TREATMENT OF ADULTS WITH CHILDHOOD TRAUMA AND CHRONIC DISEASE

A Theoretical Framework for Treatment of Adults With Childhood Trauma and Chronic Disease

Doctoral Project

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ABSTRACT

The confluence of childhood trauma and comorbid chronic disease in the United States places a significant burden on the healthcare system and on individual quality of life. Considerable advances in the field of psychoneurobiology demonstrate the interrelatedness of chronic early life stress and adult chronic diseases yet there is little research demonstrating consistent efficacy of current psychotherapy treatment methods for adult victims of childhood trauma and comorbid chronic disease. This qualitative study aimed to propose a conceptual framework for psychotherapy that integrates physiological and psychological consequences of childhood trauma over the lifespan, by exploring the efficacy of current psychotherapeutic treatment modalities for the target population, the psychoneurobiology of childhood trauma and chronic diseases, and application of the findings to a new psychotherapeutic approach incorporating the interrelatedness of physiology and psychology to address the underlying impairments of chronic disease. Findings highlighted a significant treatment gap for the target population. This includes challenges in identification, diagnosis, complex symptomology, disparate populations and research methods, and deficits in training of medical and psychological practitioners. Findings demonstrated efficacy of psychoneurological interventions such as eye movement desensitization and reprocessing, and mind-body approaches. It is hoped that these findings may contribute to a new approach to psychotherapeutic framework for treatment of adult victims of childhood trauma and comorbid chronic diseases.

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CHAPTER ONE

Overview of the Study

Health and well-being in the United States is threatened today by a confluence of three related trends: childhood trauma, and chronic physical and mental illness. In recent testimony to the U.S. Government House Oversight and Reform Committee, childhood trauma was identified as a severe, and growing, problem affecting communities across the United States (Houry, 2019). Adverse childhood experiences (ACEs) are a subset of childhood trauma involving physical, emotional, or sexual abuse, physical or emotional neglect, witnessing domestic violence, or living in a home with substance abuse (Merrick et al., 2018). ACEs are linked to five of the 10 leading causes of death (Centers for Disease Control and Prevention [CDC], 2019a). The long-term effects of ACEs are widespread, resulting in a cascade of physiological and neural damage, leading to prolonged activation of the body's stress system, damaging the nervous, immune, and endocrinological subsystems as well as creating vulnerability for a broad spectrum of chronic physical and mental illnesses in adult life (De Bellis & Zisk, 2014; Teicher et al., 2016).

In high-income countries such as the United States, chronic diseases are the cause of approximately 75% of deaths (Harris, 2019). The National Center for Chronic Disease Prevention and Health Promotion (2022) defined chronic diseases as conditions that persist for at least 1 year, may limit activities of daily living, and/or require regular medical attention. An infographic by the CDC (2019b) stated that six out of 10 adults in the United States suffer from a chronic disease, and that four in 10 adults have two or more. According to the National Center for Chronic Disease Prevention and Health Promotions, 90% of the United States $4.1 billion in annual healthcare expenditures are for people with chronic physical and mental health conditions, making it a compelling area of research from many aspects.

The relationship between chronic disease and psychopathology is complex and interdependent, and the pathways between the two are not well understood (Ohrnberger et al., 2017). Mental health disorders, such as depression and anxiety, appear to increase the risk of chronic disease (Scott et al., 2016); whereas the onset of chronic disease can in turn increase the risk of mental health disorders (Sporinova et al., 2019). Comorbidity complicates diagnosis and treatment of both physical and psychological conditions (Isvoranu et al., 2021). Raghupathi and Raghupathi (2018) suggested that the trajectory of chronic disease can be mitigated by timely diagnosis and treatment of mental health disorders; conversely, untreated mental health comorbidities can exacerbate chronic disease (Scott et al., 2016). Prince et al. (2007) concluded that there can be no health without mental health—a statement adopted by the World Health Organization (WHO, 2013) in the organization's Mental Health Action Plan.

Based on current information, it appears that adult patients with chronic disease fall into one of three categories. The first group is those adults diagnosed with one or more chronic diseases who have no history of mental health disorders, and who are adaptive and resilient enough to weather the transition, able to embrace the wellness-in-the-foreground model of disease (Patterson, 2001). The second group are people who similarly have no history of mental illness, but after diagnosis with chronic disease develop depression and anxiety as a consequence of the changes; these people experience the illness-in-the-foreground model (Patterson, 2001), where their disease begins to define them and shape their lives. The mental health issues of this group are generally served by traditional models of psychotherapy such as CBT (White, 2001).

The final group includes adults diagnosed with chronic disease who have a history of significant preexisting psychiatric disorders. Recent research emphasizes the strong link between adult chronic diseases with comorbid psychiatric disorders and ACEs (Berens et al., 2017).

ACEs have been identified as the highest risk factors for adult psychopathology, often leading to mood, personality, and substance-use disorders in adulthood (Marusak et al., 2015). Merrick et al. (2018) determined that 61.55% of study participants had experienced at least one—and often more than one—adverse childhood experience. The economic burden of increased healthcare costs, government services, and increased spending in the criminal justice system for adult survivors of childhood trauma was recently estimated to be $830,928 per case (Peterson et al., 2018).

Despite these findings, there is a noticeable lack of research regarding treatment methods for adult survivors of childhood trauma with comorbid chronic disease. An increased understanding of the mental health consequences has resulted in an increase in research over the last few years on treatment for childhood trauma (van Nieuwenhove & Meganck, 2017) and for treatment of adults with chronic disease and mood disorders (Sachs-Ericsson et al., 2017). With the increased diagnosis of both ACEs and chronic disease, the need for an integrated case conceptualization of ACEs and comorbid chronic disease to address this complex set of physiological and psychological pathology is clear. A systematic review of the literature was used to identify how adverse experiences of childhood coupled with adult chronic disease may be treated through a new conceptual model of psychotherapy that integrates both physiology and psychology.

Background of the Problem

By the middle of the 20th century, chronic diseases were the leading cause of illness and death in the United States National Center for Chronic Disease Prevention and Health Promotion, 2022), a status that has not changed in 7 decades. Nearly 60% of adults meet criteria for multimorbidity (more than two concurrent chronic diseases), with a significant increase over

the last 3 decades (Kingston et al., 2018). The rise in the incidence of chronic disease has a concomitant impact on quality of life, families, the national economy, employment productivity, and healthcare costs. The reasons for the increase are multifaceted. In a study commissioned by the National Center for Chronic Disease Prevention and Health Promotion, Bauer et al. (2014) identified poor nutrition, low physical activity, use of alcohol and nicotine, and high blood pressure as risk factors for chronic disease. More recent research has identified other factors: the increase in environmental toxins (Zhuang et al., 2018); social determinants (Cockerham et al., 2017); the state, availability, accessibility, and acceptability of healthcare in the U.S. (Goudge et al., 2009), variations in standards of care (Wennberg, 2002), the continued dominance of the biomedical model of healthcare over a mind–body approach (Astin et al., 2003), and the prevalence of mental health comorbidities in people suffering from chronic disease (van de Pavert et al., 2017).

Mental illness has seen a similar trajectory over past decades (Olfson et al., 2019). Despite an increase in the use of mental health treatment in the United States, the prevalence of mental health disorders continues to rise (Mojtabai & Jorm, 2015). At the same time, the link between adult psychopathology and childhood trauma, especially ACEs, has become evident (Devi et al., 2019; Hughes et al., 2017). In a landmark study on ACEs, Felitti et al. (1998) concluded that the effects of childhood trauma on adult health are strong and cumulative. Findings from more recent research links affective and psychotic disorders in adults to childhood trauma, concluding that childhood adversities associated with maladaptive family functioning (e.g. parental mental illness, child abuse, neglect) were the strongest predictors of mental health disorders (van Nierop et al., 2018). One of the difficulties posed in treatment of adults with childhood trauma is the neurobiological changes that occur during early childhood stressors,

resulting in increased stress response (Lippard & Nemeroff, 2020). Lippard and Nemeroff (2020) concluded that effective treatment for adult psychopathology when childhood trauma is present would benefit from a better understanding of the neurological substrates impacted by ACEs. ACEs have also been linked to chronic diseases (Sonu et al., 2019). Wittbrodt et al. (2019) found that early childhood trauma had a negative effect on stress-responsive brain areas connecting to the heart, which could contribute to adverse outcomes in patients with coronary artery disease.

The complex interrelationship between ACEs, chronic disease, and serious mental illness poses challenges for psychotherapeutic treatment. Although clinical depression and anxiety are classified as mood disorders, they are also significant symptoms of other disorders, including posttraumatic stress (PTSD). Research supports the hypothesis that these disorders may not respond to normal standards of care when they are associated with childhood trauma. Yu et al. (2019) found patients diagnosed with major depressive disorder and a history of childhood trauma showed evidence of the trauma in the significant disruption of resting state networks in brain connectivity. Lippard and Nemeroff (2020) found compelling differences in the origin and pathologic process of depression in adults with early trauma compared to adults with depression and no reported history of childhood trauma. Vythilingam et al. (2002) found reduced hippocampal volume in patients with major depression and early life trauma. In addition to changes in brain physiology arising from childhood trauma, ACEs have been shown to create insecure attachment together with long-term illness and medically unexplained symptoms (Adshead & Guthrie, 2015). Dagan et al. (2018) found that the link between ACEs and cellular aging is moderated by attachment security.

