

The effect of the COVID-19 pandemic on young children's biological ageing

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Abstract

This study investigated how exogenous variation in exposure to the COVID-19 pandemic impacted biological ageing across early childhood. A sample of socioeconomically diverse pregnant women were recruited from New York City in 2019 to participate in a longitudinal study of child development ($N = 93$). Saliva samples were collected from infants to assess epigenetic age at 1-month postpartum. By the start of the pandemic, infants ranged in age from 0 to 9.5 months old, thus experiencing different durations of pandemic exposure in the first year of life. At 30 months, children returned to the laboratory to provide a second saliva sample ($N = 52$; 59% Female, 50% Hispanic). There was no evidence of large effects of pandemic exposure on trajectories of biological ageing from 1 month to 30 months.

Keywords epigenetics, COVID-19, longitudinal

Lay summary

While numerous studies have examined the effect of the COVID-19 pandemic on children's psychological development, few studies have examined biological signals of growing up during the pandemic. Biological age, or one's age on a cellular level, is associated with overall health and well-being and is also sensitive to stressful exposures in children. This study explored how growing up during the COVID-19 pandemic impacted young children's biological ageing. We used a natural experiment design to assess whether greater exposure to the social experience of the pandemic (i.e., lockdown) in the first year of life was associated with altered patterns of biological ageing. Overall, we found no large effect of exposure to the social experience of the pandemic on biological ageing across the first few years of life.

The COVID-19 pandemic caused large disruptions to the typical child rearing environment, with potential consequences for developmental trajectories. For example, a scoping review by [Zuniga-Montanez et al. \(2024\)](#) found that young children's language-learning environments, and subsequent language skills, declined modestly due to the pandemic. Other systematic reviews find similar deleterious effects of the pandemic on the mental health of children and mothers ([Panchal et al., 2023](#); [Penna et al., 2023](#)). However, the majority of this literature relies on cross-sectional and self-reported data, which may prematurely raise the alarm for children's developmental outcomes due to biased estimates (see [Firestein et al., 2022](#) for expanded discussion). Quasi-experimental designs with longitudinal data are necessary to improve our understanding of the pandemic on the youngest generation of children. In addition, little research to date has

examined physiological alterations in children due to the pandemic. The present study leverages a natural experiment design to estimate the impact of exposure to the social experience of the pandemic in the first year of life on trajectories of biological ageing across early childhood.

Biomarkers of pandemic exposure

DNA methylation is a widely studied epigenetic marker that reliably changes over the life course and may also cause downstream effects on physiological systems that may negatively impact overall health and well-being ([Weaver, 2014](#)). Critically, numerous studies have documented DNA methylation's sensitivity to stressful life experiences across the lifespan ([Blaze & Roth, 2015](#)). In the context of COVID-19 infection, studies have identified

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DNA methylation differences in patients infected with the virus (Corley et al., 2021; Huoman et al., 2021), with the ability to predict infection even one year after recovery from severe illness (Balnis et al., 2022). Less work has sought to examine epigenetic differences based on exposure to the *social* experience of the pandemic, rather than viral infection. For example, environmental disruptions, social isolation, economic uncertainty, and other pandemic-related stressors within families may have left measurable imprints on stress-sensitive processes like DNA methylation. However, little work has sought to detect such biomarkers of pandemic-related conditions.

Biological ageing as indexed via epigenetic clocks is one measure that may be particularly sensitive to stress-related perturbations. An accelerated epigenetic age—that is, a biological age that exceeds one's chronological age—is robustly associated with both adverse lifetime experiences and negative health outcomes in adults, such as morbidity, cardiovascular disease, and cancer (Horvath & Raj, 2018). Accelerated ageing has been posited as a biomarker of physiological “wear-and-tear” in that it is associated with social determinants of health (e.g., poverty, air pollution, cumulative lifetime stress), and deleterious health outcomes (Horvath & Raj, 2018). Notably, recent work has extended detection of these patterns to *within* childhood itself, suggesting that these indicators of biological weathering may emerge prior to the onset of serious disease.

The DunedinPACE clock appears particularly sensitive to detecting these patterns in pediatric samples. This clock is often conceptualized as a speedometer as it is designed to predict the pace of biological ageing per chronological year (Belsky et al., 2022). A recent meta-analysis found that, amongst numerous clocks examined, DunedinPACE was the only one sensitive to detecting socioeconomic disadvantage in pediatric samples (Willems et al., *in press*). In addition, it is also predictive of some outcomes within childhood, such as poorer overall health (Del Toro et al., 2024), greater body mass index (Raffington et al., 2021), and poorer cognition (Niccodemi et al., 2022; Raffington et al., 2023b). Collectively, these studies suggest that greater adverse experiences even within childhood are predictive of an accelerated biological age, with potential implications for developmental trajectories. One longitudinal study tested repeated measures of epigenetic clocks collected pre- versus post-pandemic, and found no differences in the rank-order stability of biological ageing in older children and adolescents (deSteiguer et al., 2025). However, it is unknown if these null findings will persist in a younger cohort of children.

Estimating the effect of the pandemic

There has been mixed evidence to date regarding the effect of the pandemic on young children's development. In some cases, there is evidence of deleterious effects. For example, a longitudinal study from Japan found children aged 3–5 years old who had been exposed to the pandemic scored lower on measures of language, socioemotional development, and motor skills compared to a pre-COVID comparison group (Sato et al., 2023). However, results were inconsistent across age groups and assessment type. Indeed, younger children in this same study (aged 1–3 years old) seemed to perform slightly *better* in these skills compared to their pre-pandemic peers (Sato et al., 2023). In addition, a recent investigation comparing over 50,000 births from the years 2018–2022

found significant but small effects of the pandemic on infant developmental milestones, with declines of 2–3% in the domains of communication, problem-solving, and personal-social skills (Johnson et al., 2024).

