

ABSTRACT

SHARER, CHRISTY. Quality of Child Care as a Protective Mechanism for Impacts of Maternal Depression on Cellular Aging. (Under the direction of Dr. Kate Norwalk).

Maternal depression is an established risk factor for various child outcomes related to physical, psychological, cognitive, and socio-emotional development. While maternal depression rates remain high in the United States, there are significant barriers to identification and accessing treatment. Bronfenbrenner's bioecological model is used to guide the conceptualization of risk and protective factors influencing children within a critical time of development in early childhood. This study explores potential factors related to child care quality within center-based early child care settings which could buffer the impacts of exposure to maternal depression on child development through cellular aging using the FFCWS data set. Results indicate certain dimensions of child care quality may be protective against advanced cellular aging for those never exposed to maternal depression, but the effects of high-quality child care may not be strong enough to impact cellular aging for those exposed to maternal depression. These findings are encouraging for the application of research specifically focused on protective factors in center-based child care identified through measures of cellular aging and suggest more attention is warranted to address and diminish the impacts of maternal depression on child development.

Quality of Child Care as a Protective Mechanism for Impacts of Maternal Depression on Cellular
Aging

by
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DEDICATION

This dissertation is dedicated to my family and support system. To my mother, for always being a phone call away and reminding me of my childhood dreams. To both of my parents, your celebrations of my milestones still mean so much to me, even as an adult. To my husband and children, thank you for supporting these dreams by moving 500 miles during a pandemic. We spent so many hours together gathered in my office area while you (and the dogs) visited me as I sat working at my computer. To my friends, thank you for checking in and asking about my journey. Finally, thank you to Ms. Kim and Ms. Valerie for loving my children and being there for me during chaotic and sometimes hard morning drop-offs.

BIOGRAPHY

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INTRODUCTION

Perinatal mental health disorders are one of the most common complications from pregnancy and childbirth (American College of Obstetricians and Gynecologists, 2018). Although there has been a considerable amount of research focused on prevention and intervention of maternal depression, about 400,000 children are born to depressed mothers each year and around 12% of women experience depression during or within the year following pregnancy (Earls, 2010). This suggests that widespread strategies to reduce maternal depression have not been adopted and implemented successfully across the United States. Moreover, only about 30%-50% of caregivers with depression are likely to be diagnosed, while only 15% of those who are diagnosed are likely to receive treatment (Cox et al., 2016). The estimated economic cost of untreated maternal depression for mother-child dyads is \$22,647 and the cost of untreated maternal mood and anxiety disorders combined is \$32,000 for dyads from conception through age five (Diaz & Chase, 2010; Luca et al., 2020). Maternal depression is impacted by numerous factors and in turn impacts children, as exposure to maternal depression has been shown to contribute to several developmental and health-related outcomes in children (Cox et al., 2016). The impact of maternal depression also appears in measures of genetic aging in children exposed to maternal depression, suggesting that exposure to maternal depression may contribute to rapid cellular aging (Mitchell et al., 2016).

Since widespread access to and utilization of mental health supports during the perinatal period has not been achieved in the United States, researchers have begun looking at other factors within early childhood which may serve as protective mechanisms against the impact of maternal depression. In consideration of other settings in which children spend much of their time outside of the home, child care settings have emerged as a plausible area to study. Specifically, the quality of child care may serve as a protective factor for risk factors related to

family-systems variables, including maternal depression (Burchinal, et al., 2010). Beyond direct prevention and intervention for maternal depression to reduce exposure and mitigate its impact, experiences with nurturing and responsive caregivers within early child care sites could serve to counterbalance some of the negative effects associated with maternal depression through the caregiver-child relationship. The associations between exposure to maternal depression and child care quality on long-term outcomes for children have not been well studied, especially in terms of the moderating impact that high-quality child care could have on these associations (Charrois et al., 2020). The present study attempts to address this gap in the research by examining the associations between maternal depression exposure, child care quality, and cellular aging outcomes in children and adolescents.

Theoretical Framework

This study was guided by Bronfenbrenner's bioecological framework. This model offers a multimodal approach to identifying influential factors contributing to child development at both individual and systems levels of considerations. This theoretical foundation can serve as a guide for research focused on factors impacting child outcomes, such as exposure to maternal depression, while allowing researchers to consider other factors that may simultaneously impact child development, including child care quality and socioeconomic status (Brooks-Gunn, 1995).

Bronfenbrenner's original ecological model and updated bioecological model of human development frames child development as occurring within bidirectional proximal processes of interactions, such as with caregivers, as well as more distal processes, such as interactions between caregivers and educators and local, state, or federal policies (Bronfenbrenner, 1995; Bronfenbrenner & Morris, 1998). Relationships with caring adults, peers, and caregivers are hypothesized to influence child development directly at the microsystem level (Dietrichson, et

al., 2020). Additionally, development is considered within the context of transactions with other individuals and with the environment (Rutter et al., 1995). Interactions between caregivers and teachers or caregivers and health care providers, which do not involve direct interactions with the child, form the next layer of the system termed the mesosystem. At more distal levels, children are influenced by the exosystem, which includes local policies or even mass media, followed by the macrosystem which includes attitudes and values of the culture, and finally the chronosystem which represents the influence of time on the other levels of influence.

Maternal depression represents a proximal risk factor for adverse developmental outcomes within the family microsystem. Maternal depression may impact maternal sensitivity and responsiveness, which in turn can impact the maternal-child relationship. Specifically, maternal depression can impede the mother-child attachment process, increasing risk for emotional, behavioral, and social-developmental difficulties for the child (Stewart, et al., 2003; Sword, et al., 2008). This relationship between mother and child can be conceptualized to influence the child's development throughout their lifespan. Similarly, relationships with other adults such as child care providers and quality of child care experiences can influence a child's development. A high-quality child care setting may serve as a protective factor for child development. Bronfenbrenner's model can guide research focused on these risk and protective factors and even the potential interplay between them. Given this consideration of risk and protective factors influencing child development, it is plausible to use Bronfenbrenner's framework in research exploring whether child care quality serves as a potential protective mechanism for the influence of exposure to maternal depression. Results of longitudinal research indicate that high-quality interactions with adults, both maternal and non-maternal, are a strong predictor of skill development in children (NICDH, 2002).

Factors Impacting Maternal Depression and Access to Treatment

There are numerous factors which can increase a woman's risk for depression. One of the largest genetic studies involving samples of siblings and twins estimates the heritability of perinatal depression as being between 44% and 54% respectively, with 33% of the genetic variance unique to *perinatal* depression (Viktorin et al., 2016). Stressors such as unplanned or unwanted pregnancies, poor social support, low self-esteem, previous experiences of depression, stressful events, or trauma/abuse exposure can all serve as risk factors for perinatal depression (Dagher et al., 2021). Certain women may also have greater neurobiological sensitivity to fluctuations in hormones associated with pregnancy and birth which predispose them to greater risk of perinatal depression (Dagher et al., 2021). Sociodemographic considerations such as the availability of child care may impact maternal depression (Johnson & Padilla, 2019). Mothers who experience poverty are at increased risk for depression, with some estimates suggesting the prevalence in low-income mothers is double the national average (Earls, 2010; Knitzer et al., 2008). Despite these known risk factors, many of those experiencing maternal depression are still not receiving treatment or support. In one Early Head Start research study, 52% of mothers reported elevated levels of depression during pregnancy or their child's first year, which was correlated with aggressive behavior in children between the ages of one and three, but only 23% of families reported that at least one family member received mental health services (Administration for Children and Families, 2006). Unfortunately, many of the factors associated with poverty can limit mothers' access to mental health treatment, including lack of health insurance, transportation, or money to pay for services (Beeber et al., 2008). The availability of high-quality child care could reduce at least one of these barriers to treatment, which could improve outcomes for children of depressed mothers.

Impact of Maternal Depression

Maternal depression serves as a proximal risk factor within a child's family microsystem which can impact physiological, cognitive, social, and mental health outcomes. Infants whose mothers experience postpartum depression are at risk for issues related to physical development, such as low weight and length in infancy (Stewart, et al., 2003). Children of mothers with depression are less likely to be ready for school at age five compared with peers who are not, even after controlling for confounding factors (Isaacs et al., 2012). This, along with higher rates of behavioral aggression in children whose mothers were depressed during infancy, can lead to higher risk of grade retention, enrollment in special education services, or even educational drop out (Onunaku, 2005). Maternal depression is also linked with both internalizing and externalizing symptoms in children. A systematic review of longitudinal studies found that children of depressed mothers may have 70% higher odds of developing depression as an adult or adolescent (Tirumalaraju et al., 2020). Maternal depression specifically may be more impactful than paternal depression, in heterosexual couples, for child outcomes including both internalizing and externalizing behaviors (Connell & Goodman, 2002).

Maternal depression can have both direct and indirect mechanisms of influence on adverse outcomes. For instance, maternal depression may negatively impact the caregiver-child relationship and attachment process, as caregiver mental health struggles is one of the biggest risk factors for insecure infant attachment (Reeves & Krause, 2019). Maternal depression can impact the quality and quantity of parent-child interactions and caregivers' ability to meet their children's social and emotional needs, as depression symptoms can reduce caregiver sensitivity and responsiveness (Field, 1995; Knitzer et al., 2008; Onunaku, 2005). Other factors, such as genetic vulnerabilities and intergenerational or epigenetic transmission of diseases can also

impact child outcomes; however, studies have supported the idea that daily interactions, parenting behaviors, and the quality of the parent-child relationship have the largest impact on infant development (Knitzer et al., 2008). Depression symptoms may also impact maternal views of children's behaviors such that those with depression symptoms may be more likely to rate their children as being more difficult (Thomason et al., 2014). This may also impact parenting behaviors. Maternal and paternal depression rates were correlated with negative parenting behavior and aggressive behavior in children, with children ages one to three of mothers with chronic depression at higher risk for these outcomes (Administration for Children and Families, 2006).

Research on the impact of maternal depression on child outcomes has focused largely on White middle-class families. There may be differential impacts across sociodemographic factors, such as race and ethnicity, related to maternal depression (Malik, et al., 2007). Within analysis of the Head Start FACES dataset, child behaviors at the beginning of the first year in Head Start positively predicted maternal depression at the end of the first year for African American/Black families, which was not found in Hispanic mothers or those from other racial/ethnic groups (Baker et al., 2020). This suggests there may be cultural influences impacting maternal depression warranting further exploration. There may also be higher rates of maternal depression among parents of young children who are involved in the child welfare system (Administration for Children and Families, 2019). Poverty can be thought of as a mechanism through which maternal depression risk is increased, and both poverty and depression may negatively impact parent-child interactions and lead to poorer child outcomes related to developmental delays, achievement gaps, physical health, and mental health issues (Knitzer et al., 2008). The

compounding effects of poverty and maternal depression could ultimately serve to limit a child's ability for income mobility and therefore increase the likelihood of remaining in poverty.

Cellular Aging

Most research exploring the impact of maternal depression has focused on academic, psychological, or social-emotional outcomes. However, advancing technology has provided the opportunity to further examine the biological impacts of exposure to early adversity. Epigenetic changes refer to the ways in which behaviors and environment can impact genetic changes, such as whether a gene is turned on or off (CDC, 2022). Exposure to stress results in both behavioral and hormonal changes which can result in physiological processes that speed up cellular aging and cause further epigenetic changes, increasing risks related to chronic diseases and mental health struggles (Belsky et al., 2015). The impact of accumulation of stress on biological processes and systems can be measured through markers of cellular aging, which may help to explain how exposure to early stressors confers risk for negative lifelong health outcomes. Specifically, evidence from epigenetic studies suggests that the experience of early maltreatment “gets under the skin” and affects cellular aging through processes such as DNA methylation and telomere erosion (Cecil, Zhang, & Nolte, 2020; Shalev et al., 2013). Measures of cellular aging including epigenetic age, measured through numerous methylation marks made in DNA, and biological age, which has been studied extensively using telomere length as a biomarker, are of interest to researchers focused on the impact of early adversity and experiences within the environment (Rentscher et al., 2020). Epigenetic and biological aging are terms used to reflect these different approaches to measure the more global concept of cellular aging which can be compared with chronological aging.

