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Childhood Trauma and Chronic Disease

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In the United States, six out of every ten Americans have been diagnosed with one chronic disease (Center for Disease Control, 2022). The high prevalence of chronic diseases among Americans has numerable consequences, including physical pain, disability, depression, social isolation, and financial burden to individuals and healthcare systems (Harris & Wallace, 2012). The development of chronic diseases is often attributed to genetic predisposition and lifestyle choices. While these are two important risk factors, it is also important to consider other factors, such as childhood trauma, its impact on the neuroendocrine system, and the potential health consequences that may emerge in adulthood.

Problem Overview

Until the 1990s, minimal research was conducted on the relationship between childhood trauma, high-risk health behaviors, and chronic disease in adults (Felitti et al., 1998). However, from 1995 to 1997, the CDC conducted the Kaiser Permanente Adverse Childhood Experiences (ACE) Study – initiating the first study regarding childhood trauma and its future health consequences in adulthood. In addition to poorer quality of life, the financial burden of adverse childhood experiences related to productivity loss, child welfare, and corrections systems is estimated to have an approximate $210,000 lifetime per-victim cost (Peterson et al., 2018).

According to the 2017-2018 National Survey of Children's Health (NSCH), 30% of children have experienced one adverse childhood experience while 14% have experienced two or more. The Child Trends Brief of 2018 estimates the percentage of children who have experienced at least one ACE to be 45%. Further, 61% of non-Hispanic black children have experienced at least one ACE, followed by 51% of Hispanic children, 40% of non-Hispanic white children, and 23% of non-Hispanic Asian children (Sacks & Murphey, 2018).

Since the Kaiser Permanente Adverse Childhood Experiences Study was published in 1998, the concept of childhood trauma impacting the development of chronic diseases has been recognized by healthcare professionals, but there is still little research regarding the potential childhood trauma-induced physiological changes that manifest as chronic disease later in life as a result of changes to the hypothalamic-pituitary-adrenal (HPA) axis related to chronic stress, lifestyle choices of adults with ACEs, intergenerational trauma, and other factors that will be explored in the literature. In further exploring how childhood trauma and chronic diseases are connected, healthcare professionals can use this information to develop a deeper understanding of the prevention and management of chronic diseases.

Definition of Terms

Adverse Childhood Experience (ACE)

A traumatic occurrence that takes place during childhood (0-17 years old). Examples include physical, emotional, or sexual abuse, neglect, divorce of parents, substance abuse by a family member in the home, and maternal trauma while in utero (CDC, 2019).

Hypothalamic-Pituitary-Adrenal (HPA) Axis

A neuroendocrine system that regulates the body's stress response and the synthesis and release of hormones including cortisol and adrenocorticotropic hormone. Additionally, the HPA axis assists in regulating immunity, digestion, and emotions (Kuhlman et al., 2015).

Resilience

"The process of adapting well in the face of adversity, trauma, tragedy, threats, or significant sources of stress… resilience involves "bouncing back" from these difficult experiences" (Palmiter, 2020).

Posttraumatic Growth (PTG)

Positive change(s) experienced as a result of previous hardships, traumas, or crises in an individual's life. These changes are evident in the following five aspects: appreciation of life, relationships with others, new possibilities in life, personal strength, and spiritual change (Collier et al., 2016).

Purpose Statement/PICO Question

The purpose of this literature review is to further explore how processes such as hypothalamic pituitary adrenal (HPA) axis dysfunction that results in prolonged elevated cortisol levels, adverse childhood experiences, intergenerational trauma, in-utero experiences, and resilience facilitate the relationship between childhood trauma and the development of chronic diseases in adulthood. Therefore, the PIO question is stated as follows:

What are the factors that mediate the relationship between childhood trauma and the development of chronic diseases in adulthood?

Theoretical Framework

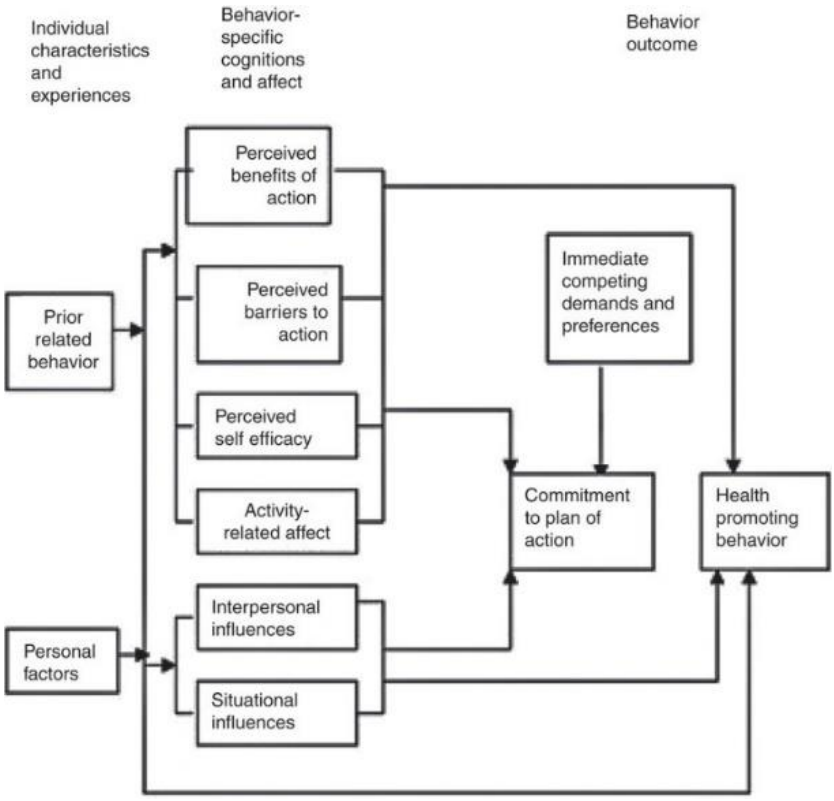
The theoretical framework chosen to guide this review of literature is Nola Pender's Health Promotion Model. The Health Promotion Model encompasses four important assumptions: individuals seek to monitor and regulate their own behavior; individuals interact and transform within their own environment; health professionals are considered part of the individual's environment and influence their decisions and perceptions; and the presence of a self-initiated plan of action to implement or change a health behavior (Pender, 1982). When addressing chronic disease development in the context of ACEs and trauma, the Health Promotion Model empowers the individual to prioritize their health through self-initiation and positive health behaviors.