There is also evidence of heterogeneity across demographic subgroups. It is well established that socioeconomically disadvantaged communities were more likely to experience higher levels of infection, mortality, and economic challenges (Abrams et al., 2022). However, there is also some evidence to suggest positive family-level effects of pandemic restrictions for this subgroup. For example, studies found that some low-income families with young children reported more positive parent–child interactions (Kalil et al., 2020), improved maternal mental health, and improved maternal sleep quality during the pandemic compared to pre-pandemic cohorts (Premo et al., 2023).

In a previous study, we leveraged the environmental shock of the COVID-19 pandemic using a pre-existing sample of pregnant and recently postpartum mothers (Sperber et al., 2022). At the start of the pandemic, infants in this sample ranged between 0 and 9.5 months of age. We leveraged this naturally-occurring variation in exposure to the pandemic in the first postpartum year to examine differences in child development and maternal mental health across the first few years of life. Notably, we observed no differences in child behavior, language, or maternal mental health at 12 or 24 months postpartum. However, these analyses were restricted to parent-reported measures of child development. In addition, this previous work found that parents who reported greater disruptive life events due to the pandemic also reported poorer mental health at 1 and 2 years postpartum, though no associations were observed with child development. Though this finding is not exogenous like the previous analysis, it does suggest some association between COVID-related disruptions and family functioning. In the present study, we extend these analyses to physiological measures of biological ageing, chronic stress, and laboratory-based assessments of cognition.

The present study

The present study examines the effect of the duration of pandemic exposure in the first year of life on trajectories of biological ageing across early childhood. Using a natural experiment design, we investigated whether greater exposure to the pandemic in the first year of life was associated with changes in epigenetic ageing from 1 month to 30 months of age. In addition, we examined the association between pandemic-related disruptive life events and trajectories of biological ageing. Based on the previous literature with children and adults, we hypothesized that greater exposure to the pandemic, as well as experiencing a greater number of disruptive life events, would be associated with an accelerated pace of children's early biological ageing.

As a follow-up to our previous study (Sperber et al., 2022), we also examined the effect of these exposures on a series of behavioral, cognitive, and physiological outcomes at 30 months. These outcomes include parent reports of socioemotional problems and language ability in addition to lab-based assessments of receptive vocabulary, executive functioning, and hair cortisol concentrations. We hypothesized that greater exposure to the pandemic and disruptive life events would be associated with higher child hair cortisol concentrations and lower performance on cognitive measures.

Method

Participants

A socioeconomically and racially diverse sample of pregnant mothers from New York City (NYC) was recruited prior to the onset of the pandemic as part of a prospective study of child development. Mothers were informed that data collection timepoints would occur during the last 5 weeks of pregnancy, then at 1-month postpartum, and then every 6 months postpartum until the child reached 36 months of age. Participants needed to meet the following inclusion criteria: (1) be at least 18 years of age; (2) live within 1 hr of the laboratory space by public transportation; (3) be carrying a singleton; (4) have no known neurodevelopmental disorders with the fetus; (5) be fluent in English or Spanish; and (5) be at least 35 weeks pregnant.

Procedure

Between June 2019 and March 2020, 93 mothers came into the laboratory where they provided informed consent and completed a battery of surveys. One month after the birth of their child, mothers returned to the lab, at which time a saliva sample was collected from the infant to assess epigenetic age. At the time of pandemic onset in mid-March 2020, in-person data collection was paused and subsequent data collection was conducted remotely to the extent possible for the duration of pandemic-related restrictions.

The next possible timepoint by which families could safely return to the laboratory for assessments was June 2021, when the oldest infants in the study were 30 months of age. At this laboratory visit, a second sample of saliva was collected from children to assess epigenetic age. In addition, a trained research assistant administered a battery of cognitive tests to the children and collected a hair sample to assess hair cortisol concentration. Finally, mothers completed surveys of their child's development.

These secondary outcomes (cognitive development, hair cortisol, and parent surveys of development) were assessed among a subsample of participants and are described in greater detail in the Supplement. All study procedures were conducted in alignment with the ethical standards established by the Declaration of Helsinki and approved by the Institutional Review Board of Teachers College, Columbia University.

Analytic sample

Many families moved out of NYC during the COVID-19 pandemic, thus substantially reducing the number of participants who returned for in-person assessments. Of the initial 93 families in the cohort, 66 families completed at least one follow-up measure at the 30-month visit. For the present study, we restricted analyses to these participants that returned for the 30-month appointment. We utilized multiple imputation with 25 iterations to account for missing data on covariates, any pre-COVID assessments, and the disruptive life events measure. We did not impute the dependent variable; only valid scores were included in the final sample for each respective outcome of interest.

Measures

Pandemic indicators

Duration of pandemic exposure. Details on the pandemic exposure measure have been described elsewhere (see Sperber et al., 2022). Briefly, we selected a cut-off date of March 22nd, 2020 to signify the start of lockdown, as this was the first day that NYC enacted social distancing requirements and required all non-essential personnel to remain home. Using the infant's birthday, we then calculated the number of days each family would experience the first postpartum year under these pandemic conditions, with higher scores indicating greater pandemic exposure. The distribution was such that infants experienced a range of 2.5–12 months of pandemic conditions during the first year of life (see Figure 1).