Epigenetic Age: DNA Methylation

The process of DNA methylation is a complex one linked with a variety of biological influences and outcomes, including cellular aging. DNA methylation refers to a chemical reaction in which a molecule, a methyl group, is added to DNA which then affects how DNA acts in the body, such as by turning off a gene so it does not make a particular protein (National Cancer Institute, 2011.). This can have benefits, such as suppressing tumors, but can also lead to negative outcomes such as increased risk for diseases (Jiang et al., 2007). Signals from the central nervous system can produce rapid changes in DNA methylation, especially through the effects of cortisol (Mitchell et al., 2016; Zannas, 2019). Researchers studying results from 13,089 individuals concluded that estimates of epigenetic age based upon DNA methylation patterns predicted mortality from all causes better than chronological age or traditional risk factors across racial and ethnic groups (Chen et al., 2016). Exposure to early life adversity is associated with accelerated aging found in measures of DNA methylation in adolescence, with evidence that changes to DNA methylation earlier in life are more impactful to epigenetic aging than changes experienced later in life (Simpkin et al., 2016). Analysis of DNA methylation in pediatric samples has demonstrated more rapid pace-of-aging and related decline in those who live in more disadvantaged neighborhoods and families (Raffington et al., 2021). Other research has found exposure to violence in childhood results in an older epigenetic age and even heart rates which are more similar to those found in adults, even when controlling for demographic variables including income, sex, and education (Jovanovic et al., 2017).

Biological Age: Telomere Length

Stress may get “under the skin” in other measurable ways and through different biological processes, specifically related to shortened telomere length and reduced telomerase

activity which are also associated with accelerated cellular aging (Epel et al., 2004). Telomeres are protective “caps” found at the ends of human chromosomes which naturally shorten each time a cell divides as a part of the typical aging process (Jiang et al., 2007). Telomeres help to provide stability to chromosomes and protect against chromosomes prematurely terminating replication (Gotlib et al., 2015). This shortening of telomeres through division can serve as a molecular clock and marker of biological aging (Shalev, 2012; Shalev et al., 2013). Once telomeres reach a critically short length, cell replication terminates, and cells enter a state of senescence (Shalev, 2012). There are compensatory processes for telomere erosion which utilize an enzyme called telomerase to preserve telomere length; however, telomerase is suppressed in most cells as humans age (Jiang et al., 2007). Furthermore, cortisol may diminish the activity of telomerase, as exposure to stress and the release of cortisol may be associated with shorter telomeres for both adults and children (Gotlib et al., 2015; Kroenke et al., 2011; Tomiyama et al., 2012).

Individuals exposed to adverse childhood experiences have a greater risk for dysregulated cortisol production (Miller et al., 2011). It is hypothesized the “wear and tear” of dysregulated biological stress responses may lead to more rapid cellular aging (Nelson et al., 2021). For those exposed to early adverse experiences, dysregulation of HPA axis activation and resulting increased cortisol production, stemming from repeated or chronic stress exposure, may lead to oxidative stress that reduces telomere length in later life (Shalev, 2012). In a study of adult women, those with the highest levels of perceived stress over greater periods of time had shorter telomere lengths than those in the low stress group, corresponding to a decade’s worth of aging (Epel et al., 2004). In adults with chronic PTSD, those with childhood trauma have shorter telomere lengths compared with those who experienced trauma at a later age (O’Donovan et al.,

2011). Oxidative stress may inhibit telomerase and has been shown to damage telomeres for certain cell types invitro (Lin et al., 2012). It is hypothesized that early exposure to adversity speeds up this genetic aging process by more rapidly shortening telomere length due to inflammation or cell stress (Rentscher et al., 2020).

Health behaviors may also speed up this erosion. For instance, each year of smoking one pack of cigarettes per day resulted in an increased telomere erosion by 18% in women aged 18-76 (Valdes et al., 2005). Diseases, such as chronic HIV or hepatitis, may accelerate telomere shortening; in turn, telomere shortening contributes to aging and diseases (Jiang et al., 2007). Deficiency within telomere maintenance processes can increase risk for chronic disease through accelerated biological aging (Gotlib et al., 2015; Jiang et al., 2007). Shorter telomere length is associated with negative health outcomes such as chronic diseases, including cardiovascular disease, dementia, diabetes, and cancer, while longer telomere lengths are associated with protective factors such as positive social supports and mindfulness practices (Nelson et al., 2018). Less is known about the aging process and changes to telomere length that occur naturally at earlier stages of the lifespan, as many studies have focused on telomere length in adults (Gaydosh et al., 2020). Analysis using data from the Future of Families and Child Wellbeing Study (FFCWS) revealed that telomere length increased to a small but statistically significant degree during adolescence (Gaydosh et al., 2020). Research focused on telomere length has primarily included White adults with higher socio-economic status (SES); however, differences have been found in telomere length between those assigned female and male at birth as well as between White and Black adults suggesting there may differences among groups (Gaydosh et al., 2020). Lower socio-economic status may be a contributing factor to shorter telomere length, but research is mixed as this correlation has not been demonstrated consistently (Lin et al., 2012). It

is believed that inflammatory activity associated with anxiety and depression may further exacerbate telomere erosion (O'Donovan et al., 2011). Therefore, it is plausible that protective factors which reduce the development of depression and anxiety and address lack of access to resources may in turn reduce cellular aging.

Association between Measures of Cellular Aging

The nature of the association between DNA methylation and telomere erosion has yet to be identified. However, research has led to hypotheses that DNA methylation may lead to telomere erosion in some instances, while in other situations both may be affected simultaneously by causal factors (Lerea, 2023). For instance, epigenetic changes such as DNA methylation at specific subtelomeric regions (i.e., the space between telomeric caps and chromatin) containing specific genes have demonstrated associations with telomere length (Mendioroz et al., 2020). It may be that telomere erosion contributes to epigenetic changes, such as DNA methylation, or that the lack of DNA methylation maintains telomere length. (Mendioroz et al., 2020). In a meta-analysis of seven large cohorts, DNA methylation at 823 DNA sites across 557 genes was associated with telomere length, after controlling for age, sex, and ethnicity, with most of these associations demonstrating a negative association between higher methylation levels and shorter telomere lengths (Lee et al., 2019). These associations have been studied in terms of both risks related to accelerated aging and protective factors related to reversed accelerated aging or even delayed aging. Analysis of biomarkers at multiple time points within longitudinal studies is recommended to be able to study the direction of changes in humans, which has been a limitation of many relevant research studies thus far (Mitchell et al., 2016).

Cellular Aging: Maternal Depression and Other Early Life Adversity

Much of the research on early adversity and its impact on cellular aging has focused on experiences of exposure to violence. Exposure to violence in childhood, especially multiple forms of violence such as bullying, witnessing maternal domestic violence, or experiencing physical abuse, has been shown to facilitate more rapid telomere erosion for children whose telomeres were measured at age five and again at age ten when compared with children not experiencing such exposure (Shalev et al., 2013). Similarly, some research suggests that advanced epigenetic age, as indicated by DNA methylation, is associated with early life adversity which includes threats of harm, while adverse experiences without a threat of harm may not yield these outcomes (Sumner et al., 2019). Results from a meta-analysis support the association between rapid cellular aging and early adversity, especially for threat-related adversity, whereas family SES and deprivation were not found to be related to advanced cellular aging (Colich et al., 2020). Taken together, research examining early adversity and cellular aging suggests exposure to violence and threat are associated with advanced cellular aging, whereas exposure to deprivation or neglect may not.

Far less research has examined exposure to maternal depression, which does not inherently result in exposure to violence or threat of harm for offspring, as a predictor of cellular aging. As such, the mechanisms by which maternal depression may impact cellular aging are largely unknown. However, researchers have theorized that maternal depression may indirectly impact cellular aging through increased cortisol levels and oxidative stress. For example, infant exposure to maternal depression over a 6-month period has been found to relate indirectly to shorter telomere length through increased cortisol reactivity (Nelson et al., 2018). In other research, maternal depression scores and covariates including maternal age, gestation age, BMI,

and substance use accounted for 35% of the variance in placental telomere length in females (Garcia-Martin et al., 2021). Exposure to maternal stress and parenting behaviors also affects DNA methylation during both antenatal and postnatal development, respectively, which may ultimately result in outcomes such as stress-associated behaviors and psychopathology for children (Mitchell et al., 2016). Exposure to maternal stress increased methylation when measured during adolescence in those assigned male or female at birth, while paternal stress only impacted methylation in those assigned male at birth (Essex et al., 2011). Maternal influence has been found to have a stronger association with child telomere lengths than paternal influence, with total heritability estimated to be around 70% across numerous studies (Broer et al., 2013). This suggests a unique impact of maternal depression, both genetically and through environmental exposure.

The developmental timing of stress exposure may also impact cellular aging. For instance, exposure to stress may also disrupt typical patterns of physiological development. While infants between the ages of 2 and 15 months typically experience decreases in cortisol reactivity, which has known impacts on cellular aging, those who are exposed to maternal depression may experience fewer of these natural decreases over time (Nelson et al., 2018). Fifteen-year-olds who experienced adversity during infancy and preschool periods of development demonstrated different methylation patterns than those who had not (Essex et al., 2011). However, exposure to maternal depression beyond early childhood may still lead to more rapid cellular aging. Exposure to mothers experiencing recurrent depression resulted in shorter telomere length and increased cortisol reactivity to stress in adolescent girls (Gotlib et al., 2015). Focusing on specific time periods and chronicity of exposure to adversity such as maternal

depression may yield greater insights regarding the impact to biological or genetic aging during known periods of sensitivity.

Finally, risk factors associated with maternal depression may also directly affect cellular aging, reflecting a nexus of interactions among types of early adversity. For example, analyses using the FFCWS dataset exploring the association between telomere length and maternal depression did not yield statistically significant correlations between the two; however, there were correlations with covariates including maternal poverty, suggesting that this risk factor for maternal depression may also directly impact telomere length (Thompson & Henrich, 2023). However, this study is limited by its use of an averaged score of maternal depression across four waves spanning eight years. Other analyses of the FFCWS demonstrate that paternal incarceration impacts telomere length in children and adolescents as well as maternal depression, with maternal depression accelerating telomere erosion for children with incarcerated fathers (Del Toro et al., 2022). Taken together, these findings suggest a complex network of interactions between factors such as genetic predisposition and environmental experiences which may influence cellular aging, which aligns with Bronfenbrenner's bioecological model. Given the impacts of maternal depression on both caregiver and child-related functioning, greater attention needs to be focused on existing community resources which could potentially be harnessed to improve outcomes for children exposed to maternal depression. Child care has emerged as one area of focus for its potential role in mediating the impact of maternal depression on child outcomes, considering research that has demonstrated child care can improve outcomes for children facing other types of early childhood adversity (Charrois et al., 2020).

CHILD CARE IN THE UNITED STATES

Child care is often a necessity when full-time parental care is not feasible due to work or training outside of the home. In 2022 in the United States, 65.9% of unmarried mothers of children under the age of 3 participated in the labor force, slightly higher than the 65.4% of married mothers (Bureau of Labor Statistics, 2023). Within married couples, both parents were employed in 61.8% of families and 69% of single mothers of children under 18 were employed in 2022 (Bureau of Labor Statistics, 2023). Due to the increasing needs for child care across the United States, public attention has turned to topics related to availability and quality of child care. Access to high-quality child care has become a central focus at the federal, state, and local levels and agencies have developed various guidelines for assessing child care quality and fostering efforts to improve access to high-quality child care (Zaslow et al., 2016).

Within both research and practice, child care quality has often been defined broadly along two dimensions using structural and process indicators (Magnuson & Shager, 2010). Structural indicators include factors such as child-to-teacher ratio or teacher education level and are conceptualized as indirectly impacting a child's daily experiences. Process indicators include aspects directly impacting a child's daily experiences, such as curriculum, activities, and interactions with peers and caregivers, which are often rated through observations. Methodological issues have emerged in research focused on quality of child care due to differing ways of defining quality even within these two dimensions, variability in length of time children were exposed to child care settings, instability within settings, and heterogeneity in the use of standardized quality assessment tools (Keys et al., 2013; Perlman et al., 2016). A tool commonly utilized to assess quality for center-based care is the Early Childhood Environment Rating System (ECERS). The tool, currently in its third edition, includes a summary score and seven

subscales across items focused on: space and furnishings, personal care routines, language and reasoning opportunities, activities, interaction, program structure, and parents and staff (Harms et al., 2005; Neitzel et al., 2019). A major criticism of this tool and other similar standardized tools is that they do not account for the content of curriculum or teaching practices (Burchinal, 2018). This is a valid concern especially when studying childhood academic outcomes and school readiness. However, this tool may be appropriate for research focused on the provision of safe and stable environments and nurturing relationships within early child care.

