to predict diseases associated with age-related decline. When epigenetic age is significantly higher than chronological age, it is referred to as epigenetic age acceleration (EAA), which is considered a robust marker of accelerated biological aging and increased health risk. Through this mechanism, environmental factors such as ACEs can influence gene activity without altering the underlying DNA sequence.

There is often a discrepancy between epigenetic age and chronological age. For instance, when an individual's epigenetic age advances at a faster rate than their chronological age, this is manifest as EAA. Research has shown that EAA can serve as a valid biomarker of biological aging.[21] Supporting this notion, EAA has been demonstrated to be an important predictor of age-related diseases,[22] and all-cause mortality.[23]

Although previous reviews[24] have examined the intergenerational effects of early environmental exposures on health and disease, and systematic reviews and meta-analyses[25] have focused on the associations between parental ACEs and adverse offspring outcomes (e.g., preterm birth, low birth weight, developmental delays, and behavioral problems), systematic syntheses specifically targeting the association between maternal ACEs and offspring epigenetic aging remain limited. Existing studies span multiple life stages—including the prenatal period, neonatal period, and childhood—and employ diverse types of epigenetic clocks, contributing to considerable complexity in the findings. Some studies have observed a significant positive association between maternal ACEs and offspring epigenetic age acceleration (EAA), whereas others have found no clear main effects, only suggesting interactions involving potential moderating variables.

Given the rapid growth of research in this field and the heterogeneity across existing evidence, this paper aims to systematically synthesize empirical studies on the association between maternal ACEs and offspring epigenetic aging using a scoping review approach. Given the heterogeneity in study designs, epigenetic clocks, and outcome measures, a scoping review is appropriate to map the existing evidence and identify research gaps. Specifically, we seek to address the following three questions: (1) What relationships between maternal childhood adversity and offspring epigenetic age have been reported in the existing literature? (2) How have ACEs and epigenetic age been measured in relevant studies? (3) What are the current gaps in the research?

Methods

This study utilized the scoping review methodology developed by Arksey and O'Malley.[26] Scoping reviews allow researchers to map the landscape of the research area, summarize and interpret the research findings, identify research gaps in the existing literature, and provide directions for future research, practice, and policy.[27] Compared to other review methods like systematic reviews, scoping reviews provide a broader overview of evidence from studies that coalesce around more general research questions. Thus, it is especially appropriate for disciplines with emerging evidence.[28]The current study followed the recommendations of Arksey and O'Malley, who organized the scoping review process into five stages:

Stage 1: Develop the Research Questions

The central research questions of this review are: (1) What evidence currently exists concerning the association between maternal Adverse Childhood Experiences (ACEs) and offspring epigenetic age? (2) How have ACEs and epigenetic age been operationalized and measured in the relevant literature? (3) What are the principal gaps and limitations in the existing body of research?

Stage 2: Identify Relevant Studies

Prior to the search, the research team met with university librarians to select electronic databases and define search parameters and keywords. The search was limited to English-language articles published between January 1995 and January 2026 (coinciding with the original ACE study). Four databases (PubMed, Cochrane Library, Embase, and Web of Science) were searched using terms related to mothers, maternal ACEs, and offspring epigenetic age. Full search strategies for databases are included in the supplemental materials upon request. The search yielded 1362 articles. All articles were exported into Endnote and 650 duplicates removed. Results of the literature search are depicted in the PRISMA diagram (Fig. 1).

Stage 3: Select Articles Using Inclusion and Exclusion Criteria

One researcher (NJH) screened the titles of all 1362 records and identified 4 potentially relevant articles. Subsequently, two researchers (NJH and XZM) independently applied the inclusion and exclusion criteria to the abstracts and full texts. To be eligible, studies had to be original epidemiological research with a population-based cohort design; mother participants were required to be aged ≥ 18 years at the time of study enrollment; and offspring participants had to be aged < 18 years at the time of DNA methylation measurement. Included studies covered two types of populations: individuals who self-reported exposure to at least one ACE item from the WHO ACE-IQ (Adverse Childhood Experiences International Questionnaire) before age ≤ 18 years, and individuals without any history of ACE exposure, reflecting the typical structure of epidemiological studies. The WHO ACE-IQ was adopted as the inclusion criterion because its items have been validated across multiple countries. Epigenetic age had to be measured using DNA-microarray-based methylation assays. Studies that assessed epigenetic age using non-DNA-methylation methods or that did not provide information on participants' ACE status were excluded. Animal or cell studies, as well as studies reporting only intergenerational effects without directly measuring offspring epigenetic age, were not included.