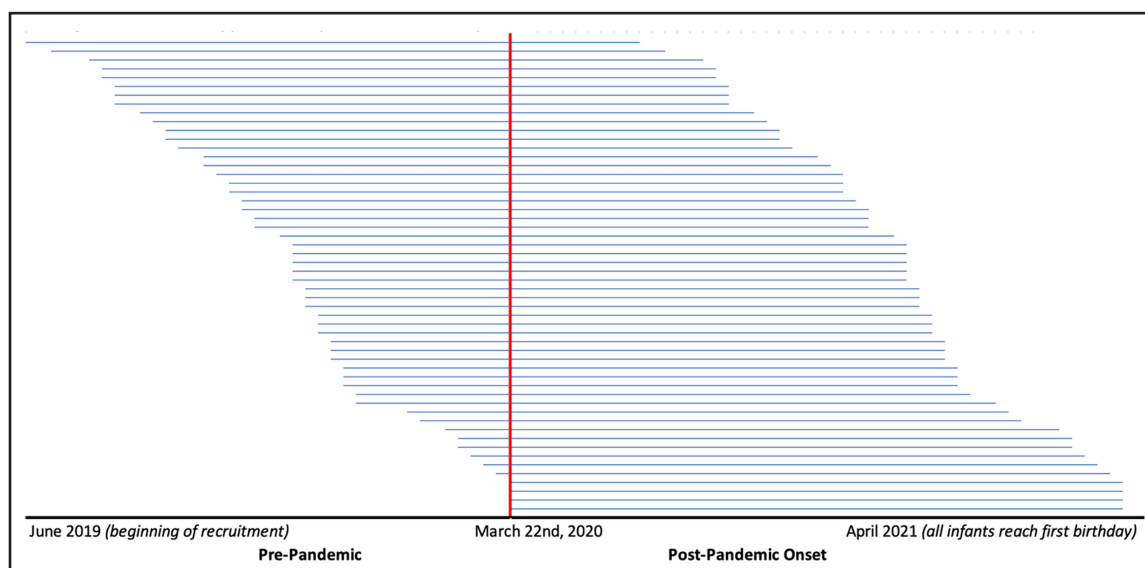


Figure 1 Distribution of pandemic exposure across the sample at recruitment. *Note.* $N = 52$. Each line reflects the pandemic exposure of a participant enrolled in the study that provided an epigenetics value at 30 months, sequential in age. The red line indicates the beginning of lockdown in NYC (March 22, 2020). The left side of the figure represents the amount of time each child spent alive prior to the pandemic in the first year of life. The right half of the figure represents the amount of pandemic exposure in the first year of life. Figure adapted from Sperber et al. (2022).

In previous work, we demonstrated that this indicator was not associated with observable participant characteristics, thus making it a reasonably exogenous indicator of pandemic exposure in this sample (Sperber et al., 2022). This variable was available for all participants; there was no missing data.

Disruptive life events. During the 12-month remote visit, mothers completed a modified version of the Epidemic-Pandemic Impact Inventory (Grasso et al., 2020; $n = 61$). Participants were presented with a checklist of 71 events that may or may not have happened to them or someone in their household due to the COVID-19 pandemic. Items ranged in their severity across seven different domains, including Work or Employment (e.g., “Laid off from job or had to close own business”), Home Life (e.g., “More conflict with child or harsher in disciplining child or children”), and Infection History (e.g., “Death of close friend or family member from this disease”). Mothers indicated whether each item impacted themselves, a person in their home, or none of the above. A composite score was generated by summing across all positively endorsed items experienced by either the participant or someone in their home. One participant’s score was deemed invalid as they endorsed the most extreme answer choices for each item on the scale. This observation was set to missing and scores were standardized.

Biological age. Due to challenges in getting families to return to the laboratory after pandemic-related lockdowns, some children provided their saliva sample several months after the intended collection date. Specifically, eight children provided a saliva sample during the 36-month laboratory visit ($M = 38.3$ months; $SD = 1.8$ months). We retained these observations to maximize sample size but include a dummy indicator for timepoint of saliva collection as a covariate in analyses. The methods used to process DNA methylation data and calculate epigenetic age have been described in detail elsewhere (Sperber et al., 2025). Here, we describe the pipeline in brief.

DNA methylation processing. Saliva samples were collected by a trained experimenter using Oragene DNA collection kits and subsequently frozen at -80°C ($n = 58$). Next, samples were shipped for processing at The University of Texas at Austin where DNA was extracted and eluted from each sample. At this stage, six samples were deemed unusable due to low DNA concentration and were destroyed. Remaining samples first underwent bisulfite conversion, then were assayed using the EPIC 850 K Infinium Methylation Beadchip Array (Illumina, Inc., San Diego, CA, USA), and then scanned for fluorescence intensities. These methylation intensities were stored as IDAT files for preprocessing.

Pre-processing pipeline. Samples were processed using the *minfi* package (Aryee et al., 2014) and Illumina’s quality control metrics were followed using the *ewastools* package (Just & Heiss, 2023). Each sample passed the bisulfite conversion threshold and examined for discrepancies between predicted vs. reported sex and genetic relatedness. Next, background fluorescence was filtered using detection p -values and number of hybridizing beads, and “preprocessNoob” was used to correct for dye-bias (Triche et al., 2013). Finally, sex chromosome and cross-reactive probes were removed, and principal components analysis (PCA) was used to derive cell type composition (Middleton et al., 2022).