Outcomes Associated with Child Care

As conceptualized by Bronfenbrenner, early experiences could influence long-term outcomes for children through impacts on early development influencing later development (Bronfenbrenner, 1995). However, research focused on outcomes related to child care has yielded mixed results regarding the benefits or impacts for children and families. Child outcomes linked to child care have also been defined and studied in myriad ways and child care settings themselves can vary widely, which can make comparing results across studies difficult. For instance, one limitation of Early Head Start and Head Start research is that program offerings can vary across locations as they may include center-based, home-based, or mixed (center- and home-based) services. Despite these limitations, researchers have been able to identify three main factors related to child care which can influence outcomes, such as school readiness and behaviors prior to the transition to kindergarten: quality, quantity, and type of child care (Belsky et al., 2007).

Results from studies focused on the impact of both structural and process indicators of child care quality are mixed (Magnuson & Shager, 2010). Proposed reasons for these mixed results include limited variability in items included in current assessment tools, low inter-rater

reliability, and an overall trend of improvements in quality of child care settings leading to limited variability in quality across centers included in research (Burchinal, 2018). A full review of these mixed outcomes is beyond the scope of this paper; however, it is important to acknowledge the lack of clarity and consistency in findings related to child outcomes and child care quality. When considering factors contributing to child care quality, child-teacher interactions, curriculum, and the educational levels of teachers and directors produce slight gains in child outcomes such as language, math, pre-literacy, and social skills (Soliday Hong et al., 2019). Availability and stability of high-quality child care are also key factors to consider. Maternal depression was associated with maternal perceptions related to available child care options, even after controlling for previous depression and current parenting stress in one longitudinal study (Johnson & Padilla, 2019). Therefore, access to and awareness of available high-quality child care may be protective for maternal mental health, in addition to the potential benefits conferred directly for children who attend high-quality child care.

Much like the impact of maternal depression, the influence of child care quality may be seen across the lifespan. Longitudinal data has suggested that high-quality child care is associated with educational and cognitive benefits in adulthood (Campbell et al., 2001; Campbell et al., 2012). Those with exposure to higher quality care within the first 4.5 years of their lives had lower externalizing behaviors and better academic outcomes at age 15 (Vandell et al., 2010). Types of care did not emerge as a significant predictor of outcomes related to problem behaviors or academic outcomes (Vandell et al., 2010). These findings indicate that exposure to higher quality care continues to yield benefits and may promote benefits even a decade later. The authors argue that since development across the lifespan builds upon earlier experiences and effects may not be seen until later in life, which they refer to as sleeper effects, it is plausible to

consider the impact of early child care even later in life (Vandell et al., 2010). Furthermore, for those who are biologically at higher risk of developing depression, high-quality child care may offer a protective effect (Charrois et al., 2020).

High-Quality Child Care: Factors Impacting Exposure

There are likely systemic issues impacting access to high-quality child care, and perhaps even more so for low-income households or historically marginalized and racially minoritized families. In a study of 80% of all preschool classrooms in the United States, the average summary score from the Early Childhood Environment Rating Scale, Revised (ECERS-R) of all 692 classrooms was 3.83 out of a possible 7, and only 14.5% fell into the highest category using another assessment tool (Classroom Assessment Scoring System) (LoCasale-Crouch et al., 2007). Results of a cluster analysis revealed the poorest quality classrooms had the largest proportion of children from families living in poverty and the highest population of ethnically and racially minoritized children (LoCasale-Crouch et al., 2007). These outcomes may reflect the impact of systemic racism and funding issues which have resulted in disparate access to robust educational opportunities for students across the United States.

The influences of income and child care quality are difficult to disentangle and may in fact be interactive. Exposure to poverty during early childhood may be most influential for development and outcomes later in life, such as high school graduation rates (Duncan & Brooks-Gunn, 2000). Higher quality child care is often more expensive or available in higher income geographical areas. In this regard, quality of child care may be one pathway through which poverty impacts children (Duncan & Brooks-Gunn, 2000). Access to high-quality child care often requires economic resources, in addition to access to transportation and work schedules

that align with center hours. Specifically, child care in general may not be affordable or accessible, let alone higher quality child care, and parents may be left with limited options.

Empirical research has provided deeper insights into what factors may affect whether children are exposed to high- or low-quality child care. It is important to consider natural differences which may exist between those who access high-quality child care and those who access lower-quality child care. Three factors predicted length of time in high-quality early child care in one study: family income positively predicted length of time whereas maternal separation anxiety and child birth order negatively impacted length of time (Bustamante et al. 2022). In terms of length of time in low-quality child care, income and mothers' employment attitudes had a positive association with time spent in lower-quality child care whereas relationship status, age and sensitivity were negatively associated with time in lower-quality child care (Bustamante et al. 2022). This suggests there may be an interaction between other sociodemographic factors and low-quality child care. Exploring outcomes of community-based and family child care situations, rather than standardized early interventions programs such as the Abecedarian Program, may yield more realistic considerations for the impact of child care quality considering these naturally occurring differences (Votruba-Drzal et al., 2004).

Attention has largely focused on center-based child care quality, but consideration regarding the quality of family-based care is also important given that 58% of children in the United States under the age of five who attended child care regularly received care outside of a child care center in 2019 (National Center for Education Statistics, 2021). Other research has suggested that children may be likely to spend more time in center-based care as they near the transition to kindergarten, while time spent in relative care remains stable and time spent in home-based child care decreases (NICHD, 2004). Factors such as maternal education and

income level are associated with the use of center-based care rather than relative care, whereas Hispanic and Black children may spend more time in relative care and children of single mothers may have more time spent in both types of care overall (NICHD, 2004). There may be greater access to family-based care compared with center-based care when parental child care is not available early in a child's life, and children may remain in relative care consistently throughout their early years. While family-based care, including licensed and non-licensed home center and relative care, can confer benefits to children and parents through the provision of safe and stable care, family-based care can be more difficult to regulate and to provide public policies and funding.

Quality of Child care: Impact on Children of Depressed Mothers

Child care quality may be especially impactful for children exposed to maternal depression, since high-quality care is conceptualized as including safe, stable, stimulating, and nurturing environments and interactions with child care providers. Bronfenbrenner conceptualizes developmental outcomes in terms of those factors which are promotive of healthy development or those which reduce dysfunction (Tudge et al., 2016). Promotive effects on development may differ across individuals depending upon other contextual factors, which reflects Bronfenbrenner's focus on process-person-context-time within his bioecological systems theory (Tudge et al., 2016). Bronfenbrenner's model identifies that family characteristics such as access to resources may contribute to differential impacts of exposure to early childhood education, as the accumulation of risks and family resources can influence responses to interventions (Brooks-Gunn, 1995). Demographic factors such as maternal education and family income-to-needs ratio may impact children's cognitive skills, but research has shown that the home environment can mediate the impact of these factors (Duncan & Brooks-Gunn, 2000;

NICHD, 2002). This is also seen within research which demonstrates that higher quality child care may be more impactful for children from lower income families, especially in terms of socioemotional outcomes between the ages of two and four (Votruba-Drzal et al., 2004). Therefore, it is reasonable to suggest that high-quality child care may confer benefits related to the promotion of healthy development or the reduction of dysfunction in children exposed to maternal depression.

Limited research has specifically focused on the impact of quality of child care for children with depressed mothers. In one longitudinal study, higher quality child care moderated the impact of maternal depression on child behaviors at the age of seven or eight (Charrois, 2020). Furthermore, those children who were in a high-quality child care setting did not experience the same difficulties, such as hyperactivity/inattention and depression/anxiety, later in childhood when compared with peers in low-quality settings even if their mothers had a clinical perinatal mood disorder (Charrois, 2020). However, results indicated that perinatal mood disorder had a stronger influence on risk for later negative outcomes than socio-economic factors (Charrois, 2020). In another longitudinal study, the Wisconsin Study of Families and Work, low-quality child care for children exposed to maternal depression and anger at age 4.5 resulted in more behavioral problems and impaired prosocial functioning in first grade (Goelman et al., 2014). Quality of child care was found to buffer the impact of exposure to maternal mental health struggles for both short-term and long-term outcomes (Goelman et al., 2014). In a subsample of the NICHD Study of Early Child Care, researchers found that high-quality non-maternal child care did not provide a buffering effect for risks including maternal depression on outcomes at age 24 or 36 months (NICHD, 2002). In other analyses from a larger sample, a buffering effect was found for higher quality non-maternal care on the relationship between

maternal depression and children's positive engagement with their mothers at 36 months (NICHD, 2003). Therefore, research remains mixed in terms of the buffering impact of child care quality for children exposed to maternal depression, which could be due to the timing of exposure.

Although limited research has explored the association directly, there still may be benefits of high-quality child care for depressed mothers and their children. In a randomized control study of Early Head Start, maternal depression rates were lower during the program and two years after completion of Early Head Start when compared with rates in a control group (Chazan-Cohen, et al., 2007). Factors which served as mediators between program participation and maternal depression included aggressive behaviors in children at age two and three, parenting distress, and spanking reported at age two (Chazan-Cohen, et al., 2007). These results suggest that interventions aimed at improving child outcomes may indirectly impact maternal outcomes, with effects that may even accumulate over time.

CURRENT STUDY

Children exposed to maternal depression may be at higher risk for negative health outcomes, and these potential effects could be seen through measures of epigenetic or biological aging. Measures such as those related to DNA methylation and advanced cellular aging "might be useful as a surrogate end point in evaluation of programs and policies to address the childhood social determinants of lifelong health disparities" (Raffington et al., 2021, p. 1). In addition to these risk factors which can be measured through studying cellular aging, protective factors may also be identified through similar methods. For instance, access to environments outside of the home which provide stimulation, nurturing relationships with caregivers, and safety may offer opportunities that children otherwise may miss out on when they are exposed to stressors such as

maternal depression (Shonkoff and Philips, 2000). Although outcomes including academic, economic, and mental health functioning following child care exposure have been mixed, limited research thus far has focused on health outcomes related to child care quality. An extensive search yielded no articles focused on child care exposure and cellular or biological aging. This provides support for the exploration of this research question focused on the potential moderating effect of child care quality on the relationship between child health outcomes and maternal depression. Therefore, the purpose of this study is to examine whether there is an association between maternal depression exposure and cellular aging, and if quality of child care moderates this association. This study was also focused on the potential impact of poverty level on the association between maternal depression and cellular aging. The selected dataset also has a diverse sample in terms of race, ethnicity, and income level of participants to account for the limitations of previous research centered around White, middle-income participants. This study was guided by the following research questions and hypotheses:

R1: Is exposure to maternal depression at age one related to accelerated cellular aging at age nine or 15? It was hypothesized that exposure to higher levels of maternal depression at age one would be positively associated with accelerated cellular aging as measured by telomere length and DNA methylation at ages nine and 15.

R2.1: Does exposure to high-quality child care at age three buffer the impact of maternal depression exposure at age one on cellular aging? It was hypothesized that higher quality child care at age three would buffer against the negative impacts of maternal depression exposure at age one on cellular aging at ages nine and 15.

R2.2: Does the association between maternal depression and cellular aging vary due to poverty status? It was hypothesized that poverty status, as defined by poverty ratio, at age one would

strengthen the association between exposure to maternal depression at age one and cellular aging at ages nine and 15.

Methods

This study utilized data from the Future of Families and Child Wellbeing Study (FFCWS), previously the Fragile Families and Child Wellbeing Study. The FFCWS is a longitudinal study which began between 1998 and 2000 with 4,897 families including approximately 3,600 unwed parents and 1,100 married couples in 20 U.S. cities (Reichman et al., 2001). The original purpose of this study was to explore the challenges and capabilities of unmarried parents and associated child outcomes over time using a diverse sample by following families beginning at birth. About 3,595 parents participated in the most recently published wave, 15 years after birth. Participants were recruited and interviewed at birth (Reichman et al., 2001). The study employed a stratified random sample of 20 U.S. cities with 200,000 or more people, with births sampled within hospital locations (Reichman et al., 2001). Criteria for inclusion included parents over the age of 18, written or verbal fluency in Spanish or English, a biological father who was living, and that there were no plans to place the child for adoption (Reichman et al., 2001). The sample includes parents and their children who have been tracked since birth, including individuals who have historically been excluded from longitudinal studies or other relevant research such as low-income families, mothers with lower educational attainment, and racially and ethnically diverse families.