Pender's Health Promotion Model is widely utilized due to its practical nature. In 2021, Habibzadeh et al., applied Pender's health promotion model to implement educational interventions in patients with heart failure. In their experimental study of 80 patients, a pretest was conducted to assess the patients' levels of understanding regarding the heart failure disease process. In addition, the researchers utilized the Health-Promoting Lifestyle Profile II (HPLP-II),

a tool used to measure and assess participants' health-promoting behaviors. Following the pretest, patients were provided with educational content based on Pender's health promotion model. The educational intervention resulted in improvement in quality of life and health promotion. This research study exemplifies the importance of encouraging health promotion in individuals with chronic diseases. Because 30-45% of children experience at least one adverse childhood experience, they have an increased risk of developing a chronic disease (Sacks & Murphy, 2018). With the knowledge of their increased risk, the health promotion model can be applied to encourage a proactive approach to prevent and manage chronic disease, even if an individual could be more susceptible due to childhood trauma.

Figure 1

Nola Pender's Health Promotion Model



Note. Figure 1 contains Nola Pender's Health Promotion Model, outlining the individual's experiences, behavior, perceptions, and behavior outcome.

Literature Review

Using the CINAHL and EBSCO databases, accessed through the Southern Adventist University McKee Library website, literature from 2016 to 2022 was obtained. Keywords used to search for literature included: childhood trauma, HPA axis, adverse childhood experiences, chronic diseases (including cardiovascular, autoimmune, anxiety, depression, insomnia, and diabetes), and resilience. Literature was selected for review based on the thoroughness of the research and the insight it provided into answering the PIO question. Literature was excluded based on the degree of limitations of the study and relevance to the PIO question.

Presentation of Literature

Hypothalamic-Pituitary-Adrenal (HPA) Axis Dysfunction

When discussing the impact of childhood trauma on the various body systems, the hypothalamic-pituitary-adrenal (HPA) axis must be considered. The paraventricular nucleus of the hypothalamus is responsible for producing corticotropin-releasing factor (CRF), which regulates and initiates the HPA axis. During stressful situations, CRF is released and binds to pituitary corticotropes, resulting in the release of adrenocorticotropic hormone (ACTH) into the circulatory system. Next, ACTH acts on the adrenal cortex, stimulating glucocorticoid secretion. The release of glucocorticoids (specifically cortisol) regulates the physiological changes that occur in response to stress (Smith & Vale, 2006). Development of the HPA axis is especially vulnerable during childhood.

Beginning in utero, maternal HPA axis activation and possible fetal effects have been studied for potential interaction. Riis et al., 2019, conducted a longitudinal study of 45 pregnant women and their children to explore prenatal maternal HPA activity on offspring neuroendocrine-immune (NEI) regulation. NEI dysfunction is associated with disease

pathophysiology (Riis et al., 2019). Researchers collected saliva cortisol assays of each pregnant woman during five prenatal studies between 24- and 38-weeks' gestation. In a five-year follow-up study, their 45 children provided cortisol and cytokine level samples via saliva. Riis et al. found that among the male children, average prenatal maternal cortisol did not impact his NEI activity or functioning; however, prenatal maternal cortisol levels were associated with higher positive cortisol-cytokine relations at age five in female children. In these female children, dysregulated cortisol-cytokine relations result in poor regulation of inflammatory cytokines, contributing to the development of chronic diseases. Despite this result, the researchers suggest that additional research with a larger sample will need to be conducted for more definitive results.

To further explore the role of maternal psychological well-being and future offspring health outcomes, Plant et al., 2016, conducted a longitudinal cohort study in which maternal depression was assessed during pregnancy at both 20 and 36-weeks' gestation and offspring childhood maltreatment and depression was assessed ongoingly (n = 103 offspring). The researchers also collected high-sensitivity C-reactive protein (hs-CRP) and awakening cortisol levels in the 25-year-old offspring. The researchers found that prenatal maternal depression exposure was strongly correlated with elevated offspring hs-CRP at age 25. Prenatal maternal depression did not exhibit an impact on adult awakening cortisol levels; however, childhood maltreatment was positively associated with elevated awakening cortisol levels. Limitations of the study include poor sample diversity and the collection of only one index of inflammation (hs-CRP) and HPA axis function (awakening cortisol).

In their 2018 experimental study, Kuhlman et al., sought to examine the interaction between HPA-axis reactivity to an acute stressor and exposure to various types of childhood

trauma as predictors of chronic mental health disorders in a sample of 121 youth ages 9 to 16 years old, of which 84.7% had experienced at least one traumatic event. Using the Socially-Evaluated Cold Pressor Task to evoke HPA-axis activation, the researchers found that the average youth exhibited a 66% increase in cortisol from their baseline to their peak response to the stress task. This spike in cortisol levels is important when considering the effects of chronic, repeated exposure to childhood trauma and its manifestations on the various regulatory body systems. A limitation of this study is the cross-sectional nature of the data.

To further evaluate how childhood trauma impacts cortisol regulation, O'Conner et al., 2020, conducted an observational study in which the cortisol levels of 154 participants ages 18 and 63 years old were collected. In this 7-day study, cortisol samples were gathered immediately upon waking, at 15 minutes, 30 minutes, 45 minutes, 3 hours, 6 hours, 9 hours, and 12 hours each day. The researchers found that participants who formerly experienced childhood trauma presented with lower cortisol upon awakening (CAR) and flatter wake-peak to 12 hours (WP-12) cortisol slopes compared to the control group. The researchers hypothesize that low CAR levels are a result of repeated HPA axis activation during childhood, effectively blunting or reducing cortisol response over time.

Finally, Kuzminskaite et al. 2020 conducted a longitudinal cohort study of $n = 2778$ participants regarding the relationship between childhood trauma, the HPA axis, the immune-inflammatory system, and the autonomic nervous system (ANS). The researchers utilized the Childhood Trauma Interview and collected separate and cumulative markers of the HPA axis (cortisol levels and fluctuations), the immune-inflammatory system (C-reactive protein, interleukin-6, tumor necrosis factor-α), and the ANS (cardiac function). This study exhibits a more thorough collection of inflammatory and HPA axis activation markers compared to Plant et

al., who only used hs-CRP and awakening cortisol levels. The sample analyses showed little support for childhood trauma having a significant impact on the separate or cumulative stress systems. The researchers acknowledge that a limitation of this study is the potential recall bias of a retrospective childhood trauma assessment.

The preceding five studies in which the HPA axis, cortisol levels, and inflammatory markers are studied present some evidence to suggest that the relationship between childhood trauma and the development of chronic diseases later in life could be attributed to dysregulation of the HPA axis during fetal development and childhood.

Adverse Childhood Experiences

Following the publication of the original 1998 (Felitti et al.) adverse childhood experiences (ACEs) study, researchers have continued to further explore the exact mechanisms linking ACEs and future health outcomes. ACEs have a significant role in the conversation regarding childhood trauma and future development of chronic diseases.