When assessing psychotherapy patients who struggle with physical illness, it is vital to address the developmental history of trauma (Adshead & Guthrie, 2015). Bryan (2019) found

that ACEs are widespread and cumulative, affecting the developing brain, as well as the hormone and immune systems. Bryan concluded that trauma-informed treatment is vital for adults with ACEs. Tottenham and Sheridan (2010) concluded that neurobiological consequences of early life stress generally present mainly in the amygdala and prefrontal cortex in systems regulating emotion. In a study of 70 adult women whose experience of early life stress varied from none to severe, Kaiser et al. (2018) focused on neurobiological consequences of threat-related ELS and found that exposure to severe ELS resulted in complex physiological changes in static and dynamic connectivity in the brain in adulthood, including changes in corticolimbic circuitry, some of which acted as mediators of the changes. They concluded that there was a need for further research on how ELS generates adult stress-related disorders, and the role of neurobiological resilience in achieving healthy functioning.

Statement of the Problem

Early childhood trauma has consequences that extend far beyond childhood (Dye, 2018). The interrelationships among ACEs and adult psychological and physiological disorders are complex (Scott et al., 2011). Although considerable research is available on the pathogenic effects of childhood trauma (Copeland et al., 2018; Dube, 2018; Dye, 2018), very few, if any, studies addressed effective psychotherapeutic modes of treatment for adult victims of childhood trauma with chronic mental and physical comorbidities. Findings from research studies on the long-term disruptive effects of childhood trauma have not yet been integrated into current clinical psychotherapy practice (Berens et al., 2017). This population, which appears to be widespread (Andersen, 2015), would benefit from a well-developed model of psychotherapy that addresses the interrelatedness and complexity of ACEs, physiological impact, and chronic disease comorbidities. Psychotherapy for an adult with comorbidities of chronic disease and

childhood trauma would benefit from a trauma-informed approach; considering the underlying impairments in physiology, the theoretical model should also address any attachment rupture. Doing so requires an integrated case conceptualization of ACEs and comorbid chronic disease to enable an effective psychotherapeutic treatment plan. Psychotherapists working with this population should also be trained in the physiology of trauma, as well as the psychology of chronic disease, neither of which are required subjects in most counseling psychology masters' programs. The continued increase in Americans with comorbid mental and physical diseases is evidence that current, non-collaborative treatment approaches are not successful. This is the case even though healthcare spending in the United States continues to rise. The costs are incalculable, but include impacts to the U.S. economy, communities, employers, families, and overall quality of life for the target population and, often, their families.

Purpose of the Study

The purpose of this systematic literature review (SLR) was threefold. The first objective was to examine the efficacy of psychotherapeutic treatment modalities for adults with childhood trauma and comorbid mental and physical illnesses. The second was to understand how recent research in psychoneuroimmunology (PNI) and related fields can inform the treatment of adult victims of childhood trauma with comorbid mental and physical illness. The third objective as to develop a model of psychotherapy that addresses the interrelatedness of physiology and psychology, using a basis of trauma-informed care, adjusted to address the underlying impairments of chronic disease.

RQ1. How efficacious are current psychotherapeutic treatment modalities in the treatment of adults with ACEs and comorbid physical and mental illness?

RQ2. How has recent research into psychoneuroimmunology and related fields informed the treatment of comorbid mental and physical disease?

RQ3. How has recent research in psychoneuroimmulogy informe. What model of psychotherapy can be developed that addresses the interrelatedness of physiology and psychology across the lifespan, using a basis of trauma-informed care, and adjusted to address the underlying impairments of chronic disease?

Theoretical Framework

Adults with childhood trauma and chronic diseases in the 21st century face longer lives than their predecessors. Medical advances over the past few decades have resulted in increased life expectancies, and with longevity has come an increased susceptibility to disease in later life (Whitley et al., 2016), exacerbated by an alarming increase in environmental toxins and their negative impacts on aging physiology (Vriens et al., 2019). This study reviewed connections between adults with ACEs and chronic disease to determine best treatment options.

Three types of theoretical frameworks were used to provide supporting theoretical foundations for the research questions. The first addresses current psychotherapeutic treatment modalities for adults who present with symptoms of chronic childhood trauma. The relevant psychotherapeutic models include psychodynamic theory, CBT, mindfulness-based CBT, eye movement desensitization and reprocessing (EMDR), neuropsychotherapy, and trauma-informed care. These models are reviewed in the context of adult survivors of childhood trauma who present with comorbid chronic physical and mental health disorders. The second theoretical framework is polyvagal theory. Stephen Porges (2011) introduced polyvagal theory as a model of neural regulation of the autonomic nervous system (ANS) by the vagus nerve. The vagus nerve is bidirectionally influenced by the brain and body organs, and it controls muscles

involved in speaking, sucking, swallowing, and breathing. Vagal tone increases on exhalation. When stress is chronic, the sympathetic nervous system becomes consistently dominant, and the vagal break provided by the peripheral nervous system occurs less frequently. Deep, intentional breathing slows down the respiratory rate and lengthens exhalation, which in turn activates the vagal brake, enabling the peripheral nervous system to take over resolve the "hijacking" by the brain's fear response organisms (Porges, 2011). Polyvagal theory explains the mechanisms by which stress responses can retune the ANS to remain in defensive states. In turn, these changes lead to physiological changes and dysregulation, while simultaneously compromising the social engagement system, removing any opportunity to coregulate through social interactions. Polyvagal theory can be used to inform the psychotherapeutic treatment of trauma, with the goal of returning the ANS to a healthy state (Porges, 2011).

The third theoretical approach is the successful aging theory, first developed by Rowe and Kahn (1998, 2015). Rowe and Kahn's successful aging paradigm focuses on three important elements of well-being as individuals age: having a low probability of disease and disability, possessing good cognitive and physical capacity, and having active engagement in life. Rowe and Kahn (1998, 2015) posed three questions about aging: What does successful aging looks like? What can each individual do to succeed at the developmental life task of aging? and What changes can be made in American society to enable individuals to age successfully? The model describes how experiences of individuals over their lifetime and environmental influences determine the quality of aging. Although the impacts of aging on adults with ACEs are not well understood, aging is an additional stressor. The successful aging model may be useful, in a theoretical model of psychotherapy for adults with ACEs and chronic disease, in determining how to build resilience in this population.

The third theoretical approach, proposed by Zolnikov (2015), includes a modification of the successful aging model, The original model by Rowe and Kahn (1998, 2015) was primarily intended for relatively high-income populations; Zolnikov proposed an adaptation of the model that extends its applicability to low- and middle-income populations by incorporating considerations of the environment in the aging process as well as access to health care. These approaches to aging align with the research questions by focusing on elements promoting successful aging that can be applied in a trauma-informed setting. Chronic diseases usually exacerbate the difficulties posed by aging, and the additional trauma of ACEs only increases the challenges. Considering these three theories, and their effect on development and successful aging, this research focused on navigating trauma-informed care in the successful aging theory and Zolnikov's newly adapted successful aging model. This study sought to shed light on the magnitude of adverse development, which contributes to poor growth across the lifespan, and how best to treat and improve it.

Significance of the Study

This study adds to the body of literature addressing successful treatment of adults with ACEs, by expanding it to consider the comorbidity of chronic disease. Although the population of individuals with childhood trauma and chronic disease spans all life stages (Raab et al., 2012), this study focused on the adult population, with particular attention to the aging processes. This population experiences higher susceptibility to early mortality, disability, and significant impaired functioning in later life (Bartels, 2004), exacerbated by the negative effects of the rapid increase in environmental toxins on aging physiology (Vriens et al., 2019). Treatment of this population is challenging and fragmented, with little attention paid to the common etiology of adult mental and physical health disorders. Although there is evidence that suggests that the

trajectory of chronic disease can be mitigated by timely diagnosis and treatment of mental health disorders (Chapman et al., 2005), there is less data about how an integrated approach to childhood trauma and chronic disease in adults can improve the quality of aging. This latter topic, however, has been recently researched in a large cohort study in the Netherlands conducted by Noteboom et al. (2021), who concluded that treatment programs for childhood trauma should include interventions that address both physical and mental illness.

There are economic considerations at play too. Chronic diseases account for more than 75% of US healthcare spending (Raghupathi & Raghupathi, 2018). The prevalence of significant mental health disorders, often originating from ACEs, together with the physical and sometimes cognitive limitations of chronic diseases, poses a real challenge to effective psychotherapy. Awareness of the unique challenges of aging has increased since the development of the successful aging theory (Rowe & Kahn, 1998).This study provides a new approach to treating the complexities that result from childhood trauma. Given the interrelatedness of ACEs and chronic disease, addressing them in an integrated manner, using a conceptual psychotherapy model adapted to the complex interpersonal neurophysiology involved, could improve both quality and quantity of life for aging adults.