Epigenetic clocks. We calculated several epigenetic clocks using genome-wide DNA methylation data. Given its sensitivity to stress-related processes in pediatric samples (e.g., Willems et al., *in press*), we focus on DunedinPACE as the primary outcome of

interest. We report the results of several other popular clocks examined in the literature in the Supplement (Horvath, PedBE, PhenoAge, GrimAge, and Epigenetic-g).

The Horvath clock is the most widely researched multi-tissue clock trained to predict chronological age across the lifespan (Horvath, 2013). Similarly, the Pediatric-Buccal-Epigenetic clock (PedBE) was trained to predict chronological age using epithelial tissues from a pediatric sample (McEwen et al., 2020). These first-generation clocks were calculated using the *methclock* package (Pelegi-Sisó et al., 2021). The PhenoAge (Levine et al., 2018), GrimAge (Lu et al., 2019), and DunedinPACE clocks (Belsky et al., 2022) were calculated via the *dnaMethyAge* package (Wang et al., 2023). As second- and third-generation clocks, they are robust predictors of overall health and mortality risk (Belsky et al., 2022; Levine et al., 2018; Lu et al., 2019). Finally, we calculated the blood-based Epigenetic-g clock using publicly-available code (https://gitlab.com/danielmccartney/ewas_of_cognitive_function), which is a predictor of general cognitive functioning in older adults (McCartney et al., 2022).

After obtaining the estimated epigenetic age according to each clock’s specifications, values were inspected for their distribution. One value of the PedBE clock at 30 months was winsorized due to a low outlier. Next, each clock was residualized for technical artifacts (i.e., plate, slide, and array), child chronological age at the time of data collection, and cell type composition (proportion of leukocytes vs. epithelial cells) to estimate accelerated ageing. At this stage, the clock distributions were re-investigated and 1 value on the PhenoAge clock was winsorized due to a low outlier. Finally, the accelerated ageing values were standardized.

Covariates

We replicated the covariates used in a previous publication that leverages this natural experiment design (Sperber et al., 2022), which includes the following characteristics: levels of prenatal anxiety, depression, and perceived stress as reported via surveys; maternal years of formal education; maternal race and ethnicity; and child age at the time of the assessment. One covariate used in the previous study (maternal receptive vocabulary scores) was excluded from the present analysis due to missing data. In addition, we adjusted for whether the saliva sample was collected at the 30-month or 36-month visit.

To reduce the number of covariates included in linear analyses due to the decreased sample size, we utilized PCA to reduce the measures of prenatal mental health. Prenatal measures of anxiety (assessed via the Beck Anxiety Inventory; Beck et al., 1988), depression (Patient Health Questionnaire; Kroenke et al., 2009), and perceived stress (Perceived Stress Scale; Cohen & Williamson, 1988) were entered into PCA and a single component was extracted with an eigenvalue of 2.11 and factor loadings ranging from 0.52 to 0.61. This component explained 70% of the variance across the measures. The component was labeled “Prenatal Mental Health” and included as a covariate in analyses, in addition to those previously listed.

Baseline balance, attrition, and weighting procedures

We next examined associations between the duration of pandemic exposure measure and children’s epigenetic age at 1 month. Since all 1-month samples were collected prior to the pandemic, these epigenetic profiles should in theory be unassociated with the exogenous indicator (e.g., similar to “baseline balance” in

an experimental design). Surprisingly, there was slight variation in 1-month epigenetic scores based on duration of pandemic exposure (Table S1): greater pandemic exposure was associated with elevated Horvath ($\beta = 1.27$, $SE = 0.16$, $p = .061$), PedBE ($\beta = 1.49$, $SE = 0.18$, $p < .001$), and PhenoAge score ($\beta = 1.33$, $SE = 0.16$, $p = .02$) at 1 month, indicating some bias in pre-pandemic epigenetic profiles. Scores did not differ by pandemic exposure for DunedinPACE at 1 month, the primary outcome of interest. Due to these patterns, results are presented both with and without adjustment for “baseline” (i.e., 1 month) epigenetic age scores.

A previous investigation found that families who completed follow-up visits during the pandemic tended to be more advantaged than the original sample (Sperber et al., 2022). Similar trends were observed in the present study (Table S2): families who returned for the 30-month visit were more highly educated ($OR = 2.26$, $SE = 0.66$, $p < .01$), reported higher incomes ($OR = 1.11$, $SE = 0.06$, $p = .063$), were more likely to be White ($OR = 2.86$, $SE = 1.59$, $p = .059$), and less likely to be Hispanic than the original sample ($OR = 0.29$, $SE = 0.15$, $p = .017$). Importantly, families who returned for the 30-month visit did not differ from the original sample on their duration of pandemic exposure in the first year of life ($OR = 1.38$, $SE = 0.33$, $p = .181$). Additionally, attrition did not vary based on any of the 1-month epigenetic measures (Table S2).

To account for missing data and differential patterns of attrition, we implemented multiple imputation and inverse probability of attrition weighting (IPAW) procedures, which in combination have shown to be robust to missing panel data in cohort studies (Seaman et al., 2012). First, a variable reflecting whether a participant remained in the sample after the pandemic was regressed onto demographic characteristics to generate propensity scores. The inverse probability of each participants’ odds of remaining in the sample were extracted and their distribution was examined. Next, we implemented multiple imputation with chained equations and 25 iterations to impute missing values using correlated auxiliary variables.