In 2019, Cubbin et al. examined data from a previous wellbeing survey to assess for potential associations between familial childhood adversities (FCAs) and a set of chronic diseases among 2,409 women ages 30-57 years old. The researchers found that FCAs during childhood were associated with the development of one or more chronic diseases (diabetes, hypertension, high cholesterol, and heart disease). The data revealed that diabetes and high cholesterol were the most observed associated chronic conditions, suggesting that dietary habits could be a potential mediating factor between FCAs, ACEs, and chronic disease. An important limitation of this study is the lack of family history of these chronic diseases in participants' family members, which could contribute to the development of these diseases.

The role of ACEs in specific ethnic minority groups is often understudied. Santoro et al. (2020) sought to address this gap in their study of ACE scores, anger expression, stress, and physical health in a sample of 132 adult Asian-Indian Americans. The participants completed an electronic survey that measured ACEs, anger expression, stress levels, personal health history, self-rated health perception, and physical illness symptoms from which that data was then analyzed to determine that ACEs are a significant predictor of increased anger expression, self-perceived stress levels, and higher quantity of chronic health conditions. Further, 94% of participants with three or more ACEs reported at least one previously diagnosed medical condition. When considering health disparities in minority groups, Santoro et al. (2020) contributes valuable insight into the role of trauma and the resulting health outcomes.

The impact of ACEs on physical health is not only an anomaly that has impacted American adults but presents as an international concern. Lin et al., 2021, studied the impact of ACEs on middle-aged and older adults in China using a population-based cross-sectional study using data collected from a survey of 11,972 male and female Chinese residents, ages 45 years and older, who had at least one chronic illness. Of the sample, 80.9% had experienced at least one adverse childhood event and 18% reported four or more. Like Cubbin et al. (2019), Lin et al. (2021) also found that individuals who experienced four or more ACEs had increased risks of chronic disease development compared to those without any ACEs. The researchers acknowledge that recall bias regarding ACE indicators is an important potential limitation of the study.

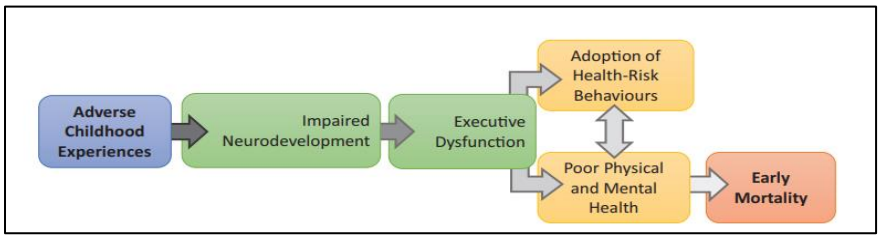
Although many studies have exemplified positive associations between ACE scores and chronic disease development, there are still knowledge gaps as to how ACEs potentially cause disease. Wheeler et al., 2019, assessed the association between ACEs, relationship distress, and

health. Using a community sample of 96 individuals, most of whom self-identified as an ethnic or racial minority (n = 81), who also completed three healthy relationship workshops, the participants completed an ACE survey, medical history questionnaire, and Behavioral Self-Regulation for Effective Relationships Scale (BSRERS). Based on this data, the researchers found that more childhood adversity was associated with greater relationship distress in adulthood. Because higher ACE scores are associated with lower relationship effort and increased relationship distress, individuals are more likely to experience chronic stress due to these unhealthy relationships. The chronic stress may then manifest as poor physical health (Wheeler et al., 2019).

In further exploring the physiological mechanisms that link ACEs to chronic disease, Trossman et al. (2021), conducted research with the hypothesis that executive functions (EFs) serve as a mediating mechanism in the causal pathway for development of chronic diseases in those who have experienced ACEs. EFs are self-regulating cognitive processes that allow individuals to participate in purposeful behaviors (e.g., working memory, planning) (Trossman et al., 2021). EFs begin in infancy and develop into early adulthood; however, ACE exposure may disrupt EF development. In their study of 84 undergraduate students, the researchers conducted an ACE survey, Barkley Deficits in Executive Functioning Scale (BDEFS), health behaviors questionnaire (HBQ), and stress questionnaires on each participant. The data indicated that higher quantities of ACE exposure were significantly correlated with executive dysfunction, contributing to health-risk behaviors that eventually lead to the development of chronic conditions. This chain of events can be visualized below in Figure 2. The results of this study further emphasize and coincide with the results of the previous Wheeler et al. (2019) results regarding the role of intimate relationship distress in physical health.

Figure 2

Proposed Neurodevelopmental Model



Note. The neurodevelopmental model that connects ACEs with early mortality in a chain of events in which executive function is disrupted, resulting in health-risk behaviors and poor health outcomes.

Specific Disease Development

As Cubbin et al. (2019) and Santoro et al. (2020) have found, childhood trauma has been found to be associated with certain abnormal lab values that can be associated with chronic disease development and diagnosis of at least one chronic disease. These findings prompt investigation into how childhood emotional trauma can result in diseases within specific body systems.

In 2020, Brew et al. performed a study in which the transgenerational effects of childhood emotional trauma, specifically bereavement, were associated with chronic inflammatory diseases in offspring. While studying three generations of Swedish families (n = 453516 participants spanning the three generations), the researchers investigated how the death of the third generation impacted the second-generation's offspring. For those children whose second-generation parents experienced early life bereavement, their risk of developing asthma, atopic dermatitis, and autoimmune diseases before age three was elevated, despite the sex of the offspring. The researchers attribute this elevation to alteration of the HPA axis in offspring, reduction of cortisol production, and therefore, a "pro-inflammatory" immune response in

addition to inherited epigenetic gamete changes. Brew et al. (2020) recognize that a limitation to this study is the assumption that the loss of a parent was emotionally traumatizing, when this may not have been true in all participants.

To further the research on specific disease development related to childhood trauma, Allen et al. (2019) acknowledged that while ACEs were associated with poor health outcomes, the prevalence of cardiovascular disease development is not well known. In this study, Allen et al., 2019, surveyed 12,229 low-income, uninsured adults, 48% of whom completed an ACE survey. The results indicated that low-income adults have even higher rates of ACEs than previous estimates. Further, ACEs were associated with higher rates of many different cardiovascular disease risk factors, including obesity, smoking, hypertension, and physical inactivity. According to the World Health Organization, ischemic heart disease is the number one cause of death globally (2020) – a disease that is escalated by the aforementioned risk factors. However, Allen et al. (2019) also found that ACE scores in this sample were not associated with high cholesterol or type 2 diabetes, in contrast to the findings of Cubin et al., 2019. Considering the results of this study, the researchers suggest that providers consider utilizing trauma-based approaches to patient care.