Limitations and Delimitations

The primary limitation of this study was that it was not a longitudinal empirical study of adults with childhood trauma and comorbid physical and mental diseases; no new empirically generated data are presented here. Theoretical studies based on review and analysis of findings of prior research studies are naturally limited by factors such as the data gathered, the target populations, the analysis of other researchers, unreported variables, methodologies, and different

data analytics techniques that were not normalized across relevant studies. Additionally, the studies may not have specifically addressed the research questions of this study, so any conclusions extrapolated may be at variance with real world findings. Research populations vary widely across the studies reviewed; results are not necessarily representative of any one segment of the population. Many of the studies reviewed were conducted in the U.S., but regional differences in availability, models, and provision of heath care are not accounted for. Another limitation is that little consideration is given to other variables involved in successful aging, such the effects of spirituality, social relationships, socioeconomic status, gender, and other possibly confounding factors; nor the variables of psychotherapy, such as strength of the therapeutic alliance. The effect of socioeconomic status is mitigated by the availability of psychotherapy in most states in the U.S. to individuals across all socioeconomic segments of the population: individual health insurance plans, private pay, and Medicare and Medicaid plans.

The percentage of the U.S. population with comorbid mental disorders arising from ACEs and chronic disease is relatively high; this study focused specifically on adults and the aging population even though ACEs and chronic disease can be found in younger stages of the lifespan. This study did not address any confounding factors of aging and psychotherapy, but rather focused specifically on psychotherapy based on the common etiology of childhood trauma and chronic disease.

Definitions and Key Terms

Adverse childhood experiences (ACEs). An ACE is a potentially traumatic experience that occurs between birth and the age of eighteen, such as chronic physical, emotional, or sexual abuse; having a parent who abused drugs or alcohol or was incarcerated; exposure to domestic violence; or divorce (Slack et al., 2017). ACES are a subset of childhood trauma.

Childhood trauma. The experience of chronic adverse events by a child that is emotionally painful or distressful, often resulting in lasting mental and physical effects.

Comorbidity. The cooccurrence of mental and physical disorders in the same person, regardless of the chronological order in which they occurred or the causal pathway linking them (Druss & Walker, 2011).

Immunosenescence. The changes of the immune system associated with age (Elwenspoek et al., 2017).

Inflammaging. The condition of chronic, low-grade sterile inflammation characterized by an age-related increase in the levels of pro-inflammatory markers that result in higher vulnerability for accelerated aging and premature death (Ferrucci & Fabbri, 2018).

Intersubjectivity. The experience of joining two subjective inner worlds (Siegel (2020).

Metaflammation. The final conversion of a chronic low-grade inflammation into risk factors for chronic disease. Metaflammation has been associated with many chronic diseases (Egger et al., 2019).

Neuroception. The neural processes, existing separately from perception, that can identify and assess environmental and other risks beneath the cognitive layer of consciousness (Porges, 2018).

Neurobiology. A branch of life sciences that deals with the anatomy, physiology, and pathology of the nervous system.

Neurophysiology. A branch of the physiology and neuroscience that studies the measurement and evaluation of nervous system function

Neuroplasticity. A general umbrella term that refers to the brain's ability to modify, change, and adapt both structure and function throughout life and in response to experience.

Trauma. An occurrence that has inflicted emotional pain, distress, or shock.

Trauma informed care. Treating those who have experienced trauma in a manner that acknowledges their experiences but does not trigger further trauma.

Unconscious. The region of the brain containing memories, emotional conflicts, wishes, and repressed impulses that are not directly accessible to conscious awareness but that have dynamic effects on thought and behavior.

Organization of the Doctoral Project

This project is be organized into five chapters: (a) an overview of the study, (b) literature review, (c) methodology, (c) results, and (e) discussion. In chapter one, the background and identification of the problem of aging adults with ACEs and chronic disease are presented. A theoretical study was used to identify how adverse experiences of childhood coupled with adult chronic disease pose a significant challenge to traditional mental health treatment interventions for the aging population. Limitations and delimitations of this study were addressed.

Chapter two provides a literature review of research studies on ACEs and chronic disease and identification of PNI effects of childhood trauma and ACEs with special attention to the aging population. The greater the number of ACES, the higher the risk for poor mental and physical health in adulthood (Felitti et al., 1998). Current psychotherapy treatment approaches for comorbidities of ACEs, chronic disease, and aging, are reviewed and assessed for efficacy. Chapter three provides a discussion of the methodology. For this theoretical study, a qualitative review was used to address the identified questions of this study. Chapter four identifies the research findings as they relate to the identified research questions. Finally, in Chapter five, an

interpretation of the research findings is proposed and an examination of how the results supports the proposed theoretical framework. A discussion of the implications for professional practice, contribution of this study to the literature, recommendations, and reflection on the findings conclude this chapter.

CHAPTER TWO

Literature Review

This section of the literature review explores current and recent research on childhood trauma, ACES, complex trauma, and the interpersonal neurobiology (IPNB) of trauma. Researchers have found that adverse, potentially traumatic, events during childhood may have lasting effects on health and well-being throughout an individual's lifetime (Berens et al., 2017; Bryan, 2019; Chang et al., 2019; Dye, 2018; Hughes et al., 2017; Merrick et al., 2017; Sonu et al., 2019). The review explores the mechanisms and long-term effects of ACEs and childhood trauma on adults through the lifespan. It establishes the PNI effects of childhood trauma and examines the mechanisms of trauma on the developing brain and immune system. Studies reviewed examine how the mechanisms of adverse experiences in childhood can lead to life-long impairments in mental and physical functioning. Current psychotherapeutic treatment modalities for adults with childhood trauma are reviewed for efficacy and opportunities. Finally, the findings are assessed against the theoretical frameworks identified earlier.

Trauma

Childhood Trauma

More than two thirds of children in the United States experience at least one traumatic event by the age of 16 (Substance Abuse and Mental Health Services Administration, 2020). More than 650,000 children were reported to child welfare or protective services across the United States in 2016 as victims of child maltreatment (Children's Bureau, 2018). The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5, American Psychiatric Association, 2013) provided a definition of trauma as experiences that have the potential for serious harm—"actual or threatened death, serious injury, or sexual violence" (p. 271). This

definition excludes psychosocial events and does not directly address developmental trauma. Van Der Kolk (2014) proposed an expanded definition to include developmental trauma, addressing the implications of traumatic experiences in the developing brain. In the American Psychiatric Association's (APA) *Handbook of Trauma*, Dalenberg et al. (2017) introduced broader criteria for the occurrence of trauma, including a "shattered assumption" or a "turning point" (p. 24): whether an event fundamentally shatters the view of self and the world, or changes the direction of a life. Across the globe, children are exposed to traumatic events that may be too overwhelming for their developing brains to process, shattering their sense of safety. These events include one time or occasional incidents such as car accidents, serious illness, loss of a loved one or a beloved pet, being a refugee, hospitalization, and other similar experiences. An event not perceived as especially traumatic by a parent or caregiver can be highly traumatizing to a child, such as moving home or changing school. When young children experience trauma, they experience both physiological and psychological reactions (Dye, 2018).

The first few years of life provide foundational experiences for the formation of a young child's psychological and physiological development, affecting physical, mental, social, and emotional development processes. Traumatic childhood experiences include physical, sexual, or emotional abuse, neglect, or witnessing relational violence. Childhood maltreatment can be unintentional or intentional, including deliberate attempts to hurt the child physically, emotionally, or sexually, or it can be through omission, with neglect. Children exposed to early life adversity may experience lasting effects on health and well-being through the lifespan (Agorastos et al., 2019; Sonu et al., 2019). Research findings have demonstrated that not only do the effects of childhood trauma last well into adult life, they also affect long-term health and

functioning and increase vulnerability to other forms of trauma experienced during the lifespan (Copeland et al., 2018; Curran et al., 2018; van Assche et al., 2020). Brain development during early childhood is especially susceptible to the adverse effects of stress that results from childhood trauma (Sciaraffa et al., 2018). Chronic childhood trauma generally results in disruption of some brain regions with long-lasting impacts to both physical and mental health, intimate and social relationships, cognitive functioning, and sense of self (Dye, 2018). A systematic review of 25 controlled neuroimaging trials of emotional, physical, or sexual childhood maltreatment found evidence of long-term effects on the brain associated with different types of childhood trauma (Cassiers et al., 2018).