Analytic plan

Longitudinal analyses: epigenetic ageing

OLS regression with robust standard errors was used to examine the effect of the pandemic on epigenetic ageing in toddlerhood. Covariates were steadily introduced to observe the changing association between each predictor and epigenetic age at 30 months. Model 1 presents the partial correlation between each pandemic exposure measure and epigenetic age, residualized for technical artifacts, cellular composition, and chronological age. This association is informative mainly for the duration of pandemic exposure measure as this variable is arguably exogenous from potential sources of bias. Next, Model 2 introduces adjustment for the demographic covariates listed above, which are chiefly important for the disruptive life events measure since this is not an exogenous indicator. Finally, Model 3 further adjusts for 1-month epigenetic age. This final coefficient likely provides the best estimate of the effect of the pandemic for both measures as it adjusts for each child’s pre-pandemic epigenetic “baseline.” This step is particularly important given that there was unequal spread in pre-pandemic epigenetic scores by duration of exposure for some clocks.

All models were weighted using the IPAW described above. The final sample was restricted to participants who provided a

valid epigenetic sample at the 30-month appointment and had non-missingness on baseline covariates. Missing values on the 1-month epigenetic age value and the disruptive life events measure were handled via multiple imputation. All measures were standardized to the sample. DNA methylation data pre-processing and epigenetic clock calculation were conducted in R. Subsequent analyses occurred in Stata v.18.

Cross-sectional analyses: developmental outcomes

For developmental outcomes and hair cortisol concentration at 30 months, we implemented OLS regression with robust standard errors. These results are reported in the Supplement. For these exploratory outcomes, the analytic sample was restricted to those who provided a valid score for each developmental outcome; no imputation procedures were used. The IPAW calculated above were applied to OLS models to offset the effects of differential attrition. All measures were standardized to the sample. Analyses occurred in Stata v.18.

Results

Descriptive statistics of the sample

Table 1 reports the descriptive statistics of the analytic sample. Mothers reported an average household income-to-needs ratio of 6.1 ($SD = 7.5$, range = 0–26.7) and 15.4 years of formal education ($SD = 3.6$). 59% of the children were female. Half of the mothers identified their ethnicity as Hispanic, while 20% identified as Black, 39% as White, and 41% as some Other race. In the first postpartum year, infants experienced an average of 7.6 months of life during the pandemic ($SD = 2.4$) and mothers reported experiencing 11 pandemic-related disruptive life events ($SD = 6.3$).

At 1 month of age, the average DunedinPACE score was 1.36 ($SD = 0.05$), which increased to a mean of 1.42 ($SD = 0.08$) at 30 months. This increase in the pace of ageing was statistically significant according to a paired t -test ($t(38) = -4.10$, $p < .001$). Among the other epigenetic clocks examined, a significant increase in biological age was also observed for the Horvath and PedBE clocks, whereas a significant decrease was observed for GrimAge (Table S3).

Correlations among key variables

Table 2 reports correlations among all the epigenetic clocks and variables of interest. For this table, epigenetic scores have been adjusted for technical artifacts and cell composition (i.e., scores have not been residualized for chronological age). At 30 months, chronological age at the time of data collection was slightly correlated with the PedBE, GrimAge, and PhenoAge clocks, but these magnitudes did not reach statistical significance (r ’s range 0.14–0.21; p ’s range .13–.31). We detected some evidence of an association between different clocks at 30 months: four of the six clocks were significantly correlated with at least one other clock. DunedinPACE demonstrated the largest number of significant associations at 30 months, positively correlating with PhenoAge, GrimAge, and Epigenetic-g (r ’s range 0.28–0.33; p ’s $< .05$). Less consistent associations were observed between longitudinal measures of epigenetic age, indicating low stability in profiles over time. DunedinPACE scores were marginally correlated from 1 month to 30 months ($r = 0.29$, $p = .08$).

Table 1 Descriptive statistics of analytic sample.

	N	Mean (%)	SD	Min	Max
<i>Pandemic exposure measures</i>					
Duration of pandemic exposure (<i>months</i>)	66	7.61	2.40	2.53	12
Disruptive life events	60	11.02	6.33	0	25
<i>Demographic characteristics</i>					
Child is female	66	59%			
Mother is Black	66	20%			
Mother is other race	66	41%			
Mother is White	66	39%			
Mother is Hispanic	66	50%			
Income-to-Needs (<i>winsorized</i>)	64	6.05	7.45	0	26.73
Years of maternal education	66	15.41	3.63	8	22
<i>Epigenetic clock estimate</i>					
DunedinPACE – 1 month	39	1.36	0.05	1.27	1.51
DunedinPACE – 30 months	52	1.42	0.08	1.24	1.58

Note. DunedinPACE scores reflect the estimated rate of ageing per chronological year, unadjusted for technical factors.

Table 2 Correlations among epigenetic clocks and variables of interest.