Type 2 diabetes, which also ranks number nine on the World Health Organization's list of top ten leading causes of death globally (WHO, 2020), has also been implicated in the consequences of childhood trauma. In 2019, Campbell et al. conducted a three-wave, longitudinal study from 1995 to 2014 during which the researchers analyzed the mortality causes of 3,023 participants, both with and without adverse childhood experiences. The results of the analysis indicated that adults with both ACEs and diabetes have a mortality rate of 2.3 times that of adults without diabetes or an ACE. It is important to note that this study is not suggesting that

ACEs contribute to diabetes, but rather that ACEs and diabetes together increase mortality in comparison to those with an ACE only or diabetes only. The researchers attribute these results to the possibility that the increased mortality of diabetes is compounded by the 66% increased risk of mortality in those with at least one ACE. Further, Campbell at al. (2019) acknowledges that further research is indicated to determine a physiological cause of ACEs and diabetes resulting in increased mortality.

Insomnia, which can be distinguished as either acute or chronic, impacts 10-30% of the population, resulting in reduced quality of life (Bhaskar et al., 2016). Mishra et al., 2020, assessed poor sleep quality and physical functional limitations in the middle of life as a mechanism between childhood maltreatment exposure. Using data from the Biomarker Project of the Midlife Development in the United States study (n = 1251), the Childhood Trauma Questionnaire, and Pittsburgh Sleep Quality Index, the data results indicated that childhood maltreatment impacts sleep quality even 50 years after exposure, with members of the childhood sexual abuse sub-group experienced the poorest sleep quality in midlife compared to the emotional and physical maltreatment subgroups. Therefore, it could be deducted that poor sleep quality, and its well-studied side effects of obesity, hypertension, anxiety, depression, etc., may provide a partial explanation as to the biological mechanisms that link childhood emotional trauma to chronic disease development.

Finally, because the World Health Organization also ranks Alzheimer's disease and other dementias as the seventh leading cause of death globally (WHO, 2020), it is also important to examine the role of childhood trauma in the development of these diseases. Using data from 2,682 men in the population-based Kuopio Ischemic Heart Disease Risk Factor Study, Donley et al., 2018, analyzed the stressful and traumatic events (orphanage placement, emigration, etc.)

that participants experienced in childhood and determined that childhood stress and trauma was associated with higher rates of dementia or Alzheimer's disease development later in life. Donley et al. suggest that the origins of dementia may even start early in childhood and are exacerbated by accumulated risk factors across the lifespan that result in the development of dementia or Alzheimer's disease. A significant limitation of this study is the lack of a diverse sample that only includes men.

Resilience

An important component of the degree of impact that childhood trauma may or may not have on future health in adulthood is resilience. The following studies seek to address trauma, resilience, and future health outcomes.

With the intention of addressing literature gaps by studying ACEs, resilience, and developing measures of resilience within a community, Longhi et al. (2021) explored how higher community-wide levels of resilience could mitigate the impact of ACEs on adult mental and physical health. Through analysis of state archival data as well as Behavioral Risk Factor Surveillance System surveys, and community resilience scores, the researchers described the positive impact of community-wide contextual resilience factors on health outcomes for both adults and youths with ACEs as "remarkable" (Longhi et al., 2021), while individual resilience levels mitigated outcomes for adults with ACEs. The presence of social-emotional support, life satisfaction, social capital factors, and social cohesion within communities could be an important intervention when attempting to address the impact of childhood trauma.

Resilience may serve as a protective factor for those who have experienced childhood trauma and may be helpful in mitigating the negative effects of childhood trauma during the prenatal and postnatal periods. Watson et al., 2022, examined the perspectives of 119 pregnant

women, of whom 38% have experienced at least one ACE, on resilience and childhood trauma screening during the prenatal period through retrospective surveys. The survey responses indicated that 82.2% of women felt that prenatal care should include ACE screening and 94% believed that prenatal care should involve resilience counseling. The study provides insight into an important opportunity to provide trauma and resilience counseling in the prenatal period with the potential of mitigating the transgenerational impact of childhood trauma that Brew et al. (2020) found. This study was limited by a demographic that unintentionally excluded low-income or uninsured pregnant and postpartum women.

Posttraumatic growth (PTG) is the positive psychological changes that result due to a traumatic experience, possibly due to new perspectives and new self-understanding (Collier, et al., 2016). In an observational study seeking to explore whether emotional resilience could determine the extent of negative or positive changes following childhood trauma (N = 167 participants), Tranter and Brooks (2021) collected data using an online survey that measured childhood adversity, resilience, and posttraumatic stress symptoms. Using this data, the researchers found that resilience served as a significant mediator of positive PTG but did not necessarily impact negative posttraumatic stress outcomes. Post-traumatic growth is an important concept when considering how childhood trauma could impact health decisions in adulthood, as positive post traumatic growth could allow for improved development of a personal perspective that could enhance quality of life (Tranter & Brooks, 2021).

To address the impact of childhood trauma, which is especially prevalent in African American communities (Hampton-Anderson et al., 2021) and resilience, Giovanelli et al., 2019, conducted a longitudinal cohort study of 1,539 participants in which they aimed to explore the impact of childhood trauma on physical and mental health and mechanisms of improving

resilience in vulnerable populations. Using data from a study on the impact of Early Childhood Education programs, the researchers were able to identify important areas in the ecological system that may improve and promote resilience to childhood trauma, including increased community cohesiveness and improved education. The researchers evaluated the impact of introducing school support mediators during childhood, which later resulted in improved high school graduation rates, higher-skilled job acquisition, and reduced smoking, even in participants with an ACE score of four or higher. This study provides a valuable introduction to the ways that resilience can be promoted within communities to combat the negative effects of childhood trauma.

Lastly, Lee et al., 2019 further explored the role of resilience in those who had experienced childhood trauma in their retroactive, observational study of 1,042 male Veterans Affairs (VA) participants. They further researched the association between childhood experiences, both negative and positive, to longevity by assessing the impacts of early psychosocial stressors, socioeconomic stress, and supportive relationships and how these factors impact the resilience pathways by which the person follows. Retrospectively, the early and midlife psychosocial factors along with mortality were assessed in the participants. The research revealed that higher quantities of stressful life events in midlife were associated with having more childhood psychosocial stressors that reduced longevity, leading to utilization of the stress continuity pathway rather than the resilience pathway. This analysis suggests that negative childhood experiences increase the risk of life choices that are not within the resilience pathway; therefore, early intervention in patients with childhood trauma is essential in assisting the selection of the resilience pathway, which results in longevity.

Summary of Literature

As healthcare professionals continue to research childhood trauma, how it impacts the neuroendocrine system, the development of chronic disease in adulthood, and the role of resilience spanning all the way from the antepartum period to the end of life, much of the research is inconclusive regarding the actual biological and psychological processes that tie childhood trauma and chronic disease development together. For example, while O'Conner et al. (2020) and Kuzminskaite et al. (2020) found that cortisol levels and the stress systems were not necessarily impacted by childhood trauma. In contrast, Riis et al. (2019) and Plant et al. (2020) found that childhood trauma of participants or even their mothers contributed to increased inflammatory markers and cortisol disruptions. All of the research confirmed that ACEs are associated with poor health outcomes, and provided some hypotheses as to why, but these were only speculations.