Early childhood experience of emotional attunement acts as a stimulus to the development of neural pathways that promote self-regulation and emotional strength (Newman et al., 2015). Mother–child brain synchrony is essential to emotional attunement; it promotes interpersonal emotional coregulation, leading eventually to the child's capacity for emotional regulation, and adaptivity to social stressors (Azhari et al., 2019; Carozza & Leong, 2021). When parenting stressors result in maltreatment or neglect, the synchrony of signals between the maternal and child brains is inhibited, and emotional attunement between parent and child is impaired. In a study of 31 mother-and-child dyads, Azhari et al. (2019) examined the impact on the left medial cluster of the prefrontal cortex during mother–child shared activities. Earlier studies identified the importance of the medial prefrontal cortex in emotional regulation (as a critical coregulatory process in emotional development (Wang & Saudino, 2011). When a young child is subjected to chronic neglect or maltreatment, synchrony of the mother–child brain is absent or impaired, and emotional attunement is not achieved. Deficits in emotional attunement diminish the development of the child's capacity for attachment and emotional regulation

(Azhari et al., 2019). Azhari et al. (2019) noted that their experimental design required children to sit on their mothers' laps to offset the stress of strange surroundings and postulated that physical touch could affect the dyadic synchrony; they recommended that future study designs control for factors such as touch.

Adverse childhood events may be mediated by risk or protective variables and may not necessarily lead to traumatic reactions (Walsh et al., 2019). Evidence suggests that exposure to trauma in early life often fundamentally alters how a child processes and prioritizes emotional information (Marusak et al., 2015). Childhood emotional responses to trauma may include feelings of helplessness, shame, and guilt, dissociation, or extreme fear (Copeland et al., 2018). Chronic interpersonal trauma can result in constant reactivation of the young child's physiological stress response, especially during sensitive periods of development, and has been shown to affect neurobiological development (Cross et al., 2017). A child with a history of chronic interpersonal trauma is often more vulnerable to other childhood or adult traumatic or even nontraumatic events, in part due to the heightened stress response (Wilson et al., 2011). A survey of empirical evidence examined the changes in the biochemical stress response system resulting from exposure to childhood trauma affected several brain regions, including the hippocampus, the amygdala, the hypothalamic-pituitary-adrenal axis, and the prefrontal cortex, conceptualizing these changes as the traumatic stress response. Findings linked changes in these brain areas to impairment in children's subsequent ability to process emotional and neutral stimuli (Wilson et al., 2011).

Advances in neuroimaging techniques have made it possible to identify different areas in the brain that are affected by developmental trauma—chronic trauma that occurs during a child's critical early years, as the young brain strives to achieve development goals through brain

processes such as neural connectivity (Atkinson, 2013). Chronic reactivity of the hypothalamic-pituitary axis (HPA), together with interactions with genetic and epigenetic processes occurring during vulnerable times during development, can impact multiple domains by changing the structure, function, and functional connectivity of the prefrontal cortex, hippocampus, and amygdala (Cross et al., 2017). Atkinson (2013) suggested that these neural changes can result in dominance of the brain's survival mechanisms at the expense of the learning mechanisms, leading to a range of impairments in stress response and arousal and cognitive, social, and emotional functioning.

One of the most profound developmental disruptions of early childhood trauma is to the development of a sense of self. Erikson and Erikson (1998) wrote about the need for individuals to achieve a well-defined sense of self, or identity that persisted over time. Interaction between the young child and caregiver creates a framework for development of the child's internal working model of self (Bowlby, 1988). Ensink et al. (2016), hypothesized that childhood abuse negatively affects the young child's developing sense of self; Carlson et al. (2009) reached a similar conclusion, arguing that the self develops through an inner organization of feelings, meanings, and beliefs, arising from an organized caregiving matrix, which subsequently evolves into the sense of self through experience of self and others. When a child does not receive responsive care, a fragmented sense of self and others may occur. Montirosso and McGlone (2020) explored the mechanisms of attunement fluctuations that occur through early body interactions between mother and infant, concluding that the process of reparation—engagement, disengagement, reengagement between mother and child—contributes not only to attunement but also to the infant's first development of self-identity: the body-self. When this engagement is insufficient or absent, a sense of self-identity may be impaired (Montirosso & McGlone, 2020).

Adverse Childhood Experiences

ACES are a subset of childhood trauma that result from traumatic interpersonal experiences and other systemic socioeconomic variables, including poverty, racism, and school and community violence (Finkelhor et al., 2015). In a study conducted on children in the United States to examine the prevalence of ACEs, Crouch et al. (2019). found high rates in the study sample of 45,287 children across races and geographical environments. ACEs often result in childhood trauma, which in turn can lead to complex trauma, as the traumatized young adult struggles with trauma symptoms such as emotional dysregulation, somatic symptoms, hypervigilance, and relational failures and ruptures (Zyromski et al., 2018). Not all ACEs cause trauma (Beutel et al., 2017), and resilience can also mediate the traumatic response (Sciaraffa et al., 2018).

A seminal study conducted in 1995–1997 defined ACEs as psychological, physical, or sexual abuse of children; violence against mother; or living with household members who had mental health disorders, or were substance abusers, or who had ever been in prison (Felitti et al., 1998). Felitti et al. (1998) found a high prevalence of ACEs in the child and adult population studied and evidence of negative impacts on adult physiological and psychological health. Other categories of adverse events in childhood have since been added, including separation or divorce of parents, neglect, and socioeconomic and community factors such as homelessness, neighborhood violence, and discrimination (Cronholm et al., 2015). Screening questionnaires have been developed for ACEs and adopted in several countries, including the United States (Hays-Grudo & Morris, 2020). Many states now include ACEs screening questions in their health risk factor review, the annual Behavioral Risk Factor Surveillance System. The survey is

coordinated by the CDC and administered by state health departments (Hays-Grudo & Morris, 2020).

Bryan (2019) found that where ACEs result in trauma the hormone and immune systems can also be affected. The impact of chronic stress extends beyond neural functioning; prolonged stress exposure is associated with changes in immune system functioning, which may be causative factors in increased susceptibility to physiological and psychological disorders (Agorastos et al., 2018). Schalinski et al. (2016) studied the differential effects of type of ACEs on the severity of childhood trauma symptoms and found that preschool and preadolescent time frames are especially vulnerable for ACEs to lead to childhood trauma. They also noted that PTSD varies depending on the number or types of ACEs across all childhood age groups. In a systematic review and meta-analysis of 37 studies with a total of over 250,000 participants worldwide related to health outcomes of multiple ACEs, Hughes et al. (2017) concluded that the effects of multiple ACEs were pervasive and harmful, impacting health through the lifespan and contributing significantly to the increasing burden of chronic disease. Nurius et al. (2016) examined ACEs- and health-affecting characteristics and found that early-onset chronic illness was evident based on ACE levels. In addition to the long-term mental health impacts, ACEs are a predictor of poor physical health in adulthood, although there are mediating factors on the extent of the effects (Bellis et al., 2019; Karatekin, 2019). ACEs have been shown to increase risk behaviors, further compounding poor health problems (Garrido et al., 2018). A systematic review and meta-analysis by Li et al. (2019) determined that maltreatment in childhood significantly increases the risk of depression and anxiety disorders in adult life.

Complex Trauma

For decades the effects of traumatic experiences were generally classified in both the DSM-5 and International Classification of Diseases (ICD-11; WHO, 2018b) as PTSD, although until DSM-5, PTSD was classified as an anxiety disorder. The DSM-5 reclassified PTSD as a traumatic stress disorder but not recognize complex trauma. Despite a decade or more of empirical evidence of the complexity of severe trauma symptoms, PTSD criteria remained relatively narrow, missing the broader symptomology found in so many patients (Ford, 2017a). In the United States, the DSM is regarded as the "bible" of psychiatry to identify and diagnose mental health disorders. The American Psychiatric Association's failure to add complex PTSD (C-PTSD) as a separate diagnostic category has often resulted in ineffective or incomplete treatment attributable to incorrect diagnoses (Cosci & Fava, 2016).

As trauma research progressed, it became apparent that many chronic trauma patients' symptomologies extended beyond PTSD diagnostic criteria (Ford, 2017a). Herman (1992) introduced the term *complex trauma* after conducting a review of the evidence for a more complex form of PTSD experienced by victims of prolonged, chronic trauma. C-PTSD results from exposure to the very diverse and long-lasting impacts of multiple, chronic, invasive, and generally interpersonal events (National Child Traumatic Stress Network, 2017), and is strongly associated with childhood trauma although adults with prolonged exposure to traumatic events, such as in countries at war, can meet the criteria. The diagnosis is used primarily to describe the experience of repeated, and often chronic, traumatic events such as sexual, physical, or emotional abuse, neglect, violence, war, refugee experiences, and persecution, that produce traumatic experiences beyond the definitions of PTSD (National Child Traumatic Stress

Network, 2017). C-PTSD shares symptoms of traumatic stimuli with PTSD and has an additional symptom cluster related to disturbances in self-organization (DSO) (Karatzias & Cloitre, 2019).

Complex trauma often has an early childhood onset when a child's caregiving system fails to provide appropriate care and emotional attunement needed for the healthy development of neural processes in the brain (Spinazzola et al., 2007); the caregiving environment that should provide a source of safety and stability is instead toxic to the child. A task force of the National Child Traumatic Stress Network (2017) was formed in 2002 to identify a more adaptive classification for symptoms of relational, self-regulatory, and attributional impairments demonstrated by children exposed to chronic childhood trauma.