Participants

The current study focused on families who met the following criteria: (1) mothers participated in the Wave 1, 2 and 3 interviews; (2) the family participated in the Child Care Study at Wave 3; (3) the child lived with the mother at least half of the time at Waves 2 and 3;

and (4) biomarker data were available for the mother at Wave 5 and for the focal child at Waves 5 and 6. A total of 350 mother/child dyads met these inclusion criteria in the present study. However, only 189 of those specifically had epigenetic ages calculated using DNA methylation at Wave 5, and 182 at Wave 6.

Further refinements, described in detail in the preliminary analyses section, were made to the sample of 189 participants, resulting in a final analytic sample of 100 participants. Descriptive statistics and frequencies for this final analytic subsample are available in Tables 1 and 2. At the age of three, the mean amount of time spent in child care per day was 7.48 hours and the mean number of different child care arrangements used was 1.20. The mean age of mothers at birth was 25 years. Most mothers completed high school or earned a GED and the majority of mothers in the sample self-identified as Black and non-Hispanic. Approximately 52% of mothers in this subsample met criteria for Major Depressive Disorder at Wave 2, around 1 year of age for their child, and 55% at Wave 3, during the child's third year. Comparatively, the prevalence of major depression in mothers in the general population in the U.S. in the year following birth is estimated to be between 6.5% to 12.9% (Earls, 2010). At Wave 2, approximately 33% of the families had income under the poverty threshold and at Wave 3 this increased to approximately 41% of families.

Measures

Maternal Depression

Maternal depression was assessed in years 1 and 3 (Waves 2 and 3) via the Composite International Diagnostic Interview – Short Form. The CIDI-SF includes items focused on diagnostic criteria associated with Major Depressive Disorder and asks respondents to rate the presence of symptoms within the prior two weeks as well as the severity or duration of some

symptoms. Maternal depression indicator variables are available in both continuous and dichotomous formats. For the latter, the FFCWS data set includes constructed dichotomous variables at Years 1 and 3 (Waves 2 and 3) which indicate whether maternal participants are likely to meet criteria for major depressive disorder based upon scores from the CIDI-SF, using a cutoff score of 3. The self-administered CIDI-SF-SF has acceptable validity and reliability, and 10 items related to Major Depression were supported by factor analysis (Gigantesco & Morosini, 2008). A modified version using 8 items was included in the FFCWS, with additional items related to severity or duration of symptoms.

Cellular Aging

Saliva samples were collected from biological mothers and focal children at the 9-year follow-up (Wave 5) and again from the children at the 15-year follow-up (Wave 6 FFCWS, 2023). Samples were collected using the Oragene DNA Self-Collection Kit (DNA Genotek Inc., Ontario, Canada) and then shipped to Princeton University for processing. It is common for researchers to rely on a few different measures of genetic aging, as they can differ in terms of correlation with one another and with chronological age (Belsky et al., 2022; Field et al., 2018). For the present study, two biological markers of cellular aging at each time point were used in the primary analyses, including estimates of epigenetic age based upon DNA methylation and telomere length.

DNA Methylation

The FFCWS includes nine epigenetic clock estimates based on DNA methylation. Some of these methods (i.e., Horvath and Hannum) represent first generation clocks, whereas others (e.g., DNAmPhenoAge and DNAmGrimAge) represent second generation clocks. First generation clocks estimate biological age, whereas second generation clocks estimate concepts

such as pace of aging and mortality risk. The present study was primarily interested in estimates of biological age, so only the first-generation clocks were considered (i.e., Horvath and Hannum). The Horvath and Hannum DNA methylation age estimators have moderate to strong correlations and prediction of all-cause mortality, despite measuring different sites of DNA (Bergsma & Rogaeva, 2020). However, Horvath is considered the preferred epigenetic clock to use in pediatric samples, since it was trained using pediatric tissues. By contrast, Hannum's clock was developed using adult blood tissue, leading to biased estimates in pediatric samples and with other tissue sources (Horvath & Raj, 2018). Because the present study was interested in biological age estimates of children, Horvath was ultimately chosen as a measure of DNA methylation. Horvath estimates are close to zero for embryonic cells and yield a correlation with chronological age of $r = 0.97$ with a margin of error of 2.9 years (Horvath, 2013).

DNA methylation profiling was completed using two assays: (1) the Illumina Infinium Human Methylation450K and (2) the Illumina Infinium Human MethylationEPIC (FFCWS, 2023). Participants were randomly assigned to one of the methylation profiling assays, which remained consistent at the two time points. The use of two different assay platforms for profiling methylation of DNA derived from saliva utilized within the sample, the Illumina Infinium 450K and the Illumina EPIC methylation assays, is an important consideration for researchers utilizing the biological outcomes data from the FFCWS is that. There are differences between the CpG sites where methylation occurs included in the two assays for analyses (Van Asselt et al., 2023).

Telomere Length

Telomere length was determined through triplicate measures which resulted in an average length reported. Researchers were cautious to avoid batch effects and used reference DNA to ensure that measurements remained consistent. Researchers re-analyzed 228 samples from the

Year 9 collection using the same reagents and procedures as the Year 15 collection, with no statistically significant differences found between the repeat measurements (FFCWS, 2023). They then estimated a linear relationship between the original and repeat measurements using the 228 samples and adjusted Year 9 telomere length values by a correction factor (FFCWS, 2023). Shorter telomere lengths are associated with more rapid cellular aging than would be predicted by chronological age and are therefore suboptimal.

Child Care Quality

Information about quality of child care for center-based care is drawn from the results of the ECERS-R at age 33 months, which was completed by a research observer in the primary child care setting. A primary child care setting was defined as the non-maternal care setting in which a child spent the most time (i.e., at least 5 hours per week out of a minimum of 7 hours). Scoring criteria for the ECERS-R can vary, as validity for thresholds has not been well-established (Setodji et al., 2019). The ECERS-R was completed by observers after spending a few hours in the child care setting and this version used during Wave 3 includes 38 items across the 7 subscales focused on: the physical space (Space and Furnishings); routines related to hygiene, naps, meals and greetings (Personal Care Routines); opportunities for exposure and practice related to communication and reasoning skills (Language-Reasoning); accessibility of activities to stimulate areas of cognitive, social-emotional, and motor development such as dramatic play, music, art, and movement (Activities); interactions between caregivers and children and among children (Interaction); structure of the schedule including free play and group time and provisions for children with disabilities (Program Structure); and provisions for parents and staff (Parents and Staff). However, only one item from the Parents and Staff subscale was included, eliminating the possibility of calculating a subscale total. Observers indicated

elements of the environment or caregiver-child interactions and then scored individual items on Likert-type scale from 1 to 7, with 1 representing low quality and 7 representing highest quality, with anchored indicators available for items; subscale scores and total scores rely on calculating simple means (Clifford et al., 2010). The ECERS-R has been shown to be stable indicator of child care throughout a school year with teachers who remain in the classroom, and inter-rater reliability of over 70% was found for all indicators with 71% agreement for scores within one point of one another across all items, and internal consistency within subscales at values of 0.71 or higher and 0.92 for the total score (Clifford et al., 2010).

Poverty

Poverty was measured using a categorical variable reflecting poverty ratio (in bands such as 0-49%, 50-99%, etc.). Family income level was reported by the primary caregiver and a categorical variable was constructed by FFCWS researchers to reflect the poverty ratio. For instance, a family within the category including 100% would be considered at the federal poverty line based on household size, while a family within the category capturing 50% would be considered below the poverty line with an income which is half the poverty level.

DATA ANALYSES

The primary analyses, which examined the associations among maternal depression at age 1 (Wave 2), child care quality at age 33 months (Wave 3), and measures of epigenetic age (i.e., DNA methylation and telomere length) at ages 9 (Wave 5) and 15 (Wave 6), were conducted via a series of linear regression models. All analyses were performed in SPSS. Biological age was included as a continuous covariate in all models. For the first research question, the outcome of interest in regression models (i.e., Models 1-4) was the main effect of maternal depression on DNA methylation and telomere length at ages 9 and 15. For the second

research question (Models 5-8), the primary outcome of interest was the interaction term between maternal depression and child care quality. Finally, the main outcome of interest for regression models addressing the third research question (Models 9-12) was the interaction term between maternal depression and poverty status. All interaction terms were added individually to the main effects models and nonsignificant interaction terms, based on a nonsignificant change in R^2 , were omitted from the final models. Statistically significant interaction terms were further probed using simple slopes analysis.

Results

Preliminary Analyses

Although participants were randomly assigned to either the 450k or Epic analyses, an ANOVA analysis was conducted to determine if there were any statistically significant differences in Horvath's epigenetic age scores between the two assay platforms. Results suggest there was a statistically significant difference between these groups at Wave 5 ($F(1, 187) = 23.37, p < 0.001$) and Wave 6 ($F(1, 179) = 11.51, p < 0.001$). Subsequently, the DNA methylation profiling platform was added as a covariate to all regression models examining DNA methylation to control for these differences.

Additional preliminary analyses were conducted to screen all analytic variables for skewness and kurtosis. Among the 189 participants for whom cellular aging data were available, the majority (77%) reported no depression symptoms at Wave 2, creating significant skewness in the continuous scores of depression based upon CIDI-SF raw scores. Applying natural log transformations to this variable did not reduce skewness values to within acceptable levels. For this reason, a dichotomous variable was created to represent mothers who reported no symptoms of depression on the CIDI-SF ($n = 146$), and those that reported one or more symptoms of

depression ($n = 43$). Information regarding chronological age was not available for four of these participants and they were not included in final analyses. Because this dichotomous variable resulted in unbalanced group sizes, a total of 41 participants reporting no depression symptoms were randomly selected to create balanced groups. Specifically, for those who had a mother with any depressive symptoms at Wave 2, 20 participants had been randomly assigned to the 450k platform and 19 participants were randomly assigned to the EPIC platform. To allow for comparison, the same number of cases with no exposure to maternal depression symptoms were selected at random between the two platforms (i.e., 22 for the 450k platform and 19 for the EPIC platform). Therefore, a final sample of 80 participants were included for the analyses focused on epigenetic age using DNA methylation in the current study. An additional 20 participants were included for whom telomere length data was available, but no DNA methylation analyses were completed, resulting in a final subsample including 100 participants. Finally, due to skewness and kurtosis values outside of acceptable ranges, natural log transformations were applied to Horvath epigenetic age values for Wave 5 and 6 as well as for chronological ages at these time points. This reduced the values to within acceptable limits.

Descriptive Analyses

Table 3 provides means, standard deviations, and score ranges for all analytic variables. Overall child care quality had a mean level of 4.77 on a scale of 0-7, just below the 5.0-5.5 range considered “good enough”. Mean ECERS subscale scores were highest for those focused on interactions between the child and child care providers, the physical elements of the child care space, and the routines surrounding greetings, meals, naptime, safety, and hygiene. Overall, maternal depression symptoms were low and the means for both Wave 2 ($M = 2.70, SD = 2.68$) and Wave 3 ($M = 2.62, SD = 2.89$) were in the subclinical range. Biological outcomes at Wave 5

and 6, taken at age nine and 15 respectively, indicate a general pattern of a mean estimated age based upon Horvath's clock which is lower than chronological age (Table 3).

Bivariate correlations using Pearson's correlation coefficient for analytic variables of interest are presented in Table 4. Telomere length at Waves 5 and 6 were not correlated with Horvath's epigenetic clock estimators. However, Horvath's epigenetic clocks estimates from Waves 5 and 6 were correlated with one another and telomere length at Waves 5 and 6 were also correlated. Income level was correlated with maternal depression scores at Wave 2; however, neither of these variables were correlated with other analytic variables of interest. Child care quality measured at Wave 3 (age 3) was not correlated with any other variables.

Maternal Depression and Cellular Aging

For the first research question regarding whether exposure to maternal depression was related to accelerated cellular aging, a series of linear regressions were completed. Models 1 and 2 examined the association between maternal depression biological aging, as measured by Horvath's epigenetic clock at Waves 5 and 6, respectively. Results are presented in Table 5. Maternal depression did not emerge as a statistically significant predictor of cellular aging in either model. Additionally, adding an interaction term between maternal depression and the biological platform used did not result in a statistically significant change in R^2 value, indicating that maternal depression was not associated with Horvath's clock for either biological platform group.

Models 3 and 4 examined if maternal depression exposure at Wave 2 (i.e., child age one) predicted epigenetic aging outcomes using telomere length at Waves 5 and 6, respectively (see Table 6). Similar to the models using Horvath's clock, neither model yielded statistically significant estimates, suggesting that telomere length is not predicted by maternal depression.