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)
1. Pandemic exposure	1.00															
2. Disruptive life events	0.15	1.00														
3. Maternal education	–0.01	0.37*	1.00													
4. Chronological age 30 months	–0.37*	–0.09	0.04	1.00												
5. Horvath 1 month	0.21	0.30	0.12	–0.28	1.00											
6. PedBE 1 month	0.48*	0.30	–0.06	–0.28	0.67*	1.00										
7. GrimAge 1 month	0.35*	0.05	–0.11	–0.12	0.19	0.20	1.00									
8. PhenoAge 1 month	0.17	0.42*	0.01	–0.16	0.20	0.22	0.39*	1.00								
9. DunedinPACE 1 month	0.02	–0.29	–0.37*	0.00	–0.01	0.01	0.09	0.10	1.00							
10. Epigenetic-g 1 month	0.05	–0.07	0.15	–0.28	–0.04	0.11	–0.08	–0.04	0.06	1.00						
11. Horvath 30 months	–0.09	0.12	–0.01	0.01	0.02	0.17	–0.28	–0.18	–0.39*	0.13	1.00					
12. PedBE 30 months	–0.22	0.08	0.02	0.21	–0.04	0.14	–0.02	–0.07	–0.28	0.14	0.50*	1.00				
13. GrimAge 30 months	–0.16	–0.04	–0.29*	0.14	–0.07	–0.03	–0.17	0.39*	0.28	0.05	0.12	0.14	1.00			
14. PhenoAge 30 months	–0.07	–0.15	–0.09	0.17	0.10	–0.03	0.21	0.17	–0.10	–0.18	0.17	0.51*	0.23	1.00		
15. DunedinPACE 30 months	0.14	–0.04	–0.27	–0.02	–0.04	–0.03	0.15	0.21	0.29	–0.34*	–0.17	–0.09	0.28*	0.30*	1.00	
16. Epigenetic-g 30 months	0.08	0.01	–0.18	–0.07	0.28	0.29	–0.07	–0.01	0.29	0.04	0.10	–0.11	0.04	–0.04	0.33*	1.00

Note. * $p < .05$. $N = 66$. Epigenetic variables have been residualized for technical factors (slide, plate, and array) and cell composition.

There was no evidence of a bivariate association between either duration of pandemic exposure or pandemic-related disruptive life events with child hair cortisol concentration or executive function (Table S4). Notably, higher behavior problems were associated with higher pandemic exposure ($r = 0.26$, $p < .05$). Additionally, greater disruptive life events were marginally associated with better parent-reported language ability ($r = 0.22$, $p = .10$). This later effect was in the opposite of the hypothesized direction.

Associations among pandemic measures and biological ageing

Table 3 presents OLS models estimating the associations among the pandemic exposure measures and DunedinPACE scores at 30 months. In these models, epigenetic age is residualized for technical factors, cell composition, and chronological age at the time of the assessment. There was no significant difference in

Table 3 Pandemic exposure measures and DunedinPACE scores in toddlers.

	DunedinPACE
Duration of pandemic exposure	
1. Partial correlation	0.11 (0.10)
2. Adjusts for demographics	0.09 (0.09)
	0.10 (0.10)
3. Adjusts for 1 month Epigenetic age	
Disruptive life events	
1. Partial correlation	−0.00 (0.19)
2. Adjusts for demographics	0.28 (0.24)
3. Adjusts for 1-month epigenetic age	0.29 (0.24)
Observations	

Note. Model 1 reflects partial correlations between the outcome of interest and DunedinPACE, residualized for technical artifacts (slide and array), cell composition, and child chronological age. Model 2 adjusts for the following demographic characteristics: maternal education, prenatal mental health, child sex, maternal race and ethnicity, and a dummy indicator of whether the saliva sample was collected at the 30-month or 36-month visit. Model 3 further adjusts for 1-month DunedinPACE scores. Sample restricted to participants with a valid epigenetic age estimate at 30 months. Coefficients have been weighted using IPAW procedures and reflect standardized betas. Robust standard errors in parentheses.

DunedinPACE scores by duration of pandemic exposure in the first year of life, regardless of adjustment for covariates or baseline epigenetic age. The same pattern was observed for disruptive life events: there was no evidence of an association between disruptive life events and DunedinPACE scores, regardless of covariate adjustments. These null results were consistent across all other epigenetic clocks examined (Table S5). Across all clocks, effect sizes ranged from -0.08 – 0.12 (SE's range 0.10 – 0.14) for duration of pandemic exposure, and from -0.00 – 0.29 (SE's range 0.12 – 0.28) for disruptive life events.

Associations among pandemic measures and developmental outcomes

Tables S6 and S7 report the associations among the pandemic measures with child cognition, behavior, and stress physiology. These models adjust for child age at the time of the assessment. Once again, there was no effect of duration of pandemic exposure on behavior problems, language ability, receptive vocabulary, executive function, and hair cortisol concentrations (Table S6). Effect sizes were small in magnitude (β 's range $-.05$ – $.10$) and imprecise due to the reduced sample size for lab-based assessments (SE's range 0.15 – 0.20). In addition, the magnitude of the association between duration of pandemic exposure and behavior problems dropped substantially from bivariate correlations when adjusting for child age ($\beta = .10$, $SE = 0.15$, $p = .49$).

There was also little evidence of an association between disruptive life events and these outcomes (Table S7). Greater disruptive

life events were marginally associated with lower hair cortisol concentrations ($\beta = -.24$, $SE = 0.15$, $p = .12$). These effects were counter to the hypothesized direction. As an exploratory analysis, we examined socioeconomic factors as a potential confound to explain these effects. When including maternal education as a covariate, the effect size reduced substantially ($\beta = -.04$, $SE = 0.22$, $p = .87$). This is likely due to the confounding association between maternal education with disruptive life events ($r = 0.37$, $p < .001$) and maternal education with child hair cortisol concentration ($r = -0.44$, $p < .001$; Table S4).