Complex trauma was included as a diagnostic category in the new version of the ICD-11 (WHO, 2018b) as C-PTSD, effective in the United States in January 2022. ICD-11 introduced C-PTSD as a clinical syndrome resulting from traumatic experiences usually associated with early life chronic traumatic events of an interpersonal nature, such as child abuse or neglect (Giourou et al., 2018). These experiences are often followed by severe and persistent difficulties in affect regulation, negative self-cognition, and difficulties in sustaining relationships (WHO, 2019. C-PTSD is a more severe disorder than PTSD (Cloitre et al., 2019). Six symptom clusters characterize C-PTSD: the three symptom clusters of PTSD: reexperiencing (flashbacks and nightmares), avoidance, and hypervigilance; and three additional symptom clusters addressing new theoretical: emotional dysregulation, interpersonal difficulties, and negative self-concept (Cloitre et al., 2019). DSO symptoms can arise after experiencing traumatic events that are typically interpersonal, occurring during early childhood years, and from which the child has no means to escape the situation (Hyland et al., 2018). The additional DSO symptoms can present as trauma memories that have been dysfunctionally stored, psychological defenses employed by the

undeveloped child but maladaptive in adulthood, dissociative traits, and frequent emotional dysregulation (Knipe, 2018). The symptomology of C-PTSD differs from that produced by isolated traumatic incidents, which tend to produce quite distinct, discrete, conditioned biological and behavioral responses, as seen in the criteria for PTSD (van der Kolk, 2014). According to Knipe (2018), the main characteristics of C-PSTD include dysfunctionally stored memories of trauma, psychological defenses that may have served an undeveloped young child but which are maladaptive in adulthood, dissociative traits, and frequent emotional dysregulation.

Complex trauma has a pervasive effect on the development of the young mind and brain, resulting in disruption of healthy developmental processes, and it can have a profound impact on a child's predictable sense of self, low self-esteem, and feelings of shame and guilt (Spinazzola et al., 2007). Complications commonly associated with childhood complex trauma include attachment difficulties and a lack of boundaries, alterations in states of consciousness, impulsive and self-destructive behaviors, somatization, emotional dysregulation, and negative self-image (Ducharme, 2017; Gold & Ellis, 2017). Children and youth exposed to complex trauma are vulnerable to lifelong problems that put them at risk for subsequent traumatic exposure, resulting in cumulative psychiatric, medical, family, social, legal, and substance abuse-related problems (Spinazzola et al., 2007). Spinazzola et al. (2007) created a classification framework to examine impairments and outcomes of childhood complex trauma with domains of attachment, biology, affect regulation, dissociation, behavioral control, cognition, and self-concept.

Over the past 3 decades, advances in brain imaging such as positron emission tomography scans and functional magnetic resonance imaging have enabled a more rigorous study of functional brain development during childhood, with emphasis on the first 3 years of life, including the time in utero (Petchkovsky, 2017). Modern neuroimaging technology has

enabled the identification of different brain areas affected by developmental trauma—chronic trauma that occurs during a child's critical early years, as the young brain strives to achieve development goals through brain processes such as neural connectivity (van der Kolk et al., 2019). The chronic nature of the trauma or the existence of multiple types of trauma creates complex trauma during the developmental stages of childhood (Briere & Scott, 2015). van der Kolk et al. (2014, 2019) proposed the addition of developmental trauma disorder as a developmentally sensitive approach to classification and treatment of children with chronic or multiple traumas in the DSM's PTSD category (van der Kolk et al., 2014, 2019). They suggested that this distinction enables more specificity when addressing developmentally significant symptomology and proposed that the introduction of developmental trauma disorder into the DSM could enhance outcomes for children exposed to complex trauma at an early age (van der Kolk et al., 2019).

Interpersonal Neurobiology of Trauma

IPNB is a relatively new multidisciplinary field founded by Dr. Daniel Siegel (2020), who described it as a consilient field that draws from all branches of science to integrate common, universal findings across independent ways of knowing to expand the understanding of mind and well-being. IPNB explores how brain development is shaped by early relationships, how relationships and the brain interact to shape our mental lives, and the opportunities of neuroplasticity over time. IPNB has broad applications of value, including understanding how childhood trauma affects the developing brain (Siegel, 2020). The fields of neurobiology and attachment have revealed a set of deeply convergent findings that have shed new light on how the developing mind is influenced by the interaction of interpersonal experience and neurobiological processes (Siegel, 2020). IPNB includes several core concepts

that contribute to an understanding of the diagnosis and treatment of trauma: mind, embodied brain, relationships, mindsight, neural integration, attunement, attachment, neuroplasticity, intersubjectivity, and integrative communications. At the heart of IPNB is the concept of integration, which requires the linkage of differentiated aspects of a system, whether in a single individual or a collection of individuals. In this model, integration provides the essential mechanism of health because it promotes a flexible and adaptive way of being that brings harmony; differentiated aspects of a system are linked by integration. When integration does not occur, chaos and rigidity are present (Siegel, 2020).

Integration in the brain creates a balance and coordinated nervous system, which in turn enables empathic relationships. Trauma inhibits neural integration (Feldman, 2017). Lack of resolution of childhood trauma can be viewed as the impairment in this innate capacity of the mind to balance the differentiation and integration of energy and information flow; it impairs the brain's representational processes (Siegel, 2020). This impairment leads to a range of dysfunction in PTSDs. An example is the blockage of the consolidation of memory and resolution of the trauma, which occurs in normal development by a bilaterally activating process in which the right hemisphere becomes activated, and information can be transferred from the right to the left hemisphere. The ability to create a narrative autobiography is disabled in trauma patients.

The brain region responsible for the integrative work is housed in the prefrontal cortex. The brain has an outer neocortex, enabling perceptions of the outside world and thought; below it is the limbic area, which processes emotions, motivation, some memory, meaning, and attachment relationships; below the limbic area is the brainstem, which drives arousal of body and brain. These areas receive inputs from the spinal cord, but the prefrontal cortex is capable of

descending inhibition. Subcortical activations can be overridden as the prefrontal cortex coordinates and balances input from cortex, limbic, brainstem, and other bodily regions, which are connected to input from other people's brains through verbal and non-verbal communication. When the regulating prefrontal cortex functions cannot regulate or balance the subcortical processes, impairments in interpersonal integration occur (Siegel, 2020). An example occurs in early childhood trauma created by a caregiving environment of abuse and/or neglect. During the early years of childhood, the developing brain has many neurons but relatively few synapses, and it is largely undifferentiated. It contains the basic circuits required for processes for emotional and behavioral regulation, interpersonal relationship, language, and memory, but it relies on genetic information, and equally importantly, appropriate experiential stimulation. Maturation of the right hemisphere's prefrontal area, the development of cortical and subcortical structures in the regulation of emotions and behavior, is highly dependent on early experiences (Hodel, 2018). The early neural circuitry of the stress system resides in the early developing right hemisphere (Herzberg & Gunnar, 2020). The right brain dominates control of vital survival functions and the human stress response, and it is most active during the first 2 years of life. Infants under 2 years have greater volume in the right hemisphere than the left. Attachment experiences are believed to directly influence the experience-dependent maturation of the right hemisphere (Schore, 2017).

Attachment experiences are typically provided by the primary caregiver; these early interactions play a major role in determining how the synapses develop. Attunement describes how responsive a person is to another's emotional needs and moods (Siegel, 2020). Attunement is critical during infancy for healthy attachment and healthy development of the brain. If a caregiver is attuned to the infant's emotions and moods, it provides a critical regulatory function, supporting the structural development of self in the infant. Gradually a child develops the ability

to attune to themself—to pay attention to their own emotions and moods and to come to understand those emotions and moods. The experience of attunement enables a child to develop secure attachment, and this ability to attach persists in relationship with others throughout life. A person who is well attuned to others will respond with appropriate language and behaviors based on another person's emotional state, which leads to intersubjectivity—the experience of joining two subjective inner worlds. Siegel (2020) discussed this phenomenon and proposed that interpersonal attunement enables a conscious awareness that leads to intrapersonal attunement in the patient, resulting in new self-regulatory capacities. Attunement is a critical process in developing integration. It activates several regions in the brain, including mirror neurons, enabling a person to empathize, or resonate in themself, with what they sense in others.

During a child's development, if the caregiver is attuned to the child, and the environment is generally positive and safe, the child's brain develops the structures critical to integration, and critical linkages are formed between structures and hemispheres (Siegel, 2020). Integration of the brain enables coordination and balance of the brain system to develop in harmony over time. The brains of children who have suffered the trauma of persistent abuse or neglect have damage to their integrative fibers; their brains have not been able to maximize each brain system through integration of its various parts (Siegel, 2020). This limited integration contrasts sharply with the developmental experiences offered by an attuned caregiving environment. In the brain, integration of brain structures improves well-being; in relationships, integration can come through the linkage or sharing of family experiences and emotions (Feldman, 2017). Human beings comprise complex systems, such as the mind, the brain, and the immune system, which are capable of self-organization. Self-organization enables a system to move forward freely towards maximizing complexity and achieving integration through linkage

of the differentiated elements. Integration enables flexibility, adaptability, cohesion, energy, and stability (Siegel, 2020). Siegel (2020) described this flow as bounded on one side by chaos and on the other by rigidity. When the brain is not integrated due to unlinked differentiated parts, it will tend toward rigidity and chaos. Mental disorders that result from early childhood trauma are characterized by symptoms of rigidity or chaos, which can be viewed as failed or impaired integration (Siegel, 2020). Ultimately, in the IPNB view, trauma resolution involves enabling the mind to regain its natural process of integration across states of mind and time, which brings a deep sense of coherence.