Child Care Quality as a Moderator

The second research question focused on whether exposure to high-quality, center-based child care buffers the impact of exposure to maternal depression in early childhood on cellular aging. Moderation analyses were completed to determine whether quality of center-based care at age 33 months moderated the relationship between maternal depression in early childhood (i.e., age one) and biological age and epigenetic age at Waves 5 and 6. Results of linear regression models examining the moderating effect of child care quality on the association between maternal depression and Horvath's clock (Models 5 and 6) are presented in Table 7. The outcome of interest was the interaction between child care quality and maternal depression. There was a statistically significant interaction effect between child care quality and maternal depression on biological age at Wave 5 (Model 5). This interaction is presented graphically in Figure 1. A follow-up simple slopes analysis revealed that there was no association between maternal depression and biological aging when child care quality was low for those who were not exposed to maternal depression; however, there was a statistically significant and positive association between maternal depression and cellular age at high levels of child care quality for those who were not exposed to maternal depression. More specifically, results from the Johnson-Neyman procedure indicated that the association between maternal depression and biological aging at Wave 5 was only statistically significant when scores of child care quality were 5.27 and greater. These results suggest that higher values of child care quality are protective against biological aging in the absence of exposure to maternal depression symptoms at age 1. No other interactions were statistically significant when added to the main effects model, including those between the biological platform used and depression symptoms group ($R^2 = 0.18$, $\Delta F(5, 72) =$

1.12, $\Delta R^2 = 0.01$, $p = 0.293$) and the biological platform and ECERS-R summary score ($R^2 = 0.17$, $\Delta F(5, 72) = 0.22$, $\Delta R^2 = 0.003$, $p = 0.643$).

Since there was a statistically significant interaction with child care present in the model, additional analyses were completed to determine if there were any particular subscales from the ECERS which also demonstrated a statistically significant interaction with maternal depression. Follow up analyses indicated two subscales of the ECERS-R moderated the relationship between maternal depression symptom exposure and biological aging using Horvath's epigenetic clock, including the Space and Furnishings $R^2 = 0.275$, $\Delta F(1, 69) = 5.945$, $\Delta R^2 = 0.063$, $p = 0.017$) and Personal Care Routines subscales ($R^2 = 0.265$, $\Delta F(1, 69) = 6.561$, $\Delta R^2 = 0.070$, $p = 0.013$). Since the Personal Care Routines subscale provided the largest change in R^2 value, this interaction was probed further and a simple slopes analysis was completed (Figure 2). Those with no maternal depression exposure had reduced biological aging at values of this subscale above 5.26, representing about 50% of the values in the sample. In other words, higher ratings on the subscale related to Personal Care Routines were protective of biological aging for those not exposed to maternal depression.

For Wave 6 (Model 6), the type of biological analysis platform used and chronological age produced the only statistically significant main effects. None of the two-way interaction terms between maternal depression group and ECERS-R summary scores ($R^2 = 0.161$, $\Delta F(5, 70) = 0.644$, $\Delta R^2 = 0.08$, $p = 0.425$), the biological platform used and depression symptoms group ($R^2 = 0.156$, $\Delta F(5, 70) = 0.254$, $\Delta R^2 = 0.003$, $p = 0.616$) or the biological platform and ECERS-R summary score ($R^2 = 0.155$, $\Delta F(5, 70) = 0.108$, $\Delta R^2 = 0.001$, $p = 0.743$) were statistically significant when added to the main effects model. A three-way interaction term between depression, the ECERS-R summary scores, and biological platform was also not statistically

significant. These results suggest that child care quality did not moderate the association between maternal depression and Wave 6 measures of Horvath's clock, regardless of whether the 450k or EPIC platform was used.

Results of models examining if child care quality moderates the association between maternal depression and telomere length at Wave 5 (Model 7) and 6 (Model 8) are presented in Table 8. Child care quality did not moderate the association between maternal depression and telomere length in either model.

Poverty as a Moderator

A related research question regarding whether poverty impacted the association between maternal depression and cellular aging utilized linear regression. Results are presented in Tables 9 and 10. For measures of Horvath's epigenetic clock at Wave 5 (Model 9), the only predictor variable that was statistically significant was the biological analysis platform used for the DNA sample (i.e., 450k or EPIC). None of the two-way interaction terms were statistically significant, including those between maternal depression group and Wave 2 poverty category ($R^2 = 0.178$, $\Delta F(5, 72) = 0.847$, $\Delta R^2 = 0.10$, $p = 0.360$), the biological platform used and depression symptoms group ($R^2 = 0.179$, $\Delta F(5, 72) = 0.913$, $\Delta R^2 = 0.010$, $p = 0.343$) or the biological platform and Wave 2 poverty category ($R^2 = 0.176$, $\Delta F(5, 72) = 0.678$, $\Delta R^2 = 0.008$, $p = 0.413$). For Wave 6 (Model 10), none of the models were statistically significant including those including only the main effects and those with interaction terms for maternal depression group and Wave 2 poverty category ($R^2 = 0.144$, $\Delta F(5, 70) = 0.114$, $\Delta R^2 = 0.001$, $p = 0.737$), the biological platform used and depression symptoms group ($R^2 = 0.143$, $\Delta F(5, 70) = 0.086$, $\Delta R^2 = 0.001$, $p = 0.770$) or the biological platform and Wave 2 poverty category ($R^2 = 0.143$, $\Delta F(5, 70) = 0.013$, $\Delta R^2 = 0.000$, $p = 0.910$). This suggests poverty and child care quality did not impact Horvath's cellular aging

estimates at age 15. As with the previous research question, moderation analyses for telomere length were completed via linear regression. The models for telomere length at Waves 5 (Model 11) and 6 (Model 12) were also not statistically significant, indicating that poverty and child care quality do not impact cellular aging measured by telomere length (Table 10).

Sensitivity Analyses

Follow-up sensitivity analyses were performed using the continuous measure of maternal depression. All regression models (Models 1-12) were rerun with continuous maternal depression scores to determine if results differed. The results from these analyses yielded comparable results to models using the dichotomous depression variable.

DISCUSSION

Advances in the study of cellular aging provide new opportunities for research focused on both risk and protective factors impacting child development over the lifespan. While risk factors associated with early childhood adverse experiences have garnered much attention, limited research has specifically focused on exposure to maternal depression and even less has focused on child care quality as predictors of cellular aging. Results of the current study using the FFCWS longitudinal data set suggest high-quality child care at the age of three may offer protective benefits at age one on cellular aging at age nine using Horvath's epigenetic clock, but not for those whose mothers report maternal depression symptoms.

Maternal Depression and Cellular Aging

The first research question explored whether maternal depression was related to cellular aging outcomes. Living with a caregiver with a mental health disorder is one of the original ACEs studied by Felitti et al. (1998) who pioneered the examination of long-term effects of ACEs. Research focused on the amount and type of ACEs exposure has demonstrated numerous

long-term effects on physical and psychological outcomes, including cellular aging (Essex et al., 2013; Shonkoff, 2012). Advanced cellular aging in childhood has been associated with a variety of adverse experiences, including poverty, violence, parental stress, parental incarceration, maternal depression, and time spent in orphanages (Del Toro et al, 2022; Drury et al., 2012; Mitchell et al., 2014; Shalev et al., 2013). Given this past research demonstrating an association between adverse childhood experiences (ACEs) and advanced cellular aging, it was hypothesized that exposure to maternal depression at age one would be associated with advanced cellular aging at ages 9 and 15, as measured by Horvath's clock and telomere lengths. The hypotheses were not supported by the analyses; maternal depression did not emerge as a statistically significant predictor of cellular aging at either time point.

These findings are contradictory to prior research which has found an association between exposure to maternal depression and telomere length in infancy (Nelson et al., 2018). One possible explanation for this disparity is that the present study did not account for the chronicity or severity of depression symptoms. Exposure to chronic maternal depression is linked with worse child academic and psychosocial outcomes (Goodman et al., 2011). The presence of chronic maternal depression symptoms may compound impacts to maternal functioning and parent-child interactions, which may require more resources over time to address and counteract. This suggests further exploration of exposure to adverse experiences such as maternal depression is warranted, ideally using larger samples with more participants with both acute and chronic maternal depression symptoms compared across distinct stages of infant and child development, which has consistently been overlooked in maternal depression research (Goodman et al., 2011).

Developmental timing of exposure to maternal depression is also an important consideration. It is plausible that the strength of the influence of maternal depression varies

across developmental stages or age groups (Elgar et al., 2004). Interactions between maternal depression and other outcomes, such as child behavior problems, may also be unique across ages and stages of development in early childhood. While children require safety and stability throughout childhood, children have distinct needs across stages of early childhood development before and after new skills emerge, with infants being the most reliant on their caregivers to meet their needs. The present study was only focused on one measure of depression completed around the child's first birthday and no information was available regarding symptoms earlier in the postpartum or antenatal period. Maternal depression exposure at earlier time points within infancy may increase oxidative stress and shape infant response behavior patterns related to their own distress or interactions, thus potentially exerting stronger influence over cellular aging. Antenatal exposure to maternal stress may also influence cellular aging, as seen in research focused on fetal telomere length.

Although this study did not find a difference in outcomes related to cellular aging based upon early childhood exposure to maternal depression, other research suggests rapid telomere length erosion and epigenetic aging are impacted by exposure to early risk factors. As prior research has indicated, there may also be nuances in terms of the association between cellular aging and threat-based adverse experiences compared with neglect. Therefore, there may not be a direct influence of maternal depression on child cellular aging but rather indirect associations through the impact of maternal depression on other factors which advance cellular aging. As found in prior research, maternal depression may increase maternal stress levels and the risk of maltreatment (Baldwin et al., 2020). There may be transactional interactions between maternal depression and coercive parenting behaviors as well as child conduct problems over time (Hails et al., 2018). Consequently, it may be worthwhile to study specific parenting behaviors which

can be influenced by maternal depression regarding their impacts on cellular aging. In a study using the FFCWS Wave 3 data, mothers who experienced depression symptoms reported higher mean levels of acts of psychological and physical aggression towards their children and rates of neglect during the previous year (Taylor et al., 2009). While these considerations were not included in the present study, these factors should be integrated into future research exploring the impact of maternal depression exposure on cellular aging.

Child Care Quality as a Moderator

The second research question focused on the potential moderating effect of child care quality on the impact of maternal depression exposure at age one and cellular aging outcomes. Given that high-quality child care is associated with more positive outcomes for children, it was hypothesized that high-quality child care would provide a buffer against the impact of maternal depression on biological markers of aging, such as telomere length and DNA methylation. Findings confirmed that high quality child care did serve as a protective factor against biological aging measured by Horvath's epigenetic clock at age 9 (Wave 5), but only for children who were not exposed to maternal depression symptoms as measured at age one. These results indicate access to high-quality child care alone may not be sufficient to reduce the impacts of maternal depression exposure, but other factors such as the amount of time spent in high-quality child care may be especially salient. It remains possible that high-quality child care may buffer the impact of exposure to more acute depression symptoms, but not for chronic symptoms. Further analysis revealed a specific value of the ECERS-R summary score at which high-quality child care slowed biological aging for those not exposed to maternal depression. This value fell within the range typically considered to be "good enough" by policy makers. Two specific subscales related to dimensions of child care quality were found to moderate the relationship between exposure to

maternal depression and cellular aging for those whose mothers did not report any depression symptoms when surveyed at age 1. No associations were found with telomere length.

Findings from other research indicate potential influences between child care quality and maternal depression symptoms, as high-quality child care may be associated with reduced reports of maternal depression symptoms while low quality settings may increase depression and worry (Gordon et al., 2011). The results from this study underscore the importance for increased focus on treatment and support for maternal depression symptoms, and ideally prevention of these symptoms. There is an ongoing need for accessible treatment options for mothers experiencing depression to improve these depression symptoms and address the long-term impacts for children. Recommendations for programs to address maternal depression include incorporating a focus on parent-child interactions, which can serve as prevention or intervention for the impacts to children through improvements in the parent-child relationship (Knitzer et al., 2008). Educational programs or materials about postpartum depression for new mothers and their families may help to overcome lack of awareness or information about maternal depression.

Although child care quality may not buffer the impacts of maternal depression exposure, child care sites may be well-positioned to provide information for treatment options given the frequency with which depressed mothers may be interacting with child care providers. For instance, federally funded Early Head Start sites are required to offer prenatal and postpartum information when enrolling pregnant women. These programs are also tasked with initiating referrals or helping to connect families with services, although reports suggest caregivers with depression may not be accessing this support (Administration for Children and Families, 2006). Greater efforts focused on utilizing sites such as child care centers or pediatrician offices where there is more frequent contact with mothers experiencing clinical or subclinical depression to

provide access to information and treatment may reduce barriers to care such as those related to child care and transportation.