Discussion

The present study investigated the effect of the duration of pandemic exposure on trajectories of biological ageing in early childhood. Using a natural experiment design, we investigated whether infants who experienced more of their first year of life during the pandemic demonstrated altered patterns of biological ageing at 30 months of age. Overall, we observed no large differences in biological ageing among infants born at the start of the COVID-19 lockdown compared to those born several months before the pandemic. Additionally, we found little evidence of associations between pandemic-related disruptive life events and biological ageing in toddlerhood. These null results were consistent across six different DNA methylation clocks. Furthermore, we found no robust differences in cognition, behavior, or chronic stress physiology at 30 months of age based on these indicators.

One concern in the interpretation of these findings is the exogeneity of the duration of pandemic exposure measure. Although a previous investigation found no differences in this measure based on demographic characteristics of the sample (Sperber et al., 2022), an examination of baseline epigenetic scores collected before the pandemic found that three out of the six clocks tended to be higher for infants with greater duration of pandemic exposure. This indicates that there may have been baseline differences in epigenetic age at the start of the pandemic in our sample, which violates a key assumption of the natural experiment design. Though we adjusted for 1-month epigenetic age to remove this variance, this artifact nonetheless raises concerns for other unmeasured confounds that could challenge the integrity of the natural experiment design. While there were no differences in baseline DunedinPACE scores, the primary outcome of interest, it is critical to situate these findings within the possibility of other unmeasured confounds, biased attrition, and a sample that is underpowered to detect small effects.

Pandemic impacts on biological ageing and development

Assuming this external bias was removed via covariate adjustment, several explanations may account for the lack of a large effect of these exposures on young children's biological ageing and development. First, it is critical to acknowledge the heterogeneity of the pandemic experience across families. While it is well-documented that low-income communities were more likely to experience stressors such as material hardship and unpredictability during the pandemic (Liu et al., 2022), some studies also reported unexpected improvements to aspects of family functioning. For example, there were documented improvements to

low-income mother's mental health and sleep quality (Premo et al., 2023), the frequency of positive parent-child interactions (Kalil et al., 2020; Pitchik et al., 2021), and even children's vocabulary development (Kartushina et al., 2021) during the COVID-19 lockdown. In contrast, as observed in the present study, mothers with higher income—who likely had greater access to resources—simultaneously reported greater pandemic-related disruptive life events, and even greater depressive symptoms (Gustafsson et al., 2021). Collectively, these findings underscore the complex and nuanced experience of the pandemic across families, which likely mar any clear pattern of effects cross-sectionally. Indeed, it is likely the social experience of the pandemic varied substantially by complex individual circumstances, which we were not powered to probe in the present study.

Alternatively, it is possible that pandemic-related stressors do not impact the infant epigenome or behavioral and cognitive development at this age. Previous work in this sample found no differences in parent-reported perceived stress or mental health symptoms due to exogenous pandemic exposure (Sperber et al., 2022). This suggests that possible mediating factors such as the home environment and the quality of parent-child interactions may not have changed drastically during the pandemic, buffering the impact of these uncertain times on infant development. These null findings are further supported by previous work examining biological ageing during the pandemic in older children (deSteiguer et al., 2025). While lingering effects of the pandemic may certainly exist in some domains of child development, we detected no evidence of altered cognitive, behavioral, or physiological trajectories based on length of exposure to the incident alone during infancy.

Importantly, it is possible that there are small effects we are underpowered to detect. A post-hoc power analysis indicated that we were 80% powered to detect an effect size of 0.36. Comparatively, a recent meta-analysis reported that the size of the association between DunedinPACE and socioeconomic disadvantage in children tends to fall around 0.16 (Willems et al., in press). While these associations are not directly comparable, it does contextualize the present study's ability to detect real effects. Indeed, if the true association between pandemic exposures and biological ageing has a similar effect size as those reported in the above meta-analysis, the present study is certainly underpowered to detect it. However, this seems unlikely given recent findings from similar studies. For example, deSteiguer et al. (2025) found no change in the rank-order stability of epigenetic ageing based on exposure to the pandemic in a sample of over 400 children. Additionally, a German study of over 600 youth found little evidence of numerous measures of the pandemic on epigenetic ageing (Schowe et al., 2025). Though we cannot rule out the possibility of small effect sizes, these findings contextualized within the broader literature lead us to conclude that there is no evidence of a large, robust association between the socialized experience of the pandemic and biological ageing in a sample of children raised in a very high-risk environment during lockdown (i.e., New York City).

Measurement of biological age in early childhood

To date, little research has critically examined epigenetic clocks in very young children. While it is common to evaluate epigenetic

clock performance using chronological age and/or mean estimates, there are several challenges to applying these standards in the present study. First, the restricted age range of the sample results in small to nonexistent correlations with epigenetic age. Second, the Horvath and PedBE algorithms were trained to predict chronological age (referred to as “first generation clocks”), whereas the other clocks examined in this study were trained to predict phenotypes of interest (e.g., clinical markers of health or ageing; “second” generation clocks) or the rate of biological ageing (“third” generation clocks). Consequently, the correlation between chronological age and epigenetic age is stronger in first-generation clocks than second- and third-generation clocks (see Oblak et al., 2021 for an overview). Finally, blood-based clocks like DunedinPACE, PhenoAge, and GrimAge tend to positively skew estimates of biological age when using pediatric saliva data (Apsley et al., 2025). Therefore, it is ineffective to evaluate clock performance based on correlations with chronological age or mean values alone in this study.