Discussion

It has been widely accepted for several years that childhood trauma can result in adult mental health disorders. The link to chronic disease, immune system disorders, and other adult health problems has been less prominent and is not widely incorporated into mainstream psychotherapeutic models of treatment for adults with childhood trauma. A growing body of evidence indicates the association between childhood trauma and poor adult physiological and psychological health outcomes. Goodwin and Stein (2004) examined the relationship between types of childhood trauma and specific physical disorders, investigated how comorbidities of anxiety, depression, and substance use disorders contribute to treatment outcomes, and explored how different types of childhood trauma might predict physical disorders. Their findings confirmed that certain types of childhood disorders did appear to be associated with physical disorders in adults, that the relationship between childhood trauma and physical illnesses in adults exists independent of the existence of comorbid mental health or substance-use disorders, and that the relationships identified in the study were generalizable to the United States population.

Evidence supports a dose-response relationship between childhood trauma and adult impairments in mental and physical functioning (Kalmakis & Chandler, 2015). This topic is explored further in the section on PNI, a field that is critical to the successful treatment of adult victims of childhood trauma who have comorbid physical and mental illnesses. Malarbi et al. (2016) identified evidence for cognitive impairments in trauma-exposed children with or without a formal diagnosis of PTSD; these deficits included language/verbal skills, visual-spatial, information processing, learning and memory, and executive skills. ACEs have been shown to increase risk behaviors, further compounding poor health problems. When repeated or chronic, childhood trauma is associated with changes in neurobiology that can have adverse effects on critical neural processes. This process is facilitated by chronic HPA axis reactivity and disturbances of genetic and epigenetic processes during critical periods of development. The development of the brain, body, and immune system is highly complex and influenced by many variables; notwithstanding, childhood trauma appears to make a significant contribution to impaired functioning of mind and body in adults.

A chronic condition is a physical or mental illness that persists for more than a year, requires ongoing monitoring and treatment, and results in functional impairments (Basu et al., 2016; Buttorff et al., 2017). By the middle of the 20th century, chronic diseases were the leading cause of illness and death in the United States (National Center for Chronic Disease Prevention and Health Promotion, 2022). Seven decades later, this relationship has not changed. In high-income countries such as the United States, chronic diseases are responsible for approximately 75% of deaths (Harris, 2019), and nearly 60% of adults in the United States meet criteria for multimorbidity, with a significant increase over the last 3 decades (Kingston et al., 2018). Treatment of chronic diseases is estimated to consume close to 75% of healthcare spending in

the United States (Raghupathi & Raghupathi, 2018). Living with chronic disease can have severe impacts on an individual's quality of life (Mohammed & Hasan, 2020), family (Golics et al., 2013), healthcare costs (Raghupathi & Raghupathi, 2018), employment (Jinnett et al., 2017), and the U.S. economy (Waters & Graf, 2018).

Unlike communicable or infectious diseases such as influenza, tuberculosis, and Covid-19, which are caused by a virus, bacteria, fungus, or protozoan (Cole & Kramer, 2016), chronic diseases are typically noncommunicable and last many years. They are generally considered to be attributable to genetics, lifestyle, and environmental factors (Lin et al., 2017). Rappaport (2016) examined the effect of genetics in acquiring chronic disease and concluded that the main mechanism of genetics through the lifespan is via the interactions between genome and exposure. Risk factors for chronic diseases are complex, often interdependent, and exacerbated by low socioeconomic status (Dugravot et al., 2019), culture (Shaw et al., 2000), and health behaviors (Lee et al., 2020). Bauer et al. (2014) identified low physical activity, poor nutrition, alcohol and nicotine use, and high blood pressure as risk factors for chronic disease.. In a multicohort study of more than 116,000 participants, Nyberg et al. (2020) identified a consistent dose-response association between more healthy lifestyle behaviors and the number of disease-free years in people of both sexes and across the socioeconomic spectrum. Other research has identified variations in standards of care (Wennberg, 2002), the continued dominance of the biomedical model of healthcare over a mind–body approach (Astin et al., 2003), the state of healthcare in the U.S. (availability, accessibility, and acceptability of care) (Goudge et al., 2009), social determinants (Cockerham et al., 2017), the prevalence of mental health comorbidities in people suffering from chronic physiological disease van de Pavert et al., 2017), and increases in environmental toxins (Zhuang et al., 2018).

Traumatic experiences in childhood are the cause of many of the risk factors for chronic physiological and psychological diseases in adult life by providing additional pathways for onset and exacerbation of disease (Sonu et al., 2019). Changes in the molecular and genetic makeup of a child alter the development and function of neurological, endocrine, and immune systems (Boullier & Blair, 2018). The mechanisms by which molecular and genetic alteration occurs are biological and behavioral (Holter et al., 2021). Research on the biological implications of exposure to ACEs and adult chronic physiological and psychological diseases has led to the development of the biological embedding of childhood adversity model (Miller et al., 2011), and the concept of allostatic load, which is used for objective assessment of the consequences of chronic stressors on neural, endocrine, metabolic, immune, and gut microbial systems (D'Alessio et al., 2020). Inappropriate activation of biological mechanisms that occurs as a result of chronic stress, high cortisol levels, and oxidative stress are linked to high-risk health-related behaviors that serve as risk factors for chronic disease; these behaviors include substance abuse, lack of exercise, poor nutrition choices often leading to obesity, emotional dysregulation, reckless sexual activities and sexually transmitted diseases, and very poor overall self-care (Holter et al., 2021). Early experiences of traumatic events can also lead to distorted cognitions about self and others that contribute to the development of psychological disorders that persist into adulthood (Danese & Widom, 2020).

Chronic diseases are often diagnosed as people reach middle age after many years of poor health behaviors. The prevalence of chronic disease increases with age; it is estimated that over 80% of patients over 65 years have at least one chronic illness, and at least half have two or more (Prasad et al., 2012). Similarly, the severity of chronic diseases increases with age, as the aging process exacerbates the cellular and molecular malfunctions (Prasad et al.). Aging is a complex

process involving genetic, molecular, cellular, organ, and system-level changes. One of the mechanisms associated with chronic disease and aging is oxidative stress, which negatively affects the normal functioning of several tissues (Cabello-Verrugio et al., 2017). The mechanisms of aging have also been associated with chronic inflammation, which can activate cell damage and cell malfunction; these can cause, or worsen, chronic disease (Prasad et al., 2012).

Chronic Psychological Disorders

Despite the increase in utilization of mental health treatment in the United States, the prevalence of mental health disorders continues to rise (Mojtabai & Jorm, 2015). Data gathered from the 2019 National Health Interview Survey identified that nearly 20% of adults in the United States had received mental health treatment during the prior year, approximately 16% reported taking prescription medication, and nearly 10% had participated in treatment with a mental health professional (CDC, 2019c). Survey findings also indicated that approximately 11% of adults aged 18 and over reported regular feelings of anxiety, nervousness, or worry; nearly 5% reported frequent feelings of depression (CDC, 2019c). Chronic mental health disorders place a significant and growing burden on health, economies, and society globally (WHO, 2022). A systematic review and meta-analysis of mortality rates for people with psychological disorders found higher mortality rates than in the comparison population (Walker et al., 2015).

Two groups of mental health disorders are diagnosed most frequently in the United States: mood disorders, and anxiety disorders (Twenge & Joiner, 2020). According to the National Alliance on Mental Illness (2021), anxiety disorders are the most common mental health illnesses followed by mood disorders—primarily depression and bipolar disorders; less than 5% of the population suffer from all other disorders, which include schizophrenia,

obsessive-compulsive disorder, and borderline personality disorder. The interrelatedness of mental health disorders and the attribution of symptomology to etiology often confuses diagnosis. Chronic childhood trauma is associated with adverse mental health outcomes in later life (Copeland et al., 2018; Rybakowski, 2020). Many trauma patients in primary care are diagnosed with depression or anxiety rather than trauma, in part because these symptoms occur frequently in trauma (Meltzer et al., 2012). Meltzer et al. noted that very few urban primary care patients who met criteria for PTSD were officially diagnosed with trauma according to their medical records. As more research is undertaken in the field of trauma, awareness of the complexity of the PTSD symptom clusters is increasing. Nöthling et al. (2020) explored and synthesized the literature on several epigenetic modifications and mediators in childhood trauma and their effects on the subsequent onset of psychiatric disorders. They noted that longitudinal studies and a more consistent methodological approach in studies of this area were needed to understand cause and effect.