The systematic reviews themselves were not included in this pool. If more than one article used data from the same study, all articles were included in the review in order to capture the differing offspring outcomes examined.

Stage 4: Chart the Data

This study employed a narrative synthesis approach to extract key characteristics from the included studies, including author(s), publication year, study location, Ethnicity, biospecimens, study design, method of measuring Adverse Childhood Experiences (ACEs), and method of measuring child outcomes (see Table 1).

Table 1
General Characteristics of Reviewed Articles.

Study	Cohort	Study design	Year	Study Location	Sample size	Ethnicity	ACEs measurement	ACE groupings	ACEs	Epigenetic age calculator
Jamaji C.etal	the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study	Prospective	2021	USA	238	Does not specify	a slight adaptation of the ACE questionnaire first described by Felitti	Cumulative ACEs: 0, 1, 2, 3+	abuse (emotional, physical, sexual), neglect (emotional, physical), and household dysfunction (domestic violence, divorce, incarcerated relative, mental illness, substance abuse)	Horvath, Hannum, Skin Blood Clock, Intrinsic, Extrinsic, PhenoAge, GrimAge, DNAm telomere length
Elissa J.et al	NGHS Contra Costa County cohort	Retrospective	2025	USA	215	52% White, 48% Black	Stress and Adversity Inventory	Individual ACE	Physical Abuse, Sexual Abuse, Substance Abuse by Parent	Horvath, DunedinP.
Sosnowski.et al	the Stress and Health in Pregnancy (SHIP) cohort, the Prospective Research on Early Determinants of Illness and Children's Health Trajectories (PREDICT) cohort	Prospective	2024	USA	332	56% female; 39% Black; 25% Hispanic	10-item ACE questionnaire	Cumulative ACE score ranging from 0 to 10	emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect, loss of a parent due to separation or death, domestic violence, family member with addiction, family member mental illness, and family member incarceration	PedBE, Knight, Bohlin, EP, GA, SHIP-PREDICT
Dye.et al	ALSPAC	Retrospective	2024	USA	1018	Does not specify	Indications of exposure to adversities for the 10 ACEs that are included in the WHO ACE-IQ	Cumulative ACE score ranging from 0 to 10	emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect, loss of a parent due to separation or death, domestic violence, family member with addiction, family member mental illness, and family member incarceration	Knight, Bc

Stage 5: Summarize and Interpret Study Findings

Findings that emerged from the studies were summarized in Table 2 and interpreted in the Results and Discussion sections. Implications for future research and practice were also discussed.

Table 2
Summary of Main Findings on Maternal ACEs and Offspring Epigenetic Aging

First Author (Year)	Main Positive Findings	Negative Findings	Effect Modifiers
Dye et al. (2024)	Maternal ACEs associated with mother's GrimAge EAA (not offspring outcome, but reported as background). In male newborns: maternal ACE total score and Bohlin GAA acceleration ($\beta = 0.05$, $p = 0.05$). Maternal emotional neglect and male newborn Knight GAA acceleration. Maternal substance abuse and male newborn Bohlin GAA acceleration.	No significant association with Knight clock in either sex. No main effect of total ACE score on newborn GAA at $p < 0.05$. Prenatal depression did not mediate.	Child sex
Jamaji C. et al (2021)	Maternal ACEs (1–2 vs. 0) associated with 0.76-year higher Horvath EAA and 0.80-year higher IEAA in children (7–14 years). Maternal ACEs (≥ 3) associated with 0.04 kb longer DNAm TL in children. Parental divorce associated with accelerated Horvath EAA and IEAA in children.	No associations with Hannum, Skin & Blood, PhenoAge, GrimAge, EEAA. No dose-response (3 + ACEs not significant for Horvath/IEAA).	/
Elissa J. et al (2025)	In Black mothers, any abuse before 13, physical abuse before 18, and sexual abuse before 18 predict child Horvath EAA acceleration ($\beta = 0.81 - 1.69$ years). No associations in White mothers.	No association with DunedinPACE. No association with maternal own epigenetic age.	Race (Black vs. White)
Sosnowski et al. (2024)	The interaction between maternal ACEs and restless sleep during pregnancy is associated with EPIC gestational age acceleration ($b = 1.04$, $p = 0.04$). Only infants with both exposures showed acceleration.	No main effect of ACEs or restless sleep alone on any clock. No interaction for PedBE, Knight, Bohlin, or SHIP-PREDICT clocks.	Prenatal restless sleep
Abbreviations: DNAm TL, DNA methylation-based telomere length; EAA, epigenetic age acceleration; GA, gestational age; GAA, gestational age acceleration; IEAA, Intrinsic Epigenetic Age Acceleration; EEAA, Extrinsic Epigenetic Age Acceleration.			