With these caveats in mind, different clocks must be evaluated using different methods. For the PedBE and Horvath clocks, the significant increase in biological age estimates from 1 month to 30 months is noteworthy, as well as the accurate epigenetic age estimate of the sample at 30 months. These findings reaffirm the accuracy of these first-generation clocks during a period of rapid maturation. Furthermore, we observed a slight increase in the rate of biological ageing per year according to the DunedinPACE clock. This trend is surprising, as one might expect infancy to reflect a greater period of maturation than toddlerhood; nonetheless, the observed increase was small and may be an artifact of the small sample size or indicative of the measure's poor sensitivity during infancy.

Rather than comparing raw mean values, observing the *change* in biological age estimates over time is informative to evaluating the PhenoAge and GrimAge clocks' validity. We observed no difference in PhenoAge scores from 1 month to 30 months, and a significant *decrease* in GrimAge scores over this same period. These findings may indicate that these clocks are not sensitive to detecting differences in ageing in very young children. Previous work has reported associations between these clocks and physical health outcomes in middle childhood and adolescence (Del Toro et al., 2024), suggesting these measures can still detect meaningful variation in epigenetic age in older childhood. However, the null and counterintuitive trends observed here suggest that these effects may not extend to early childhood: since these clocks do not reliably differentiate changes in epigenetic signatures during this period of rapid maturation, they may not reflect a valid assessment of biological ageing in the first few years of life.

Epigenetic-g reflects a DNA methylation composite of cognitive abilities and is therefore theoretically distinct from the other biological age clocks examined here. To date, little work has attempted to validate this measure during early childhood, which limits the interpretation of this measure. Notably, we find positive though non-significant effect sizes among Epigenetic-g and multiple measures of cognition at 30 months of age. This aligns with previous work in older children (Raffington et al., 2023b). It is critical that future research with larger samples further interrogates the validity of this measure during childhood.

This is one of a few studies to examine longitudinal change in epigenetic ageing within early childhood, which introduces opportunities to explore how these profiles manifest in the first

few years of life. To date, there has been little validation work which examines these clocks in very young children. Notably, the small and inconsistent correlations between epigenetic age from 1 month to 30 months suggests low stability in these profiles over time. A positive sign for measurement validity during this age range are the associations among some epigenetic clocks measured concurrently at 30 months. In contrast, the counterintuitive behavior of some clocks (GrimAge, PhenoAge) raises doubts as to the validity of some measures in early childhood. Additionally, we applied saliva tissue to generate estimates using clocks created for blood tissue. Previous work finds low-to-moderate correlations between saliva and blood-based generated clocks (Apsley et al., 2025; Raffington et al., 2023a), emphasizing the need for saliva-based clocks validated across the lifespan. Greater longitudinal research is necessary to critically validate epigenetic clocks during this developmental period.

Strengths and limitations

We leveraged a natural experiment design, repeated measures, and longitudinal assessments of psychological and physiological outcomes to provide a comprehensive overview of children's developmental trajectories after the pandemic. However, the strength of these conclusions is tempered by several limitations. First and foremost, this study was limited by a small sample size, which restricted our ability to fully rule out the existence of smaller effects that we lack the power to detect. Second, we suffered from unbalanced attrition following the COVID-19 pandemic. While we attempted to off-set this analytically via weighting procedures, the overrepresentation of more privileged participants reduces the generalizability of findings. Additionally, these limitations prevented us from exploring possible moderating factors of these associations. Indeed, there may be meaningful heterogeneity in these associations that are masked, such as by socioeconomic status or race. Finally, our confidence in the interpretation of these results is restricted given the lack of validation work of these measures in pediatric samples and our use of saliva samples using algorithms generated for blood tissue.

Conclusion and future directions

This study contributes to a limited literature by reporting longitudinal associations among epigenetic ageing and developmental outcomes in the first few years of life. Future research should leverage longitudinal data using larger samples of children to examine moderating factors in these associations with greater precision. Additionally, there is a need for rigorous validation work with these measures in young children. Finally, the creation of biological ageing clocks using saliva samples in children is critical for strengthening confidence in these conclusions and for expanding the study of epigenetic ageing.

While this study contributes in-depth longitudinal data on a sample of children highly affected by the pandemic using rigorous methodology, the findings should be interpreted cautiously due to the sample size and measurement limitations described above. Therefore, we situate these findings within the broader COVID-19 and development literature as follows: overall, we find no large effects of pandemic-related conditions on the development of very young children in the psychological or physiological domains examined here.

Supplementary material

Supplementary material is available at [Child Development](#) online.

Data availability

The materials, data, and analytic code necessary to reproduce the analyses presented here are not publicly accessible.

Author contributions

JFK: conceptualization, methodology, formal analysis, writing—original draft of the manuscript. MM: software, data curation, writing—review & editing. AB: investigation, writing—review & editing. AMD: investigation, writing—review & editing. FAC: investigation, resources, project administration. KGN: funding acquisition, project administration, supervision, writing—review & editing.

Jessica Sperber Knott (Conceptualization [lead], Formal analysis [lead], Methodology [lead], Visualization [lead], Writing—original draft [lead]), Melissa Miller (Methodology [supporting], Software [supporting], Writing—review & editing [supporting]), Ariel Bellatin (Data curation [lead], Writing—review & editing [supporting]), Amanda Dettmer (Data curation [supporting], Writing—review & editing [supporting]), Frances Champagne (Data curation [lead], Supervision [supporting], Writing—review & editing [supporting]), and Kimberly Noble (Funding acquisition [lead], Project administration [lead], Supervision [lead], Writing—review & editing [lead])

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Conflicts of interest

The authors report no conflicts of interest.

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