For those who were not exposed to maternal depression symptoms, the subscale which emerged as the strongest moderator of cellular aging and maternal depression was one focused on Personal Care Routines. This subscale reflects center-based practices and routines surrounding health, safety, naps, daily greetings, and toileting needs. Items are focused on topics such as the provision of well-balanced meals, nap time, hand washing, safety, and independence related to personal hygiene (NYC Department of Education, 2021). This finding is especially important for policy makers and child care staff to consider, given that analyses from 2017-2020 of center-based care sites in New York City indicated Personal Care Routines subscales consistently scored the lowest of all six subscales within the ECERS-R (NYC Department of Education, 2021). This finding also brings up questions regarding the utility of the ECERS-R summary score for decision making and evaluation purposes. While the total summary score may be useful for communicating multiple elements of a child care setting, it may not be fully reflective of the importance or impact of the various elements it measures. State policymakers often view a score of 3.0 to 3.5 as a bare minimum, with a score between 5.0 and 5.5 often signaling quality that is “good enough” (Setodji et al., 2019). The overall average score for the ECERS-R in this subsample was nearing this “good enough” range. Another limitation of the ECERS-R, which is a commonly used tool, is that it is often used to measure caregiver-child interactions broadly and does not distinguish emotional support and instructional support as other standardized tools do (Zaslow et al., 2016). It is possible these mechanisms may also contribute protective benefits. Furthermore, there are nuances pertaining to exposure to high-quality child

care which should be considered in future research, including continuity of care with stable caregivers within child care settings (Papero, 2005).

Researchers suggest there may be differential impacts of child care for children of high and low socio-economic backgrounds, such that child care programs may confer benefits for disadvantaged families and negative impacts for advantaged families (Baker et al., 2019). This could be one explanation for the findings from the current study, as close to 40% of the families were at or below the poverty line during the child's first and third years while at least 25% of families had incomes three times over the poverty line. This variability in income level may have obscured some of the effects of child care in the current study and would be worth controlling for statistically within future research focused on child care quality. Children from low-income families who had sustained exposure to high-quality early child care and education demonstrated fewer disparities at age 26 related to educational attainment and wages than those from low-income families without this exposure (Bustamante et al., 2022). There are also individual factors to consider, in line with Bronfenbrenner's model, in terms of interactions between a child's temperament and child care. Quality of care may yield distinct impacts in children with different temperament styles, as those with negative-emotional styles or "difficult" temperaments in infancy experienced more behavioral issues in kindergarten when exposed to low-quality child care and fewer behavioral issues when exposed to high-quality child care than those with "easy" temperaments (Pluess & Belsky, 2009). These temperamental traits were not considered within the focus of these analyses but could be included in future research across measures of cellular aging which may reflect impacts of risk and protective factors.

Poverty as a Moderator

The final planned research question explored whether poverty impacted the relationship between maternal depression exposure and cellular aging, with a hypothesis that poverty would strengthen the association between maternal depression exposure and cellular aging. Results did not support this hypothesis for the selected subsample. Researchers have proposed a mediated-moderator pathway linking poverty as a risk factor for maternal depression which influences child developmental outcomes and is impacted by age of entry into high-quality child care (Papero, 2005). This suggests a more intricate network of influence for these outcomes of interest, stemming from a confluence of factors rooted in poverty and impacting both maternal and child outcomes. Specifically, poverty can impact parents and children directly and indirectly through increased maternal depression risk, the quality of affordable child care options, and even the age of child care entry in the absence of universal paid parental leave policies. It is possible that poverty levels influenced the quality of child care, maternal depression levels, and time spent in child care, which were not explored in detail in the current study beyond the examination of poverty serving as a potential moderator for depression and cellular aging.

Cellular Aging Over Time

Impacts to cellular aging differed across the two time points. It is interesting that the protective influence of high-quality child care on the association between maternal depression and cellular aging (as measured by Horvath's clock) were found at age 9 but not at age 15. Research is mixed regarding whether social-emotional and academic outcomes related to quantity, quality, and type of child care experiences endure as children age (Love et al., 2013; NICHD, 2005; Vandell et al., 2010; Vogel et al., 2010). It may be possible that some influences endure while others appear over time or disappear, or that measures of cellular aging and

mortality risk in pediatric samples have sensitivities at particular stages of development. These results may also suggest developmental timing of maternal depression exposure and child care quality may be especially salient for the impacts on cellular aging at earlier time points, but that these impacts may disappear in adolescence. Future research can explore whether these impacts are fully resolved throughout the lifespan, or if there is any evidence related to cellular aging of the “sleeper effects” discussed by other researchers given the idea that earlier experiences build upon one another over the course of development (Vandell et al., 2010).

There were also notable differences in outcomes related to the measure of cellular aging used. Analyses of the initial subsample of 350 participants demonstrated differences in estimates of cellular aging across the platforms used (i.e., 450k vs EPIC), with no evidence to suggest these differences were caused by demographic differences associated with randomization to the platforms. Other analyses of blood samples drawn from newborn and 14-year-old participants using the 450K and updated EPIC methylation profiling platforms revealed high correlations within each sample between the two platforms and expected differences between males and females across ages were observed (Solomon et al., 2018). Therefore, it may be worthwhile exploring plausible explanations for these differences. Telomere length was not correlated to Horvath’s clock, suggesting these are distinct measures of cellular aging. The results of these analyses suggest different measures of cellular or biological aging may have varying sensitivity to distinct environmental factors and this may be influenced by the methylation analysis platform utilized. Researchers suggest ongoing efforts to better understand the cellular mechanisms of aging and biological age estimators in conjunction with the environmental, developmental, and individual factors which may influence them (Horvath & Raj, 2018).

Limitations and Future Research

There are some notable limitations to this study that highlight areas in need of future inquiry. Additional considerations are warranted for the use of some epigenetic clocks in pediatric samples since most epigenetic clocks were not developed or trained using pediatric samples. Horvath's epigenetic clock may also be limited in its ability to discern risk and protective factors compared with second generation clocks such as GrimAge. When compared with age acceleration based upon Horvath's clock using twin studies, age acceleration based upon GrimAge is a stronger predictor of mortality separate from genetic influences (Föhr et al., 2021). Prior research has focused on measuring both risk and protective factors using GrimAge. Emotional regulation and self-control may moderate some of the relationships between cumulative stress, insulin resistance, and adrenal sensitivity on GrimAge (Harvanek et al., 2021). Therefore, second generation clocks are promising outcomes of interest in studies focused on known risk factors influencing these later outcomes and may also adequately capture protective factors, highlighting the biological embedding of these experiences. Other variables of interest, such as age of menarche and early exposure to abuse, have been found to predict GrimAge but not outcomes based upon the first-generation epigenetic clocks such as Hannum's and Horvath's (Hamlat et al., 2021). This may be a function of the established superiority of this measure, possibly due to its unique utilization of CpG sites, especially for predicting relationships with environmental factors and aging or because epigenetic clocks may represent distinct aspects of epigenetic aging based upon different biological processes (Hamlat et al., 2021; Horvath & Raj, 2018). However, since there is limited research using GrimAge estimates following pediatric samples as they age, it is difficult to discern the precision of GrimAge in pediatric samples (Joyce et al., 2022). Furthermore, effect sizes for research focused on early life adversity and

accelerated development tend to be small (Belsky, 2019). Therefore, while second generation clocks may lend themselves to the study of social risk and protective factors, this application within pediatric samples remains unclear and is worthy of ongoing research.

Caution is also warranted in interpreting the results of the present study, as the association between maternal depression and child outcomes may be more complicated than can be accounted for by the analytic methods used in this study. The creation of a dichotomous variable including caregivers with no depression symptoms in the 2 weeks preceding the completion of the CIDI-SF at Wave 3 and those with any symptoms (ranging from 1 to 8) limits variability compared with using a continuous variable. Although the purpose of this study was not confined to a focus on clinical depression, there may be limitations to including those with any subclinical depression symptoms, such as those with a CIDI-SF score of 1, and those who may meet criteria for clinical depression in the same group. At the same time, even one symptom of depression can be impactful for caregivers and children alike, especially for those who may be experiencing a symptom such as thoughts of death or suicide. Therefore, it is also important to recognize that content, severity, and frequency of depression symptoms may be highly influential for caregiver and child outcomes. Although these analyses did not differentiate between dimensions of depression symptoms such as hopelessness, suicidal ideation, or changes in appetite, activity level, mood, or sleep, it is valuable to recognize the potential variability in impact from these symptoms on caregivers and children. The CIDI-SF also only focuses on the two-week time period preceding completion. Future research may be strengthened by considering multiple measures of maternal depression over time and controlling for the types of depression symptoms experienced.

The current study included a preliminary analysis focused on clarifying the relationships between maternal depression and cellular aging, but future research aimed at examining the factors impacting maternal depression and offspring of depressed mothers and cellular aging may consider additional variables of interest. Other health indicators can also covary with measures of cellular aging, such as body mass index and chronic health conditions such as asthma (Shalev, et al. 2013). Future analyses should include these variables of interest, as well as youth biological sex since this data is readily available in the FFCWS. Ongoing research using larger sample sizes to further elucidate the unique impacts and relationships between exposure to early childhood adversity and health outcomes including cellular aging is warranted, including exploration of the factors influencing these relationships and outcomes. Likewise, timing of exposure to maternal depression symptoms and the severity and chronicity of these symptoms may impact child development and therefore more frequent or robust measures of maternal depression within longitudinal studies could be useful. Longitudinal studies such as the FFCWS data set provide the opportunity to explore dynamic interactions between both risk and protective factors on outcomes throughout the lifespan. For instance, protective factors for early life adversity and child behaviors have been identified in the FFCWS dataset, including school connectedness and neighborhood cohesion (Yoon et al., 2023). However, it can also be difficult to isolate the impact of maternal depression in a sample such as the FFCWS data set, due to the high rate of adversities experienced by participants in the sample (Thompson & Henrich, 2023). Although, in studies which used control groups of non-depressed caregivers and children, differences were still observed in biological markers of dysregulated stress response systems (Nelson et al., 2021).

It is also critical to emphasize that there may not be a simple unidirectional relationship between maternal depression and child outcomes. Contextual risk factors such as parenting

stress, partner support, and relationship satisfaction may also predict both maternal depression and child behavior problems (Malik, et al., 2007). This study also did not account for the presence of other caregivers, which may serve to mitigate some of the impacts of maternal depression. Child characteristics may influence maternal depression as well, and there may be a reciprocal relationship between maternal depression and behavior problems in children during early childhood (Baker et al., 2020; Chazan-Cohen, et al., 2007). Other analyses have supported the bidirectional influence between child aggression and parental stress and maternal depression and child outcomes such as conduct problems (Elgar et al., 2003; Heberle & Chazan-Cohen, 2022). The relationship between cellular aging and child behaviors may add more complexity to these reciprocal interactions with these environmental risk factors including maternal depression. For instance, in kindergarten children, telomere length had an inverse relationship with internalizing behaviors, such that those with shorter telomere length had more internalizing behaviors (Kroenke et al., 2012). These limitations provide valuable insights for future research using cellular aging outcomes to identify risk and protective factors in pediatric samples. Further exploration of the contributing factors, including risk and protective factors and their interactions related to cellular aging outcomes could illuminate the pathways of influence to point towards opportunities for effective intervention strategies.

Future research focused on the roles of risk and protective factors on cellular aging should consider maternal depression and child care quality as variables of interest along with other measures of environmental stressors and child outcomes. While researchers have focused more broadly on exposure to Adverse Childhood Experiences (ACEs) and cellular aging, the prevalence of maternal depression and low treatment rates suggest this is an area in need of further attention. However, research focused on ACEs can point to useful considerations for

other factors influencing cellular aging in childhood. Another analysis of the FFCWS dataset revealed that with each additional ACEs exposure, there was a 1% decrease in child telomere length and 72% of children at age 9 experienced between one and three ACEs, with economic hardship being the most common (Sosnowski et al., 2021). Further analyses may explore the bidirectional influence between maternal depression and child behaviors or temperament. Child aggression, behavior problems and behaviors related to hyperactivity can be extracted from the results of the Childhood Behavior Checklist (CBCL) administered at Wave 3, and future research may include analyses of these variables related to the associations found in the current analyses. Analyses of FFCWS suggest that mothers who perceived more support from their partners experienced fewer mental health struggles 5 years after birth (Meadows et al., 2010). Information about quality of relationships is available as well, should future researchers seek to study this as a potential confounding variable.