Results

Study Contexts

A total of 1362 initial records were identified through the search. After removing duplicates and screening based on titles, abstracts, and full texts, four studies were ultimately included in the final analysis.[29–32] All included studies were published between 2021 and 2025. As shown in Table 1, two of the four studies adopted a prospective design, while the other two used a retrospective design. Sample sizes ranged from 100 to 1500 participants. All studies assessed adverse experiences that occurred before the age of 18, and all employed array-based DNA methylation techniques to measure epigenetic age. Half of the studies utilized multi-ethnic samples,[31, 32] and only one study reported the inclusion of Hispanic participants.[32] Two studies did not report the race or ethnicity of their samples. [29, 30]All studies were conducted in the United States. Overall, although the number of studies conducted to date is limited, they show considerable diversity in terms of racial and sex composition; however, limitations in study design remain.

Measurement of Maternal Adverse Childhood Experiences

All included studies retrospectively assessed maternal adverse childhood experiences (ACEs) using self-report questionnaires. The assessments were based on the classic framework proposed by Felitti[1], covering abuse, neglect, and household dysfunction. Specifically, Dye[29] and Jamaji C[30] both used the 10-item ACE questionnaire; the former employed a cumulative score (0–10), whereas the latter categorized scores into three groups: 0, 1–2, and ≥ 3 . Sosnowski et al.[32]also used the 10-item questionnaire but dichotomized ACE exposure as “none” (0) versus “any” (≥ 1) due to the low prevalence of ACEs in their sample. Elissa J[31] combined the Stress and Adversity Inventory (STRAIN) to assess any abuse before age 13 and used Felitti-style questions to separately evaluate physical abuse and sexual abuse. Although the included studies varied in their scoring methods (continuous, categorical, or dichotomous) and dimensional focus, all targeted adverse experiences occurring before the mother's 18th birthday, thereby ensuring consistency in the core exposure construct.

Measurement of Epigenetic Age

All included studies assessed offspring epigenetic age using array-based DNA methylation technology. Biospecimen types included umbilical cord blood at birth[29, 32], peripheral blood in childhood[30], and saliva[31]. DNA methylation was profiled using the Illumina Infinium HumanMethylation 450K or EPIC BeadChip.

The selection of epigenetic clocks varied considerably across studies. Dye[29] applied the Knight and Bohlin clocks to estimate gestational age acceleration in newborns. Sosnowski[32] used the PedBE clock, Knight clock, Bohlin clock, EPIC gestational age clock, and a sample-derived SHIP-PREDICT clock. For childhood samples, Jamaji[30] calculated the Horvath pan-tissue clock, Hannum clock, Skin & Blood clock, Intrinsic Epigenetic Age Acceleration (IEAA),

Extrinsic Epigenetic Age Acceleration (EEAA), PhenoAge clock, GrimAge clock, and DNA methylation-based telomere length. Elissa J[31] employed the original Horvath clock and the DunedinPACE pace-of-aging metric.

In all studies, epigenetic age acceleration was defined as the residual from regressing epigenetic age on chronological age (positive values indicating acceleration, negative values deceleration). DunedinPACE was used directly as a measure of aging rate without residualization. Several studies additionally adjusted for cell type composition, batch effects, and technical covariates. Most studies in this review used blood samples; the sole exception used saliva samples (i.e., predominantly epithelial cells). The wide range of clocks employed indicates that no “gold standard” for epigenetic age calculation currently exists, and the discrepancies observed across different clocks reflect this reality.