Research regarding resilience has begun to provide professionals with potential avenues of intervention for disrupting the childhood trauma to chronic disease to increased mortality sequence of events despite not having solidified the pathophysiological sequence of events. Much of the research supported the promotion of both individual and community resilience to combat the immediate and transgenerational effects of childhood trauma.

Discussion and Synthesis

Based on the literature presented, it is reasonable to suggest that childhood trauma and the development of chronic disease in adulthood may be connected. Much of the research found that childhood trauma resulted in pathophysiological changes, such as neuroendocrine-immune dysregulation (Riis et al., 2019), increased inflammatory markers, and elevated cortisol levels by adulthood (Plant et al., 2016). However, results were not always consistent, with other studies denying significant increase in inflammatory markers or cortisol levels in participants with ACEs (Kuzminskaite et al., 2020). Other studies suggested causes such as increased relationship distress (Wheeler et al., 2019), chronic stress, impaired neurodevelopment, executive dysfunction (Trossman et al., 2021), and transgenerational trauma (Brew et al., 2020). Finally, the role of resilience as a protective factor in interrupting the sequence of events that links childhood trauma to disease development was introduced. Social cohesion within communities (Longhi et al., 2021), resilience counseling (Watson et al., 2022), and post-traumatic growth (Collier et al., 2016) are all resilience mechanisms with mitigating potential.

In answering the question "What is the relationship between childhood trauma and the development of chronic disease in adulthood?" the literature provides solid evidence that there is a positive relationship between the two variables. Although the exact physiological mechanisms of this relationship have not yet been solidified, the study of ACEs, the HPA axis, and chronic disease development in adults who have experienced childhood trauma suggest physiological means through which this connection occurs, although the evidence is still inconsistent.

Although the exact mechanisms for the relationship between childhood trauma and chronic disease is adulthood is not yet fully known, it is still suggested by many of the researchers that providers begin incorporating trauma-based approaches to care delivery,

especially in ACE-vulnerable populations (Allen et al., 2019). Trauma-informed care involves building a trauma-informed workforce, preventing secondary traumatic stress in staff, involving patients in treatment processes, screening for trauma, and staff training in trauma-specific treatments (Center for Health Care Strategies, 2017). Utilization of trauma-based care is an option that will allow providers to empower patients to follow the steps of the health promotion model in a self-initiated treatment plan.

Implication for Advanced Nursing Practice

Childhood trauma impacts a significant number of children. Based on the preceding literature, it would be prudent for nurse practitioners to be provided with trauma-informed care training in their program of study. Trauma-informed care training should not be limited to only mental healthcare or pediatric providers. Medical treatments implemented in primary care offices or inpatient hospitalizations can be perceived as invasive, distressing, and even triggering of posttraumatic stress disorder symptoms (Stevens et al., 2019). Implementation of trauma-informed care is limited by lack of training programs and materials. Many healthcare providers report a lack of perceived self-competence in caring for traumatized patients (Bruce et al., 2018). The increased risk of developing chronic diseases in the presence of childhood trauma has a high cost on both communities and Medicaid/Medicare. For example, one out of every four dollars in US health care costs is spent on caring for those with diabetes (Zhou et al., 2020). Chronic diseases are not only detrimental to direct medical costs, but also loss of productivity costs – impacting both the finances of individuals, communities, and governments alike.

Recommendations for Future Research

For future research on childhood trauma and chronic disease development, further exploration will need to be done to address the biological mechanisms that facilitate this

connection. Researchers have already begun evaluating the role of the HPA axis, neuroendocrine dysfunction, and inflammation; however, the results are inconsistent and inconclusive. If the exact patterns of cortisol levels, inflammatory markers, etc. can be further researched, it will become possible for an intervention to be developed.

It would also be helpful to conduct further research on the different methods of psychological intervention and their effectiveness in mitigating the negative repercussions of childhood trauma. Interventions for trauma, such as eye movement desensitization and reprocessing (EMDR), cognitive-behavioral therapy (CBT), and cognitive processing therapy (CPT) can be utilized to promote psychological well-being in trauma victims (APA, 2020), but it is not well studied in its effectiveness in mitigating chronic disease development associated with childhood trauma.

Conclusion

Childhood trauma is a widespread issue that requires the attention of healthcare providers within all specialties, as it does result in chronic disease development in adulthood, impacting the quality of life and financial outcomes of both individuals and communities. The literature strongly supports the connection between childhood trauma and the development of chronic disease in adulthood, but the biological mechanisms require further exploration so that further interventions can be developed and implemented. For now, training healthcare providers in trauma-informed care is an important change that can be made to provide the best care possible for patients who have experienced trauma, with the goal of empowering patients to make positive personal and health decisions that will promote health maintenance and disease prevention.

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Appendix

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Riis, J. L., Granger, D. A., Woo, H., Voegtline, K., DiPietro, J. A., & Johnson, S. B. (2019). Long-term associations between prenatal maternal cortisol and child neuroendocrine-immune regulation. *International Journal of Behavioral Medicine*, *27*(3), 267–281. https://doi.org/10.1007/s12529-019-09814-2	"Examine whether prenatal maternal hypothalamic-pituitary-adrenal activity moderates child neuroendocrine-immune (NEI) relations and explore the consistency of this moderating effect across gestation (Riis et el., 2019, p. 1)."	n = 45 mother/child pairs n_{female} = 25 children n_{male} = 20 children Mother's mean age 32 years	No interventions Explanatory variable: mother's cortisol levels during pregnancy Response variable: offspring saliva cortisol and cytokine levels	Researchers compared the saliva cortisol and cytokine levels for children whose mothers experienced elevated cortisol levels during pregnancy vs. children of mothers who experienced normal cortisol levels during pregnancy	In male children, maternal cortisol levels did not impact NEI activity or functioning. In female children, maternal cortisol levels were shown to be associated w/ higher positive cortisol-cytokine relations by age 5.	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Plant, D. T., Pawlby, S., Sharp, D., Zunszain, P. A., & Pariante, C. M. (2016). Prenatal maternal depression is associated with offspring inflammation at 25 years: A prospective longitudinal cohort study. *Translational Psychiatry*, *6*(11). https://doi.org/10.1038/tp.2015.155	"To investigate whether maternal prenatal depression predicts adulthood inflammation and HPA axis dysfunction and whether offspring child maltreatment moderate the effects of prenatal depression on these immune and neuroendocrine parameters (Plant et al., 2016, p. 1)."	*n* = 103 offspring, all age 25	No interventions Explanatory variable: mothers who experienced prenatal depression Response variable: hs-CRP and awakening cortisol levels of offspring	A comparison was made between the hs-CRP and awakening cortisol levels in offspring of mothers who experienced prenatal depression vs. those levels in offspring of mothers who did not experience prenatal depression	Prenatal maternal depression did not exhibit an impact on adult awakening cortisol levels; however, childhood maltreatment was positively associated with elevated awakening cortisol levels.	3B
Kuhlman, K. R., Geiss, E. G., Vargas, I., &	"To examine whether individual differences in HPA-	*n* = 121 youth (ages 9 to 16 years old)	Interventions: Socially-	The researchers compared the varying degrees	The average youth exhibited a 66% increase in	2A