There may also be nuances regarding child care quality which were not captured in the present study. Future studies could also account for length of time of exposure to child care as a measure of dose-response, as it is possible that longer time spent in a high-quality setting could provide greater benefits. Dosage or length of exposure to higher quality child care has been shown to impact child outcomes, as children with two years of Head Start involvement had better outcomes related to vocabulary and literacy compared with those who only had one (Zaslow et al., 2016). This may also differ among groups. White children who experienced more non-maternal care experienced less maternal sensitivity and positive engagement with their mothers, whereas greater maternal sensitivity and child engagement was associated with more care hours for Hispanic and Black/African American children (NICHD, 2003). Timing of care may also play a role, as more time spent in care during infancy has been correlated with lower pre-

academic scores while toddlers who spend more hours in care have been observed to have higher language scores (NICHD, 2004). While the FFCWS data set provides information about length of time spent in the setting from which the ECERS-R was calculated, there is no previous data to compare the quality across other classrooms at the same child care center or even for the classroom over previous time periods. Future research may also incorporate ongoing assessment of child care quality to enrich these analyses. While measures of cellular aging rely on ever-advancing technology, it is wise for researchers to begin including these measures routinely, especially in those focused on development beginning in early childhood.

Implications

Results from the current study encourage ongoing efforts focused on prevention and intervention related to maternal depression. The average number of maternal depression symptoms remained relatively stable between year 1 and year 3 postpartum in this subsample whereas, the percentage of the sample meeting criteria for depression based on the presence of three or more symptoms only decreased slightly. Ongoing monitoring and identification of maternal depression rates may be warranted, even beyond the first postpartum year. Poverty rates as determined by the poverty threshold also increased during this same time period. While the focus of this study was not to explore the impact of poverty on maternal depression rates, this relationship is well documented (Papero, 2005). Given that poverty is a barrier for accessing mental health treatment, it is important for policy makers to continue to work towards improved identification and treatment of maternal depression in high-risk populations within the first few postpartum years.

Although the results of this study were limited by small sample sizes, there are potential applications for future research focused on intervention planning based upon cellular aging outcomes associated maternal depression exposure as well as possible protective factors.

Developmental theorists, pediatricians, mental health providers, educators, and interventionists focused on early childhood development have acknowledged the relationships between genetic predisposition, environmental influences, and outcomes related to physical, mental, and social-emotional health. A model of biological embedding suggests early exposure to adversity influences behavior and hormonal dysregulation, which in turn, exacerbates pro-inflammatory tendencies associated with epigenetic changes programmed during childhood stress (Miller et al., 2012). Biological sensitivity theory proposes that early adversity may be especially impactful for certain children depending upon genetic, epigenetic, and psychobiological predispositions (Boyce and Ellis, 2005). Exposure to childhood adversity can increase the risks for both mental health struggles as well as shorter telomere length and early adversity, and mental health issues in later life may have an interactive effect on accelerated biological aging (Lin et al., 2012). Thus, the identification of early protective factors that can mitigate the effect of early adversity is crucial. Preventing childhood exposure to early life adversity and treating maternal depression represent overlapping areas of interest. The CDC (2023) has outlined strategies to serve as a sort of vaccine for adverse childhood experiences (ACEs), including creating positive childhood experiences and supporting strong beginnings for families. These “upstream” policies and practices to support caregiver-child systems could serve to reduce sociodemographic stressors which can influence and exacerbate maternal depression. Bronfenbrenner lectured about the importance of connecting his developmental theory to interventions or programs aimed at improving the lives of children and families decades ago (Brooks-Gunn, 1995). Connecting early exposure to adversity and early exposure to protective factors with biological markers associated with long-term disease may bolster efforts related to both maternal mental health and promoting early childhood development, such as those pertaining to access to high-quality child care.

Focusing on building social-emotional skills in early childhood, including adaptive and coping skills, may be especially important for children exposed to early adversity and those who are more biologically sensitive to the impacts (Shonkoff, 2012). Direct benefits conferred to the child through high-quality care may be identified through the conceptualization of child care as a buffer for later deleterious health outcomes related to known sociodemographic risk factors. Furthermore, conceptualizing child care as a mechanism of support for maternal depression, given that lack of child care is a known barrier to treatment, may yield greater attention for the multigenerational benefits which high-quality child care can provide. Therefore, a broader approach focused on access to high-quality child care for every child may be warranted. While access to prevention treatment for depressed mothers is still advisable, there are other mechanisms in the environment, including high-quality child care, which can reduce the impact of exposure to maternal depression on child outcomes. Within the macrosystem level, this could alleviate the onus on caregivers, who may already struggle to access resources, while harnessing the positive impact of stakeholders including child care providers.

CONCLUSION

Children may be especially at risk from the effects of adversity on accelerated development (Belsky, 2019). Exposure to adversity early in life, such as maternal depression, can impact physical and mental health outcomes in children both in the short-term and long-term. There is evidence that early adversity causes greater cellular aging than would be expected based upon chronological age, and that for those whose biological age exceeds their chronological age there are undesirable impacts to cognitive, psychological, and physical functioning (Belsky et al., 2015). Similarly, researchers have also focused on understanding what could stop or reverse accelerated aging (Field et al., 2018). This suggests that identifying risk factors and the real-time impacts of these risk factors on epigenetic aging may provide the

opportunity for delivering swift interventions that could serve as protective factors. As suggested within Bronfenbrenner's bioecological model, adaptive or protective mechanisms may contribute positively to epigenetic aging and perhaps even mitigate some accelerated aging (Belsky, 2019; Belsky & Shalev, 2016). Advancing technology can help to reveal the biological processes which are influenced by environmental experiences and impact health outcomes across the lifespan. Shortened telomere length and rapid cellular aging are linked to early childhood adversity and associated with negative mental health and physical health outcomes. The study of epigenetic and biological aging is a relatively newer advancement which can be utilized to better understand the factors impacting childhood development and the mechanisms through which known risk factors confer these outcomes. Furthermore, available measures of cellular aging may demonstrate different associations with risk factors, and possibly even with protective factors, as well as long-term outcomes. Early child care experiences around age three may be especially important for those who are not exposed to maternal depression symptoms, while it may not be able to buffer the impact of maternal depression for those who are exposed. Longitudinal data sets such as the FFCWS can provide a richer understanding of the factors impacting this advanced aging for those exposed to early life adversity, as well as protective factors which may exist within their environment or within interactions with others. As far as the author is aware, no study to date has focused on the relationship between child care quality and biological aging and limited research has focused on high-quality child care as a buffer for the impacts of maternal depression on children. Now is the time for increased attention on policies and access to prevention or intervention programming utilizing existing community resources to address the impact of maternal depression on children and families. As can be seen at the cellular level, time cannot wait.

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Table 1: Descriptives for Continuous Demographic Variables for Analytic Sample

| | <i>Mean</i> | <i>S.D.</i> | <i>n</i> | <i>Min</i> | <i>Max</i> |
|--|-------------|-------------|----------|------------|------------|
| Mother Age at Baseline | 25.15 | 5.92 | 100 | 15 | 40 |
| Mother/baby separations from Birth to age 1 (Lasting 1 week or longer) | 0.15 | 0.56 | 94 | 0 | 4 |
| Mother/baby separations from age 1 to age 3 (Lasting 1 week or longer) | 0.88 | 3.67 | 95 | 0 | 26 |
| Child Age at Entry into Current Child care Setting (in months) | 13.57 | 10.51 | 81 | 0 | 36 |
| Number of Child care Arrangement Changes Since Age 1 | 1.21 | 1.30 | 82 | 0 | 5 |
| Number of Days Spent in Child care Per Week | 4.65 | 0.92 | 81 | 2 | 6 |
| Number of Hours Spent in Child care Per day | 7.48 | 1.76 | 82 | 3 | 12 |

Table 2: Frequencies for Categorical Demographic Variables for Analytic Sample

| | Frequency | Percent |
|---|-----------|---------|
| Mother Education at Baseline | | |
| Some High School | 25 | 25.0 |
| High School Diploma or GED | 26 | 26.0 |
| Some College or Technical Training | 29 | 29.0 |
| College or Graduate School | 19 | 19.0 |
| Mother Race | | |
| White | 24 | 24.0 |
| Black | 63 | 63.0 |
| Asian | 2 | 2.0 |
| Other | 11 | 11.0 |
| Mother Hispanic/Latino | | |
| Yes | 14 | 14.0 |
| No | 84 | 84.0 |
| Baby Sex Assigned at Birth | | |
| Male | 61 | 61.0 |
| Female | 39 | 39.0 |
| Mother meets Depression Criteria Wave 2 | | |
| Yes | 52 | 52.0 |
| No | 48 | 48.0 |
| Mother meets Depression Criteria Wave 3 | | |
| Yes | 55 | 55.0 |
| No | 44 | 44.0 |
| Wave 2 Poverty Categories | | |
| 0-49% | 16 | 16.0 |
| 50-99% | 17 | 17.0 |
| 100-199% | 29 | 29.0 |
| 200-299% | 11 | 11.0 |
| 300%+ | 27 | 27.0 |
| Wave 3 Poverty Categories | | |
| 0-49% | 19 | 19.0 |
| 50-99% | 22 | 22.0 |
| 100-199% | 21 | 21.0 |
| 200-299% | 13 | 13.0 |
| 300%+ | 25 | 25.0 |

Table 3: Descriptive Statistics for Analytic Variables

| | <i>Mean</i> | <i>SD</i> | <i>n</i> | <i>Min</i> | <i>Max</i> |
|---|-------------|-----------|----------|------------|------------|
| Wave 2 Maternal Depression Score (CIDI-SF Raw Score) | 2.70 | 2.68 | 100 | 0 | 7 |
| Wave 3 Maternal Depression Score (CIDI-SF Raw Score) | 2.62 | 2.89 | 100 | 0 | 8 |
| ECERS-R Summary Scores | 4.77 | 1.47 | 100 | 1.05 | 7 |
| Biological Outcomes | | | | | |
| Chronological Age Wave 5 | 9.27 | 0.32 | 82 | 8.92 | 10.84 |
| Horvath EpiAge Wave 5 | 6.51 | 2.23 | 78 | 2.74 | 18.11 |
| Chronological Age Wave 6 | 15.50 | 0.54 | 76 | 14.76 | 17.6 |
| Horvath EpiAge Wave 6 | 11.85 | 3.21 | 78 | 7.09 | 26.68 |
| Telomere Length Wave 5 | 8.03 | 2.26 | 81 | 2.91 | 17.49 |
| Telomere Length Wave 6 | 8.28 | 2.69 | 89 | 4.48 | 17.97 |

Note. CIDI-SF = Composite International Diagnostic Interview - Short Form ; ECERS-R = Early Childhood Environment Rating Scale - Revised

Table 4: Bivariate Correlations Between Analytic Variables of Interest Across 450k and Epic Platforms

| | Pearson's Correlations (<i>r</i> , <i>n</i>) | | | | | | | | |
|------------------------------------|--|---------------------|----------------------------------|----------------------------------|------------------------------|------------------------------|-----------------------------|-------------------------|-------------------------------|
| | InWave 5 Horvath | InWave 6 Horvath | InChronological Age Wave 5 | InChronological Age Wave 6 | Telomere Length Wave 5 | Telomere Length Wave 6 | ECERS-R Summary Score | CIDI-SF Raw Score | Poverty Category Wave 2 |
| InWave 5 Horvath | 1.00 | | | | | | | | |
| InWave 6 Horvath | 0.68** (77) | 1.00 | | | | | | | |
| InChronological Age Wave 5 | 0.14 (78) | 0.06 (76) | 1.00 | | | | | | |
| InChronological Age Wave 6 | 0.05 (76) | 0.15 (76) | 0.32** (76) | 1.00 | | | | | |
| Telomere Length Wave 5 | 0.06 (67) | 0.12 (66) | 0.01 (67) | 0.07 (66) | 1.00 | | | | |
| Telomere Length Wave 6 | 0.03 (75) | 0.11 (74) | 0.08 (74) | 0.25* (73) | .41** (65) | 1.00 | | | |
| ECERS-R Summary Score Wave 2 | -0.04 (79) | -0.07 (77) | -0.10 (78) | 0.09 (76) | 0.12 (79) | 0.04 (85) | 1.00 | | |
| CIDI-SF Raw Score | 0.19 (79) | 0.10 (77) | 0.10 (78) | 0.12 (76) | -0.15 (79) | -0.02 (85) | 0.05 (100) | 1.00 | |
| Poverty Category Wave 2 | -0.16 (79) | -0.08 (77) | -0.05 (78) | -0.16 (76) | 0.14 (79) | 0.11 (85) | 0.09 (100) | -0.22** (100) | 1.00 |

p-value* < .05 *p-value* < .001

Note. CIDI-SF = Composite International Diagnostic Interview - Short Form ; ECERS-R = Early Childhood Environment Rating Scale - Revised