Content Analysis Results

Main Effects and Clock-Specific Findings

The association between maternal ACEs and offspring EAA was highly dependent on the specific epigenetic clock used. In the largest study, Dye[29] found that maternal total ACE score was not significantly associated with neonatal gestational age acceleration (GAA) when using the Knight or Bohlin clocks in the overall sample. However, sex-stratified analyses revealed a marginally significant positive association with the Bohlin clock in male newborns ($\beta = 0.05$, $p = 0.05$). In contrast, Jamaji C[30] reported that maternal ACEs (1–2 vs. 0) were significantly associated with accelerated Horvath EAA ($\beta = 0.76$ years, $p = 0.004$) and IEAA ($\beta = 0.80$ years, $p = 0.002$) in children aged 7–14 years. No significant associations were observed for the Hannum, Skin & Blood, PhenoAge, GrimAge, or EEAA clocks. Interestingly, mothers with three or more ACEs showed no significant EAA acceleration but had longer DNA methylation-based telomere length ($\beta = 0.04$ kb, $p = 0.009$). Elissa J[31] found that maternal childhood abuse (any abuse before age 13, physical abuse before 18, sexual abuse before 18) was associated with accelerated Horvath EAA only among Black mothers (β range 0.81–1.69 years, all $p < 0.05$), with no significant associations among White mothers or for DunedinPACE. Sosnowski[32] did not detect main effects of maternal ACEs on any of the five neonatal clocks, but reported a significant interaction between maternal ACEs and restless sleep during pregnancy on EPIC gestational age acceleration ($b = 1.04$, $p = 0.04$), indicating that only infants exposed to both maternal ACEs and restless sleep showed accelerated aging.

Sex-Specific Effects

Sex differences emerged as a prominent theme. Dye[29] observed that the association between maternal ACEs and neonatal Bohlin GAA was evident only in males ($\beta = 0.05$, $p = 0.05$), whereas no association was found in females. Additionally, maternal emotional neglect was associated with Knight clock GAA acceleration specifically in male newborns. In contrast, Jamaji C[30] reported consistent associations for both sexes, with slightly stronger effect sizes in males (Horvath EAA: $\beta = 0.93$ for males vs. 0.65 for females). Elissa J[31] did not examine sex differences due to power limitations but found a significant moderation by race. Sosnowski[32] did not stratify by sex owing to sample size constraints.

Effects of Individual ACE Types and Cumulative Scores

Beyond total ACE scores, individual ACE subtypes showed specific associations. Dye[29] found that maternal emotional neglect was associated with Knight clock GAA acceleration in male newborns, and parental substance abuse was associated with Bohlin clock GAA acceleration in male newborns. In female newborns, maternal parental separation and domestic violence were associated with Knight clock GAA deceleration. Jamaji C[30] reported that among all ACE domains, only parental divorce/separation was significantly associated with accelerated Horvath EAA ($\beta = 0.58$ years, $p = 0.03$) and IEAA ($\beta = 0.56$ years, $p = 0.03$) in children. In contrast, multiple ACE domains (domestic violence, mental illness, neglect, physical abuse, sexual abuse, substance abuse) were associated with longer DNAm telomere length. Elissa J[31] found that any abuse before age 13, physical abuse before 18, and sexual abuse before 18 were each associated with child Horvath EAA, but only among Black mothers.

Moderating and Mediating Factors

Sosnowski[32] identified prenatal restless sleep as a significant moderator: maternal ACEs were associated with EPIC gestational age acceleration only when mothers also reported restless sleep during pregnancy ($b = 1.04$, $p = 0.04$), representing a “second-hit” model. Elissa J[31] demonstrated that race (Black vs. White) significantly moderated the association, with effects present only in Black mothers. Dye[29] tested prenatal depression as a mediator but found no significant mediation. Jamaji C[30] adjusted for child’s own adversity and found that associations remained significant, suggesting that intergenerational transmission is not fully explained by the child’s direct exposure to adversity.

Summary of Key Findings

Table 2 provides a synthesis of the main associations across studies. In summary, the evidence suggests that maternal ACEs are associated with offspring epigenetic age acceleration, but this association is clock-dependent, sex-specific, race-dependent, and moderated by prenatal factors such as sleep. First-generation clocks (Horvath, Hannum) and second-generation clocks (GrimAge, PhenoAge) showed inconsistent results, while neonatal clocks (Bohlin, Knight, EPIC GA) also varied in sensitivity. Positive associations were most consistently reported for the Horvath clock in childhood[30, 31] and for the Bohlin clock in male newborns.[29] Null findings were common, particularly for the GrimAge, PhenoAge, and DunedinPACE clocks in offspring samples.