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Lopez-Duran, N. (2017). Hpa-axis activation as a key moderator of childhood trauma exposure and Adolescent Mental Health. *Journal of Abnormal Child Psychology, 46*(1), 149–157. https://doi.org/10.1007/s10802-017-0282-9	axis responses to acute stress moderated the relationship between exposure to different types of trauma and behavioral problems in youth (Kuhlman et al., 2017, p.1)."		Evaluated Cold Pressor Task The participants' changes in cortisol levels/HPA activation depended on their reaction to the cold pressor task.	of HPA activation reaction to the stressor task	cortisol from their baseline to their peak response to the stress task.	
O'Connor, D. B., Branley-Bell, D., Green, J. A., Ferguson, E., O'Carroll, R. E., & O'Connor, R.	"Examine whether suicide vulnerability grouping was associated with daily CAR and cortisol levels	*n* = 154 Ages 18-63 years old (*M* = 27.74 years, *SD* = 9.27 years)	No intervention Explanatory variable: childhood trauma experience	Comparisons were made between the daily awakening cortisol levels and wake-peak to 12 hours	Participants who reported a history of childhood trauma presented with lower awakening cortisol levels and	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
C. (2020). Effects of childhood trauma, daily stress, and emotions on daily cortisol levels in individuals vulnerable to suicide. *Journal of Abnormal Psychology, 129*(1), 92–107. https://doi.org/10.1037/abn0000482	across the rest of the day over a 7-day time window and whether daily stressors and emotions, including defeat and entrapment influenced cortisol levels (O'Connor et al., 2020, p. 1)."		Response variable: daily awakening cortisol levels and wake-peak to 12 hours cortisol slopes	cortisol slopes of participants who self-reported experiences of childhood trauma vs. those participants who denied childhood trauma.	flatter wake-peak to 12 hour cortisol slopes, possibly due to prolonged over-activation of the HPA axis	
Kuzminskaite, E., Vinkers, C. H., Elzinga, B. M., Wardenaar, K. J., Giltay, E. J., & Penninx,	"Examine the associates between retrospectively reported CT and markers of HPA-axis, immune-inflammatory	*n* = 2778 Ages ranging from 18 years to 65 years old, without	No interventions Explanatory variable: childhood	Researchers compared separate and cumulative markers of the HPA axis, immune-	While most of the participants who experienced childhood trauma now reported anxiety and/depression	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
B. W. J. H. (2020). Childhood trauma and dysregulation of multiple biological stress systems in adulthood: Results from the Netherlands Study of depression and anxiety (NESDA). *Psychoneuroendocrinology*, *121*, 104835. https://doi.org/10.1016/j.psyneuen.2020.104835	system, and the autonomic nervous system (Kuzminskaite et al., 2020, p. 1)."	depression/anxiety	trauma experience(s) Response variable: the separate and cumulate markers of HPA axis immune-inflammatory system and autonomic nervous system	inflammatory system, and the autonomic nervous system in participants who reported childhood trauma (via Childhood Trauma Interview) vs. these levels in participants who did not experience childhood trauma	(88.6%), the researchers did not find significant impact on the stress systems and their markers.	
Cubbin, C., Kim, Y., & Panisch, L. S. (2019).	"To contribute to the empirical literature on ACEs	*n* = 2409, ages 30-57 years old	No interventions	The researchers compared the prevalence of	FCAs were strongly associated with	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Familial childhood adversity is associated with chronic disease among women: Data from the Geographic Research on Wellbeing (Grow) study. *Maternal and Child Health Journal*, *23*(8), 1117–1129. https://doi.org/10.1007/s10995-019-02758-9	among women in the following ways: develop a measure of ACEs referred to as familial childhood adversities and examine the association between each of the two measures and a set of important chronic diseases and related conditions (Cubbin et al., 2019, p. 1)."		data collection only. Explanatory variable: experiences of familial childhood adversities Response variable: the development of chronic diseases (specifically DM, HTN, high cholesterol, heart disease)	chronic diseases between various demographics of women who all experienced at least one FCA.	the development of chronic diseases in women, especially separated, divorced, or widowed women w/ each additional FCA increasing the likelihood of developing a chronic disease by 10%.	
Lin, L., Wang, H. H., Lu, C., Chen, W., & Guo, V. Y. (2021). Adverse	"To examine associations between ACEs and subsequent chronic diseases and to assess if certain	*n* =11972 Ages 45 years and older (mean age 59.85 years, standard	No interventions Explanatory variables: ACE scores and	The researchers compared the prevalence of chronic diseases in those with no ACE scores vs.	Those who had ACE scores of four or higher exhibited positive association with development of	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
childhood experiences and subsequent chronic diseases among middle-aged or older adults in China and associations with demographic and socioeconomic characteristics. *JAMA Network Open*, *4*(10). https://doi.org/10.1001/jamanetworkopen.2021.30143	demographics and socioeconomic factors modify these associations (Lin et al., 2021, p. 1)."	deviation of 9.56 years)	socioeconomic characteristics Response variable: Development of one or more chronic illness	those with ACE scores of four or higher.	chronic disease. Socioeconomic and demographic factors did not play a role in these associations.	
Trossman, R., Spence, S.-L., Mielke, J. G.,	"To fill an important theoretical gap in	n = 84 (n_{male} =34, n_{female} = 48)	No interventions	The researchers compared executive	The researchers found that those with ACEs	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
& McAuley, T. (2021). How do adverse childhood experiences impact health? exploring the mediating role of executive functions. *Psychological Trauma: Theory, Research, Practice, and Policy*, *13*(2), 206–213. https://doi.org/10.1037/tra0000965	the ACE literature by evaluating whether executive functions constitute a biologically plausible mediating mechanism in this pathway (Trossman et al., 2021, p. 1)."	Ages 18-35 (*M* 20.68, *SD* 2.91).8	Explanatory variable: ACE score Response variable: executive function/dysfunction	function (or executive dysfunction) of those with ACEs vs. those without ACEs.	exhibited poorer executive functioning, leading to poor health decisions.	
Santoro, A. F., Suchday, S., Robbins, R. N., Benkhoukha,	"To examine the relationships between ACEs, anger expression, stress, and physical	*n* = 132 Asian Indian participants (half male, half female)	No intervention Explanatory variable: ACE score	The researchers compared chronic health condition quantity and	Participants with ACE scores of three or higher were significantly more likely to	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
A., & Zemon, V. (2021). Childhood adversity and physical health among Asian Indian emerging adults in the United States: Exploring disease-specific vulnerabilities and the role of anger. *Psychological Trauma: Theory, Research, Practice, and Policy*, *13*(2), 214–222. https://doi.org/10.1037/tra0000942	health in a sample of Asian Indian adults due to the current lack of research regarding ACE impact in specific ethnic minority groups (Santoro et al., 2021, p. 1).”	18-29 years old w/ a mean age of 23.52 years old	Response variables: anger expression and chronic health condition diagnosis, which the researchers suggest may depend on the ACE score of the participant.	anger expression in adulthood of participants with ACE scores of three or higher vs. those with ACE scores lower than three	have at least one chronic condition, specifically diabetes. These participants also exhibited higher anger expression in adulthood.	