Mood Disorders

Approximately 11% of adults in the United States are diagnosed with mood, also known as affective, disorders (National Alliance on Mental Illness, 2021). Of these, major depressive and bipolar disorders are the most common (Jaworska-Andryszewska & Rybakowski, 2019). Mood disorders are characterized by a disturbance in mood as the predominant feature. Mood disturbances are also prevalent in several psychiatric disorders, including PTSD, as a secondary characteristic (Jaworska-Andryszewska & Rybakowski, 2019). Mood disturbances generally fall into two main categories: major depressive disorders, and bipolar disorders. Depression is one of the leading causes of disability globally, with an estimated 322 million people suffering from depressive diseases worldwide and a higher incidence of depression among women than men

(WHO 2017). According to the WHO (2017), countries with the highest rates of depression span both developed and developing countries, including China, India, the United States, Russia, Brazil, and Nigeria. Countries with the lowest reported rates of depression include the Solomon Islands, Papua New Guinea, and Nepal. Culture and societal values play a significant role in a country's rate of depression. Thornicroft et al. (2017) noted that depression is undertreated for many reasons, including cultural or religious bias, shame or other social stigma, or unavailability of screening and treatment. Depression has been shown to increase the risk of chronic disease (Scott et al., 2016). Conversely, the onset of chronic disease can increase the risk of depression and other mental health disorders (Sporinova et al., 2019). Individuals with multiple chronic diseases are twice as likely to be diagnosed with depression as the general population (Birk et al., 2019). Li et al. (2019) found evidence suggesting a common biological mechanism is shared between chronic disease and depression. Comorbidity complicates diagnosis and treatment of both the physical and psychological conditions (Sporinova et al., 2019).

Depression. Depression is characterized by feelings of low mood, hopelessness, futility, sadness, anhedonia, low self-worth, sleep and appetite disturbances, poor concentration, and lack of motivation. It can be pervasive across the lifecycle, or episodic. Presentation of depression varies over the lifespan (Thaipisuttikul, 2011). Factors of risk and protections can change over time; for example, both biological risk and psychological resilience tend to increase with age (Fiske et al., 2009). Depression is one of the most common chronic diseases in older adults; adults who are aging report similar symptoms to younger populations as well as somatic complaints, comorbid chronic diseases, and sometimes memory and cognitive impairments. (Kok & Reynolds, 2017).

Depression often impairs an individual's ability to complete activities of daily living; when very severe, it has a high suicide risk at approximately 15% (Orsolini et al., 2020). The suicide rate in the United States increased 33% in the first 17 years of the 21st century, and it is the 10th leading cause of death (Weir, 2018). Major depressive disorder and persistent depressive disorder, also called dysthymia, share most symptoms, with the main difference being that with persistent depressive disorder the symptoms are prolonged, lasting for at least 2 years in adults, whereas in major depressive disorder symptoms tend to be episodic. Other less frequently diagnosed depressive disorders included in the DSM-5 (American Psychiatric Association, 2013) include disruptive mood regulation disorder, premenstrual dysphoric disorder, substance/mediation-induced disorder, depressive disorder due to another medical condition; and other specified depressive disorder, and unspecified depressive disorder.

The causes of depression are multifactorial (Otte et al., 2016). Depression may be the result of a complex interplay of genetic, biopsychosocial, and environmental factors that disrupt an individual's neurobiology (Maletic et al., 2007). A different, but related, etiology proposes a diathesis-stress model, which attributes depression to vulnerability, which can be genetic or schematic, activated by life stressors (Colodro-Conde et al., 2018). Although this model has not met with much support, it has close links to the concepts behind childhood trauma's strong correlation with depressive disorders (Lee et al., 2018). Alterations in a neurocircuitry network of several brain areas, including the brainstem, amygdala, hypothalamus, and prefrontal cortex, are believed to have a causal relationship with mood disorders (Bao & Swaab, 2019). This network includes the HP axis, which integrates the response to stress in the neural, adrenal, and immune systems; other neurocircuitry in this network plays a critical role in symptoms of

depression such as disturbed sleep patterns, anhedonia, eating disturbances, and cognitive problems (Bao & Swaab, 2019).

Bipolar Disorders. Bipolar disorders affect approximately 46 million people worldwide; in most countries, they affect slightly women more than men (Ritchie & Roser, 2018). Numbers vary across countries; the United States has one of the highest rates at 2.8% (National Institute of Mental Health, 2017). According to data collected by the National Institute of Mental Health (2017), individuals suffering from bipolar disorders have the highest rate of serious impairments at 83%. Between 4% and 19% of subjects with bipolar disorder exhibit suicidal behavior; between 20–60% have at least one suicide attempt (Dome et al., 2019). It is estimated that the suicide rate of individuals diagnosed with a bipolar disorder is approximately 6–7% (Plans et al., 2019); 20–60% of subjects with a bipolar disorder have at least one suicide attempt (Rihmer et al., 2017). Bipolar disorders occur with similar prevalence across different cultures and ethnicities globally (Ferrarri et al., 2016); severity appears to differ, increasing in developing countries, possibly from less availability of medical assistance, methodological differences, and lower quality of healthcare (Ayuso-Mateos, 2013; Zhang et al., 2017). In the United States, European and African Americans have a higher rate of bipolar disorders than Asian Americans (Kurasaki, 2002). Zhang et al. (2017) found a low prevalence of bipolar disorders in China, at .11%.. Forty et al. (2014) examined the rates of medical comorbidities in individuals with bipolar disorder and found a significantly higher prevalence of medical diseases than those without a bipolar disorder. Individuals diagnosed as bipolar had a high rate of medical and psychological comorbidities, specifically hypertension, asthma, diabetes, obesity and hypothyroidism, substance use, and anxiety disorders (Carvalho et al., 2020; Hossain et al., 2019).

Bipolar disorders are characterized by alternating episodes of depressive mood and mania or hypomania (Lutz, 2020). There are three major types of bipolar disorder: bipolar I disorder, bipolar II disorder, and cyclothymic disorder (APA, 2013). The most common age of onset is late adolescence through young adulthood (Ferrari et al., 2016). The exact causes of bipolar disorders are not yet fully understood, but genetic and biological factors play a significant role (Kerner, 2014). Risk factors include genetic and neurobiological variables (Carvalho et al., 2020); environmental factors, including childhood trauma (Brietzke et al., 2012); and psychosocial variables which may interact with genetic and biologic dispositions (Serretti & Mandelli, 2008). In surveys, 30–50% adults diagnosed with a bipolar disorder reported various forms of childhood trauma; cases of bipolar disorder with childhood trauma have a higher rate of suicide, more mental health comorbidities, especially PTSD, and earlier onset of a bipolar disorder (Brietzke et al., 2012). Protective factors for more serious presentations of bipolar disorder include compliance with a medication regimen, good nutrition and daily exercise, a strong social support structure, and mindfulness meditation practice.

Anxiety Disorders

Anxiety disorders affect more than 19% of the U.S. population (40 million adults) and are the most prevalent mental illness in the United States (Anxiety and Depression Association of America, 2021). In 2015 it was estimated that 264 million adults worldwide suffer from anxiety (WHO, 2017). Statistics vary globally: in European/British cultures, the numbers range from nearly 4% to over 10%; in Indonesia/Asia, 2.8%; in Africa 4.4%; Central and Eastern Europe 3.2%; North Africa/Middle East nearly 5%; and over 6% in Latin cultures (Remes et al., 2016). Anxiety disorders are characterized by excessive anxiety and worry (APA, 2013). Several national suicide prevention organizations, including the American Association for Suicidology

and the American Foundation for Suicide Prevention, consider anxiety as a top risk factor for suicide. Bolton et al. (2010) concluded that suicide risk is increased for individuals who have been diagnosed with an anxiety disorder, and comorbid anxiety and depression are linked to a higher suicide rate than for either single disorder. A 2-year prospective study first published in 2017 found no significant variance in survival rates for individuals with and without comorbid anxiety disorders (Abreu et al., 2018). These different findings may result from the fact that direct attribution of anxiety to suicide rates is confounded by the fact that anxiety has high rates of comorbidity with other mental health disorders, making it difficult to ascertain the exact cause of suicide (Nock et al., 2010).

The major anxiety disorders in the DSM-5 are generalized anxiety disorder, panic disorder, specific phobias, and social anxiety disorder (APA, 2013). The most common anxiety disorders in the United States are specific phobias, which affects 19 million adults, or nearly 8% of the population; social anxiety disorder, which affects 15 million adults, or nearly 3% of the population; generalized anxiety disorder, affecting nearly 7 million adults, or just over 3%; and panic disorder, which affects 6 million adults, or nearly 3% of Americans (Anxiety and Depression Association of America, 2021). Anxiety disorders are characterized by excessive feelings of worry and anxiety, which often cause physiological symptoms. Symptoms of anxiety include fear, worry about the future, feeling restless or on edge, difficulty breathing irritability, difficulty concentrating, muscle tension, sleep disturbance, and increased heart rate (APA, 2013). Individuals who are diagnosed with anxiety disorders are at high risk for other medical and psychological disorders (Anxiety and Depression Association of America, 2021). Multiple studies have identified significant associations between anxiety disorders and medical illness,

including cardiac disease, gastrointestinal illnesses, hypertension, and migraine (Härter et al., 2003; Sartorius, 2018; Niles et al., 2015).