Discussion

This scoping review systematically synthesized the existing literature on the association between maternal ACEs and offspring epigenetic aging, mapping the emerging evidence in this field. Based on four eligible studies published between 2021 and 2025, several key findings emerged. First, research in this area has expanded rapidly over the past five years, particularly in United States. Most studies focused on the negative effects of maternal ACEs, with intergenerational research predominantly concentrated on infancy and early childhood; studies examining how maternal ACEs transmit effects into adulthood remain scarce. Second, maternal ACEs appear to be associated with accelerated epigenetic aging in offspring, but this association is highly

conditional, depending on the choice of epigenetic clock, offspring biospecimen type, child sex, and maternal race. Third, the most consistent positive associations were reported for the Horvath clock in childhood[30, 31] and the Bohlin clock in the neonatal period. [29] Fourth, null findings were common, particularly for first-generation clocks (Hannum), second-generation clocks (GrimAge, PhenoAge), and the DunedinPACE pace-of-aging metric. Fifth, sex and race emerged as important moderators: male newborns may be more vulnerable to maternal ACE-related gestational age acceleration, whereas the effect in childhood was stronger among Black mothers compared to White mothers. Additionally, prenatal restless sleep was identified as a potential “second hit” factor that amplifies intergenerational effects.[32] Although epigenetic metrics in children have been explored, no gold standard epigenetic clock for accurately estimating biological age currently exists. Future research is needed to further investigate the intergenerational impact of maternal ACEs on other domains of child development and functional outcomes.

Although the present review focuses exclusively on DNA methylation-based epigenetic clocks, it is worth noting that alternative biomarkers of biological aging have also been linked to maternal ACEs[33]. For instance, Chen[34] reported that maternal ACEs, particularly when combined with relapsing/remitting depressive symptoms, were associated with shorter buccal telomere length in 3-year-old children. This parallel evidence from telomere biology supports the broader notion that maternal childhood adversity may become biologically embedded in offspring, accelerating aging at multiple molecular levels. However, given the mechanistic and methodological differences between telomere attrition and epigenetic clock acceleration, direct comparisons remain tentative.

Additionally, the association between maternal psychosocial exposures and offspring epigenetic aging may not follow a simple linear dose-response pattern; future studies should consider threshold or curvilinear effects. Folger[35] observed a non-linear pattern in the context of prenatal depressive symptoms: subclinical symptoms were associated with offspring epigenetic age deceleration, whereas elevated symptoms were not. Although that study did not examine maternal ACEs, it cautions against assuming a simple linear relationship between maternal adversity severity and child epigenetic aging. Similar non-linearity may exist for maternal ACEs. For instance, moderate levels of ACEs could trigger compensatory biological mechanisms, while high levels lead to exhaustion and accelerated aging. Future studies should test quadratic or spline models rather than treating ACE scores as purely linear.

Potential Biological Mechanisms

Although this review primarily presents associational evidence, elucidating the underlying biological pathways is essential for interpreting the findings. Two non-mutually exclusive mechanisms may explain how maternal ACEs become embedded in offspring epigenetic aging.

First, maternal ACEs may dysregulate the hypothalamic-pituitary-adrenal (HPA) axis, leading to chronic alterations in glucocorticoid levels that persist into pregnancy.[36, 37] Animal models have shown that early life stress alters methylation of glucocorticoid receptor genes, and such changes can be transmitted across generations.[37, 38] In human studies, maternal ACEs have been associated with differential DNA methylation of stress-related genes in cord blood, suggesting that the intrauterine environment is a critical window for intergenerational programming.[39]

Second, maternal ACEs may influence offspring indirectly through prenatal and postnatal behavioral pathways, including smoking, nutrition, and sleep quality. [40] For example, Sosnowski et al.[32] found that prenatal restless sleep amplified the association between maternal ACEs and neonatal epigenetic age acceleration, supporting a “second-hit” model. Chronic inflammation represents another plausible mediator: maternal ACEs are linked to elevated levels of inflammatory markers during pregnancy, and maternal inflammation can affect fetal immune and epigenetic programming via placental transfer.[41]

Notably, these mechanisms are not mutually exclusive and are more likely to form a complex causal network. However, direct tests of these mediational pathways remain limited, and most existing studies rely on retrospective designs, precluding strong causal inference. Future research should integrate multi-omics data and employ longitudinal mediation analyses to elucidate the core pathways linking maternal ACEs to offspring epigenetic aging.