Reference	**Research Question Purpose Objective Hypothesis**	**Patients Population Sample**	**Interventions Identify Independent and Dependent Variables**	**Comparisons**	**Outcomes Findings**	**Level of Evidence and Quality Grade**
Wheeler, N. J., Daire, A. P., Barden, S. M., & Carlson, R. G. (2019). Relationship Distress as a Mediator of Adverse Childhood Experiences and Health: Implications for Clinical Practice with Economically Vulnerable Racial and Ethnic Minorities. *Family process*, *58*(4), 1003–1021.	"To add to existing knowledge for the mediating potential of relationship distress between early life adversity and health in the population demonstrated as the most vulnerable to disparities in each construct (i.e., ACE, relationship distress, chronic health issues among individuals with economic disadvantage, and a racial or ethnic minority background (Wheeler et al., 2019, p. 1)."	96 individuals (13 male, 83 female), average age of 40 years old (*SD* = 12.98, Min = 18 years, Max = 65 years)	Explanatory variable: childhood trauma Response variables: Relationship distress and health problems	Comparisons were made between the relationship distress levels and health measurements of those who had experienced childhood trauma vs. those who did not.	More childhood adversity (as evidenced by ACE score) was associated with greater relationship distress in adulthood, providing a potential explanation for poor physical and mental health.	3B
Allen, H., Wright, B. J., Vartanian, K., Dulacki, K., &	"The objective of this study was to estimate the extent of ACEs in a low-	The sample consisted of 12,229 low-income,	Explanatory variables: ACE score and income level	Two comparisons were made: (1) the prevalence of	The results indicated that low-income adults have even	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Li, H.-F. (2019). Examining the prevalence of adverse childhood experiences and associated cardiovascular disease risk factors among low-income uninsured adults. *Circulation: Cardiovascular Quality and Outcomes*, *12*(9). https://doi.org/10.1161/circoutcomes.117.004391	income, nonclinical, uninsured adult population and assess the relationship between ACEs and cardiovascular disease risk factors (Allen et al., 2019, p. 1)."	nonelderly uninsured adults	Response variable: clinical indicators of cardiovascular disease	ACEs in low-income adults vs. the general population and (2) the presence of risk factors of cardiovascular disease in those with ACEs vs. those without or those with lower quantities of ACEs	higher rates of ACEs than previous estimates. Further, ACEs were associated with higher rates of many different cardiovascular disease risk factors, including obesity, smoking, hypertension, and physical inactivity.	
Brew, B. K., Lundholm, C., Caffrey Osvald, E.,	"To investigate whether early-life adversity experienced as	3 generations of Swedish families, with a base	Explanatory variables: early-life adversity	The researchers compared the inflammatory disease	Early-life bereavement experienced by women was	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Chambers, G., Öberg, S., Fang, F., & Almqvist, C. (2021). Early-life adversity due to bereavement and inflammatory diseases in the next generation: A population study in transgenerational stress exposure. *American Journal of Epidemiology*, *191*(1), 38–48. https://doi.org/10.1093/aje/kwab236	bereavement is associated with chronic inflammatory health in offspring (Brew et al., 2021, p. 1).”	population of 453,516 children	experienced as bereavement Response variables: inflammatory health in offspring	development of children whose generation 1 experienced bereavement in childhood vs. the inflammatory disease development of those whose generation 1 did not experience bereavement in childhood	associated with early-onset offspring asthma. Early-life bereavement in men was associated with autoimmune disease in offspring.	

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Campbell, J. A., Mosley-Johnson, E., Garacci, E., Walker, R. J., & Egede, L. E. (2019). The co-occurrence of diabetes and adverse childhood experiences and its impact on mortality in US adults. *Journal of Affective Disorders, 249*, 20–25. https://doi.org/10.1016/j.jad.2019.02.016	"To build on the current literature on ACEs and diabetes by addressing this gap in knowledge by examining the impact of co-occurring diabetes and ACEs on mortality in a longitudinal cohort of US adults (Campbell et al., 2019, p. 1)."	*n* = 3,023	Explanatory variable: ACE score Response variable: Development of diabetes, mortality	Comparisons were made in the mortality rates of those with diabetes vs. those with diabetes and an ACE vs. those with no diabetes and no ACE	The results of the analysis indicated that adults with both ACEs and diabetes have a mortality rate of 2.3 times that of adults without diabetes or an ACE.	3B
Donley, G. A., Lönnroos, E., Tuomainen, T.-P., & Kauhanen, J.	"This study examines relationships between childhood stress and later-age	*N* = 2682 with a mean age of 53.1, ranging from 42 to 61.3 years.	Explanatory variable: experience of childhood stress	The prevalence of Alzheimer's disease or dementia development in	Childhood stress and trauma was associated with higher rates of dementia or	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
(2018). Association of Childhood Stress with late-life dementia and alzheimer's disease: The KIHD study. *European Journal of Public Health, 28*(6), 1069–1073. https://doi.org/10.1093/eurpub/cky134	dementia, specifically Alzheimer's disease (AD) (Donley et al., 2018, p. 1)."		Response variable: future development of Alzheimer's disease or dementia	participants who experienced childhood stress vs. those who did not experience childhood stress	Alzheimer's disease development later in life. Donley et al. suggests that the origins of dementia may even start early in childhood and are exacerbated by accumulated risk factors across the lifespan that result in the development of dementia or Alzheimer's disease.	
Mishra, A. A., Friedman, E. M., Mihalec-Adkins, B. P., Evich, C. D., Christ, S. L., & Marceau, K. (2019). Childhood maltreatment	"The present study had three major aims: 1) To identify sub-groups of adults with differing combinations of childhood maltreatment exposures, 2) to	*n* = 1251	Explanatory variable: childhood maltreatment Response variables: Sleep dysfunction and physical functional	The researchers compared the sleep quality and physical functional levels of adults who had experienced childhood maltreatment vs. the sleep quality	The results reveal the role of sleep in connecting childhood maltreatment with functional impairments in adulthood as childhood maltreatment was	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
exposure and physical functional limitations in late adulthood: Examining subjective sleep quality in midlife as a mediator. *Psychology & Health*, *35*(5), 573–592. https://doi.org/10.1080/08870446.2019.1657576	understand the association of childhood maltreatment sub-group membership with subjective sleep quality in midlife, and 3) to assess poor sleep quality in midlife as a mechanism between childhood maltreatment sub-group membership and physical functional limitations in late adulthood (Mishra et al., 2019, p. 1)."		limitations in late adulthood.	and functional levels of those who did not.	shown to result in functional limitations and poor sleep in adulthood.	
Giovanelli, A., Mondi, C., Reynolds, A., & Ou, S. (2020). Adverse childhood experiences: Mechanisms	"We posited three hypotheses: (1) Cumulative ACEs from birth to 18 will predict adverse outcomes in the domains of educational attainment,	*N* = 1539 low-income adults	Intervention: Early childhood education programs Explanatory variable: ACE scores	Comparisons were made between participants with the ACE scores, early childhood education involvement, and socioeconomic	Participants with four or more ACEs were significantly less likely to obtain a high school diploma by age 25. The 2-ACE group was less	2B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
of risk and resilience in a longitudinal urban cohort. *Development and Psychopathology*, 32(4), 1418-1439. doi: 10.1017/S0954579419001382X	occupational prestige, criminal justice system involvement, and smoking in early adulthood. As the brain is uniquely sensitive to experience in early childhood, we also hypothesized that ACEs from birth to age five will be uniquely impactful on early adult outcomes; (2) Associations between ACEs and outcomes will be strongest for males and for participants in the highest poverty neighborhoods; and (3) 5HM mediators will partially to substantially explain the direct		Response variable: adverse outcomes in the domains of educational attainment, occupation prestige, criminal justice system involvement, and smoking	factors vs. those who did not participate in early childhood education and have significant parental involvement in childhood	likely to have a higher-skill job. School support mediators reduced the effects of ACEs on high school graduation. ACE group of four or greater exhibited higher likelihood of smoking. School support mediators slightly reduced the association between smoking and ACEs.	