Table 5: Results of Regression Analyses Examining Maternal Depression on Cellular Aging Using Horvath Epigenetic Clock

| Model | Predictor | Model Summary | Difference | <i>b</i> | <i>se</i> | <i>t</i> | <i>p</i> |
|--------------------------------|--|---|-------------------------------------|----------|-----------|----------|----------|
| <u>Model 1 (Wave 5)</u> | | | | | | | |
| Main Effects | | $R^2 = .17,$ $F(3, 74) =$ 4.93, $p = .004$ | | | | | |
| | Constant | | | -0.252 | 2.086 | -0.121 | 0.904 |
| | Wave 2 Maternal Depression Group | | | 0.077 | 0.062 | 1.257 | 0.213 |
| | Biological Platform Group | | | 0.209 | 0.062 | 3.352 | 0.001 |
| | (ln)Chronological Age | | | 0.741 | 0.941 | 0.787 | 0.434 |
| Interaction 1 | Wave 2 Maternal Depression Group*Biological Platform Group | $R^2 = 0.18,$ $\Delta F(4, 73) =$ 0.90 | $\Delta R^2 = 0.01,$ $p = 0.346$ | | | | |
| <u>Model 2 (Wave 6)</u> | | | | | | | |
| Main Effects | | $R^2 = .14,$ $F(3, 72) =$ 3.96, $p = .011$ | | | | | |
| | Constant | | | -1.815 | 2.14 | -0.848 | 0.399 |
| | Wave 2 Maternal Depression Group | | | 0.016 | 0.052 | 0.315 | 0.753 |
| | Biological Platform Group | | | 0.165 | 0.052 | 3.138 | 0.002 |
| | (ln)Chronological Age | | | 1.453 | 0.776 | 1.871 | 0.065 |
| Interaction 1 | Wave 2 Maternal Depression Group*Biological Platform Group | $R^2 = 0.14,$ $\Delta F(4,71) =$ 0.10 | $\Delta R^2 = 0.10,$ $p = 0.757$ | | | | |

Table 6: Maternal Depression on Cellular Aging Analyses for Telomere Length

| Predictor | Model Summary | <i>B</i> | <i>se</i> | <i>t</i> | <i>p</i> |
|----------------------------------|--------------------------------|----------|-----------|----------|----------|
| | <u>Model 3 (Wave 5)</u> | | | | |
| | $R^2 = 0.01,$ | | | | |
| | $F(1,79) = 0.96,$ | | | | |
| | $p = 0.33$ | | | | |
| Constant | | 8.795 | 0.817 | 10.762 | <0.001 |
| Wave 2 Maternal Depression Group | | -0.494 | 0.504 | -0.979 | 0.33 |
| | <u>Model 4 (Wave 6)</u> | | | | |
| | $R^2 = 0.00,$ | | | | |
| | $F(1, 87) = 0.04,$ | | | | |
| | $p = 0.835$ | | | | |
| Constant | | 8.466 | 0.938 | 9.023 | <0.001 |
| Wave 2 Maternal Depression Group | | -0.12 | 0.576 | -0.209 | 0.835 |

Table 7: ECERS-R Moderation Analyses Horvath Epigenetic Clock

| Model | Predictor | Model Summary | Difference | <i>b</i> | <i>se</i> | <i>t</i> | <i>p</i> |
|--------------------------------|---|--|---------------------------------|----------|-----------|----------|----------|
| <u>Model 5 (Wave 5)</u> | | | | | | | |
| | | $R^2 = 0.17,$ $F(4, 73) =$ $3.71,$ $p = .008$ | | | | | |
| Main Effects | Constant | | | -0.119 | 2.117 | -0.056 | 0.955 |
| | ECERS-R Summary Score | | | -0.01 | 0.021 | -0.46 | 0.647 |
| | Wave 2 Maternal Depression Group | | | 0.077 | 0.062 | 1.251 | 0.215 |
| | Biological Platform Group | | | 0.208 | 0.063 | 3.313 | 0.001 |
| | (ln)Chronological Age | | | 0.703 | 0.95 | 0.739 | 0.462 |
| Interaction 1 | Wave 2 Maternal Depression Group* ECERS-R | $R^2=0.158,$ $\Delta F(5, 72)=4.009$ | $\Delta R^2=0.04,$ $p=0.049$ | | | | |
| <u>Model 6 (Wave 6)</u> | | | | | | | |
| | | $R^2 = 0.15,$ $F(4, 71) =$ $3.21, p =$ $.018$ | | | | | |
| Main Effects | Constant | | | -1.91 | 2.214 | -0.892 | 0.376 |
| | ECERS-R Summary Score | | | -0.017 | 0.017 | -0.987 | 0.327 |
| | Wave 2 Maternal Depression Group | | | 0.015 | 0.052 | 0.298 | 0.766 |
| | Biological Platform Group | | | 0.163 | 0.052 | 3.102 | 0.003 |
| | (ln)Chronological Age | | | 1.518 | 0.779 | 1.948 | 0.055 |

Note. ECERS-R = Early Childhood Environment Rating Scale - Revised

Table 8: ECERS-R Moderation Analyses for Telomere Length

| Predictor | Model Summary | <i>B</i> | <i>se</i> | <i>t</i> | <i>p</i> |
|---|---------------|----------|-----------|----------|----------|
| <u>Model 7 (Wave 5)</u> | | | | | |
| <i>R</i> ² = 0.04, <i>F</i> (3,77) = 1.08, <i>p</i> = 0.364 | | | | | |
| Constant | | 10.398 | 3.046 | 3.414 | 0.001 |
| ECERS-R Summary Score | | -0.324 | 0.625 | -0.518 | 0.606 |
| Wave 2 Maternal Depression Group | | -2.174 | 1.852 | -1.174 | 0.244 |
| Wave 2 Maternal Depression Group*ECERS-R | | 0.341 | 0.374 | 0.911 | 0.365 |
| <u>Model 8 (Wave 6)</u> | | | | | |
| <i>R</i> ² = .002, <i>F</i> (3, 85) = 0.52, <i>p</i> = 0.984 | | | | | |
| Constant | | 9.284 | 3.206 | 2.896 | 0.005 |
| ECERS-R Summary Score | | -0.176 | 0.664 | -0.265 | 0.792 |
| Wave 2 Maternal Depression Group | | -0.71 | 1.952 | -0.364 | 0.717 |
| Wave 2 Maternal Depression Group*ECERS-R | | 0.126 | 0.401 | 0.315 | 0.754 |

Note. ECERS-R = Early Childhood Environment Rating Scale - Revised

Table 9: Poverty Moderation Analyses Horvath Epigenetic Clock

| Model | Predictor | Model Summary | <i>b</i> | <i>se</i> | <i>t</i> | <i>p</i> |
|--------------|----------------------------------|--|----------|-----------|----------|----------|
| | | <u>Model 9 (Wave 5)</u> | | | | |
| | | <i>R</i> ² = 0.17, <i>F</i> (4, 73) = 3.69, <i>p</i> = 0.009 | | | | |
| Main Effects | Constant | | -0.223 | 2.099 | -0.11 | 0.916 |
| | Wave 2 Poverty Category | | -0.334 | 0.24 | -0.39 | 0.698 |
| | Wave 2 Maternal Depression Group | | 0.67 | 0.068 | 0.985 | 0.328 |
| | Biological Platform Group | | 0.206 | 0.063 | 3.26 | 0.002 |
| | (ln)Chronological Age | | 0.751 | 0.024 | 0.793 | 0.698 |
| | | <u>Model 10 (Wave 6)</u> | | | | |
| | | <i>R</i> ² = 0.14, <i>F</i> (4, 71) = 2.95, <i>p</i> = 0.026 | | | | |
| Main Effects | Constant | | -1.717 | 2.196 | -0.78 | 0.437 |
| | Wave 2 Poverty Category | | -0.004 | 0.019 | -0.23 | 0.819 |
| | Wave 2 Maternal Depression Group | | 0.012 | 0.056 | 0.214 | 0.831 |
| | Biological Platform Group | | 0.164 | 0.053 | 3.104 | 0.003 |
| | (ln)Chronological Age | | 1.425 | 0.791 | 1.801 | 0.076 |

Table 10: Poverty Moderation Analyses for Telomere Length

| Predictor | Model Summary | <i>b</i> | <i>Se</i> | <i>t</i> | <i>p</i> |
|--|---------------|----------|-----------|----------|----------|
| <u>Model 11 (Wave 5)</u> | | | | | |
| <i>R</i> ² = 0.05, <i>F</i> (3,77) = 1.20, <i>p</i> = 0.315 | | | | | |
| Constant | | 5.508 | 2.229 | 2.472 | 0.016 |
| Wave 2 Poverty Category | | 0.912 | 0.591 | 1.542 | 0.127 |
| Wave 2 Maternal Depression Group | | 1.214 | 1.299 | 0.935 | 0.353 |
| Wave 2 Maternal Depression Group*Poverty Category | | -0.479 | 0.366 | -1.309 | 0.194 |
| <u>Model 12 (Wave 6)</u> | | | | | |
| <i>R</i> ² = .02, <i>F</i> (3, 85) = 0.46, <i>p</i> = 0.712 | | | | | |
| Constant | | 7.457 | 2.504 | 2.979 | 0.004 |
| Wave 2 Poverty Category | | 0.218 | 0.682 | 0.319 | 0.75 |
| Wave 2 Maternal Depression Group | | 0.021 | 1.504 | 0.014 | 0.989 |
| Wave 2 Maternal Depression Group*Poverty Category | | 0.025 | 0.442 | 0.056 | 0.955 |

Figure 1: Simple Slopes Analysis for the Interaction of Child Care Quality and Maternal Depression Exposure Groups on Log Transformed Wave 5 Horvath Epigenetic Age

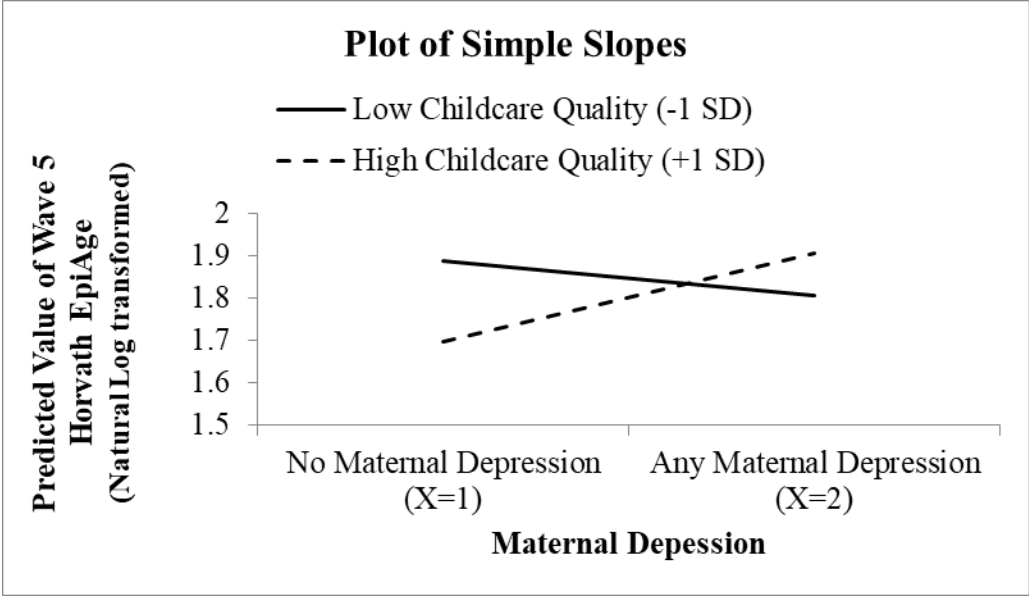


Figure 2: Simple Slopes Analysis for Personal Care Routines Subscale on Maternal Depression Exposure Groups on Log Transformed Wave 5 Horvath Epigenetic Age