Methodological Limitations

This review also identified common methodological limitations across the field. Most studies used non-probability sampling with small-to-moderate sample sizes, which can produce estimation bias and limit generalizability.[42] Although most studies employed longitudinal designs, maternal ACEs were typically measured retrospectively. While accumulating evidence supports the reliability of retrospective ACE assessments,[43–45] caution is needed when making causal inferences due to possible recall bias.[46] Furthermore, most studies relied on parental self-report to assess ACEs and child outcomes, which may introduce additional bias. Despite these limitations, a notable advance in the field of intergenerational ACE research is that an increasing number of studies have moved beyond main effect analyses to explore mediating and moderating mechanisms.

Strengths and Limitations

This scoping review has several strengths as well as some limitations. To our knowledge, it is the first review to systematically synthesize evidence on the association between maternal ACEs and offspring epigenetic aging. We followed the PRISMA guidelines, employed a rigorous search strategy across multiple databases, and included studies covering diverse epigenetic clocks, offspring ages, biospecimen types, and racial groups. Additionally, we extracted information on mediators and moderators, moving beyond a purely main-effect analysis.

Despite these strengths, several limitations should be acknowledged. As a scoping review, we did not assess the quality or risk of bias of the individual studies. Only four studies met the inclusion criteria, reflecting the early stage of this field, which precluded meta-analysis and limits the generalizability of our findings. Publication bias may have overestimated positive results. Maternal ACEs were assessed retrospectively, introducing the risk of recall bias. Heterogeneity across studies in ACE measurement, epigenetic clocks, and covariate adjustment hindered cross-study comparisons. Most studies had small sample sizes and thus insufficient statistical power. All studies were conducted in the United States and predominantly involved populations of European ancestry or specific minority groups, limiting generalizability to other regions and populations. Moreover, no study measured offspring epigenetic age at more than two time points, preventing the characterization of developmental trajectories. Finally, mediation analyses remain preliminary, and causal pathways require further validation.

Conclusions

Given that most individuals experience at least one adverse childhood experience, understanding its intergenerational impact is particularly urgent. This review shows that maternal ACEs are associated with accelerated epigenetic aging in offspring, an association moderated by factors such as epigenetic clock choice, offspring age, sex, and maternal race. The findings highlight the need to unify ACE definitions and standardize measurements to adapt to changing demographic structures. As racial composition evolves, developing assessment tools that adequately capture childhood adversity is essential. Future research should standardize ACE assessment methods, uniformly apply DNA methylation based clocks, and adequately adjust for confounders to more clearly elucidate the association between ACEs and epigenetic age acceleration.

Declarations

CRedit authorship contribution statement

All the authors listed have approved the manuscript that is enclosed, and author's individual contribution to the article was described below.

Jiahui Ni: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization, Software.

Zimeng Xu: Investigation, Formal analysis, Data curation.

Ruotong Wei: Conceptualization, Validation.

Yanfei Cao: Conceptualization.

Tian Chen: Formal analysis Methodology

Feng Zhang: Writing – review & editing, Funding acquisition.

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Figures

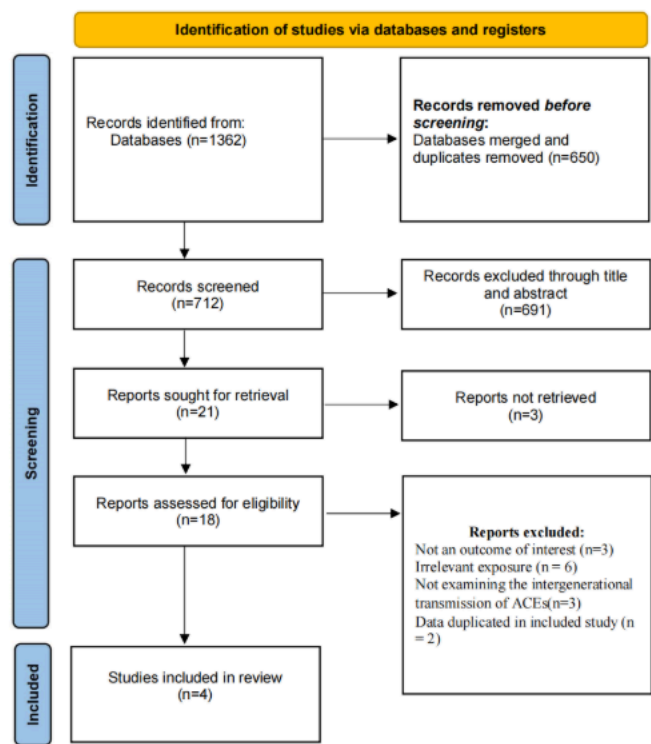


Figure 1

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