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
	effects between ACEs and outcomes (Giovanelli et al., 2020, p. 1)."					
Lee, L. O., Aldwin, C. M., Kubzansky, L. D., Mroczek, D. K., & Spiro, A. (2019). The long arm of childhood experiences on longevity: Testing midlife vulnerability and resilience pathways. *Psychology and Aging*, *34*(7), 884–899. https://doi.org/10.1037/pag0000394	"This study evaluated the independent contributions to longevity of favorable and unfavorable early experiences, including psychosocial stressors, childhood socioeconomic status (SES), and close relationships. We also examined 4 midlife psychosocial factors as vulnerability and resilience pathways potentially mediating these	*n* = 1,042 male patients from the Veterans Affairs	Explanatory variable: childhood experiences, stressful life events in midlife Response variables: Negative affect, life satisfaction, optimism	The researchers compared the longevity of participants who experienced childhood adverse events and midlife stressful life events vs. the longevity of those who did not experience those things.	More childhood psychoscial stressors was linked to reduced longevity. Higher optimism in midlife mediated the association of higher childhood socioeconomic status to higher longevity.	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
	associations (Lee et al., 2019, p.1)."					
Longhi, D., Brown, M., & Fromm Reed, S. (2021). Community-wide resilience mitigates adverse childhood experiences on adult and Youth Health, school/work, and problem behaviors. *American Psychologist*, *76*(2), 216–229. https://doi.org/10.1037/amp0000773	"This study developed community-wide measures for 118 Washington State communities of levels of adverse childhood experiences (ACEs) and resilience, and found significant mitigating effects of resilience on community-wide levels of mental health, physical health, problem behaviors, and school/work outcomes, independent of community-wide levels of ACEs, low income, and race/ethnic composition	118 Washington State communities	Interventions: The researchers developed community-wide measures for communities of levels of ACEs and resilience Explanatory variable: ACEs within the community, Resilience interventions Response variable: the mitigating effects of resilience as measured by individual and contextual resilience scores	The researchers compared the factors of individual resilience (life satisfaction, optimism) and contextual resilience (social cohesion, protective supports for youths) between the communities and compared the levels of resilience vs. the impacts of ACEs within the communities.	Outcomes for adults in communities with high individual ACE scores were mitigated by both contextual and individual resilience levels. Outcomes for youth in communities with high individual ACE scores were mitigated by only contextual resilience.	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
	(Longhi et al., 2021)"					
Tranter, H., Brooks, M., & Khan, R. (2021). Emotional resilience and event centrality mediate posttraumatic growth following adverse childhood experiences. *Psychological Trauma: Theory, Research, Practice, and Policy*, *13*(2), 165–173. https://doi.org/10.1037/tra0000953	"This study explored whether emotional resilience and event centrality could determine the degree of negative or positive changes reported following ACEs (Tranter & Brooks, 2021, p. 1)."	*N* = 167; 54.5% female; aged 19 – 95 years)	Explanatory variable: childhood ACE score Response variables: Resilience, posttraumatic growth, psychological well-being	The researchers compared the self-perceived resiliency and post traumatic growth of adults who experienced ACEs during childhood.	Following ACEs, the treatment and management of emotional resilience could result in positive effects on mental health.	3B

Reference	Research Question Purpose Objective Hypothesis	Patients Population Sample	Interventions Identify Independent and Dependent Variables	Comparisons	Outcomes Findings	Level of Evidence and Quality Grade
Watson, C., Wei, J., Varnado, N., Rios, N., Staunton, M., Ferguson, D., & Young-Wolff, K. C. (2022). Pregnant women's perspectives on screening for adverse childhood experiences and resilience during prenatal care. *Psychological Trauma: Theory, Research, Practice, and Policy*. https://doi.org/10.1037/tra0001166	"To examine the acceptability of routine screening for adverse childhood experiences (ACEs) and resilience during prenatal care. This study examined pregnant women's perspectives on ACEs and resilience screening during prenatal care in two medical centers via post-screening telephone surveys (Watson et al., 2022, p. 1)"	*N* = 119 pregnant women	Intervention: A mental health resource was provided to the women during ACE screening, although this intervention was not necessarily tested Explanatory variable: ACE and resilience screening during prenatal care Response variable: The pregnant women's perception of the screening	The researchers compared the perspectives, opinions, and recommendation of the individual pregnant women on the implementation of regular ACE and resilience screening on pregnant women.	Of the participants, 82.2% felt that prenatal ACE screenings should be included in prenatal care. 94% felt that reliance screenings and conversations should also occur during prenatal care. Many of the women also believed that good coping skills can be helpful in reducing the negative consequences of ACEs.	2B