The etiology and pathogenesis of anxiety disorders are multifactorial. Anxiety is an emotion that can result from stressors experienced in childhood, in relationships, at work, from health issues, or from the environment. Clinical anxiety can develop and may be sustained by a complex set of interacting risk factors that include genetics, neurobiology, psychology, and environmental variables including parenting style, attachment ruptures, and other forms of childhood trauma (Fonzo et al., 2016). Stressors experienced during prenatal and neonatal periods have been identified as particularly damaging to the functioning of the HPA axis, leading to dysregulation linked to impairments in brain function and development, and anxious or depressive behaviors (Schiele & Domschke, 2018). Stressors experienced during pregnancy that result in high levels of anxiety have been found to result in long-term impairments in cognition, physical health, and development of anxiety and depressive disorders (Schiele & Domschke, 2018). Fullana et al. (2020) examined the relationship between anxiety disorders and potential risk and protective factors and concluded that most of the protective factors for anxiety were reciprocal to risk factors.

Chronic Trauma and Stressor-Related Disorders

A review of trauma literature is provided in a previous section of the literature review; some additional information is included here for completeness of the section on chronic disease.

The human response to psychological trauma is one of the most important public health problems in the world (van der Kolk, 2014). Regardless of whether the trauma experience was a one-time occurrence, such as a car crash or sexual assault, a repeated set of events, or the developmental disruption of attachment trauma, if the trauma remains unresolved, the mind will

have acquired long-lasting negative impacts on its functioning (Center for Substance Abuse Treatment, 2014; Siegel, 2020). A study reviewing research on trauma in the WHO World Mental Health epidemiological surveys on trauma found that over 70% of participants experienced traumas worldwide (Kessler et al., 2017). Bauer et al. (2014) approximately 7–8% of people in the United States experience PTSD during their lifetimes, and about 8 million adults are diagnosed with PTSD annually. These numbers do not accurately reflect the reality of trauma sufferers for two primary reasons: many people with trauma symptoms do not seek or are ineligible for mental health care and others are misdiagnosed in primary care due to the complexity of the PTSD symptom clusters (Meltzer et al., 2012).

The major trauma disorder is PTSD., which was originally classified as an anxiety disorder in earlier versions of the DSM, the current version listed it in a new diagnostic category, trauma and stressor-related disorders (APA, 2013). Changes to diagnostic criteria for PTSD include a more explicit definition of trauma and exposure, additional symptoms and other criteria and specifiers, as well as the removal of a subjective perspective to the definition of trauma (Pai et al., 2017). The DSM-5 updated treatment of trauma, however, does not fully encompass the etiology and symptom clusters of the growing epidemic of childhood trauma (McKinnon et al., 2019). The characteristics of PTSD include reliving the trauma through nightmares, flashbacks, sleep disturbances, and frightening memories; emotional numbness, avoidance, hypervigilance, and impairments in memory, focus and cognition. These symptoms can be traced to changes in brain structure and function that result from stress and traumatic experiences (De Bellis & Zisk, 2014).

The DSM-5 definition of trauma emphasizes an experience of an immediate threat to life or serious injury (APA, 2013). This definition excludes stressors such as loss of a job, or a

divorce. In addition to a traumatic event, there must be a qualifying exposure (North et al., 2016). In the DSM-5, qualifying exposures are direct experience of trauma, witnessing others' trauma, and indirect experience of trauma through observation of a family member or other close associate (APA, 2013). A fourth qualifying exposure was added in the DSM-5: repeated or extreme exposure to a traumatic event, such as that experienced by the military, law enforcement, and child protective workers. (APA, 2013). The DSM-5 included a separate diagnostic cluster for children 6 years or younger, stating that PTSD can occur at any age after 1 (APA, 2013). The clinical presentation of PTSD can differ depending on developmental age, and children under six years of age are likely to express symptoms in play activities while apparently sometimes lacking obvious fearful reactions when exposed to the trauma. This subtype of PTSD specifically excludes symptoms such as blame, and negative self-beliefs, due to the immaturity of the young child's cognitive constructs and emotional states (Substance Abuse and Mental Health Services Administration, 2016).

Chronic Physiological Diseases

According to the WHO (n.d.), noncommunicable medical diseases, known also as chronic diseases, are the major cause of death globally. Approximately one in three adults worldwide suffer from multiple chronic medical conditions (Hajat & Stein, 2018). In developed countries three out of four aging adults are diagnosed with multiple chronic conditions (Hajat & Stein, 2018); this number is expected to increase significantly between 2015 and 2035 (Buttorff et al., 2017; Kingston et al., 2018). Chronic physiological diseases are responsible for more than two thirds of all deaths in the United States; heart disease, diabetes, cancer, chronic obstructive pulmonary disease, and stroke are the most common disorders (Raghupathi & Raghupathi, 2018). Other chronic medical diseases include respiratory disease, Alzheimer's disease, and

kidney disease (Raghupathi & Raghupathi, 2018). Chronic physiological diseases are often comorbid, furthering complicating treatment options. The spread of chronic diseases has a far-reaching impact on the world affecting economies, quality of life, and families sometimes with devastating results (Maresova et al., 2019; Raghupathi & Raghupathi, 2018).

Chronic diseases are generally the result of a combination of social and environmental determinants, genetics, physiology, and behavioral factors (WHO, 2012, 2018a). Research on genome sequencing has generally supported the hypothesis that the risk of getting a chronic disease is the result of genetics, exposures during a lifetime, and their interactions (Rappaport, 2016). Rappaport (2016) examined genome research on chronic disease risk and concluded that although genetics can influence the outcome of an illness, it is not a major risk factor. According to the WHO (2012), risk factors are socioeconomic determinants such as income and employment; environmental factors, including air quality, water supply, sanitation practices, housing conditions, and climate; and other variables, including the availability and quality of health care services, global ecology, and cultural factors. Other social determinants of health include immigration status, race/ethnicity, type of occupation, housing, immigrant status, access to healthy nutrition, and public spending on healthcare and prevention (Cockerham et al., 2017).

Many epidemiological studies have found an association between unhealthy lifestyle behaviors such as poor diet, lack of physical activity, alcohol, and cigarette use, sleeping a minimum of 7 hours daily, and chronic diseases (Patel et al., 2019; Patra, 2018; Petrovic et al., 2018). Stein et al. (2017) determined that recent increases in the death rate of non-Hispanic White people living outside large urban areas resulted mainly from self-destructive health behaviors. The concept that patient behavioral self-management interventions can improve

chronic disease outcomes is now widely incorporated by many U.S. healthcare providers (Dineen-Griffin et al., 2019). Although patient self-management of health behaviors can change the trajectory and in some cases even reverse chronic diseases, mental health comorbidities, particularly depression, often impair an individual's ability to make necessary behavioral changes (Druss et al., 2018). A systematic review of evidence of the effect of self-management interventions targeting both medical and psychological chronic diseases determined that an integrated intervention had a high potential for clinical efficacy (Whiteman et al., 2016).

Inflammatory dysregulation has been shown to be associated with several chronic diseases (Tsoupras et al., 2018; Zhong & Shi, 2019). Pawelec et al. (2014) identified higher inflammatory biomarkers as common in aging adults. Inflammageing is a condition that places an additional burden on aging individuals with chronic disease; it is characterized by chronic, low-grade sterile inflammation identified by elevated levels of blood inflammatory markers associated with frailty, comorbidity, and early death (Ferrucci & Fabbri, 2018). Inflammageing is both a risk and exacerbation factor for chronic disease; clinical trials suggest that it is a causal factor for cardiovascular disease (CVD), and a risk factor for chronic kidney disease, diabetes, depression, and other conditions (Ferrucci & Fabbri, 2018). Flynn et al. (2019) introduced a new term, *inflamminactivity*, to identify the decline of physical activity and intensity in old age as a contributing factor to inflammageing, and proposed that regular exercise and generally increased levels of physical activity can help to counteract the process of increased inflammation during aging, which in turns reduces the risk or exacerbation of chronic disease.

According to data from the American Public Health Association ([ca. 2012]), cancer is responsible for the highest U.S. spending in healthcare and lost productivity costs, followed closely by heart disease, diabetes, chronic obstructive pulmonary disease, and hypertension/stroke. Heart disease and cancer are the first and second leading causes of death in the United States (Ahmad & Anderson, 2021). One measure of the decline in U.S. health is the lowering of life expectancy in 2019 to 78.9 years, compared to the 81.3 years of other high-income countries; this number has not improved for 10 years, in part the result of an increasing number of deaths from CVD over the past 10 years (Global Burden of Disease, 2020).

Cardiovascular Diseases

The American Heart Association (2019) estimated that in 2016 nearly half of all adults in the United States had a CVD. According to the WHO (2021) CVDs are the leading cause of death worldwide, at approximately 18 million lives annually; four out of five of these deaths are the result of heart attacks and strokes. China leads the world in death rates for CVD, followed by India, Russia, and the United States (Roth et al., 2020). Heart disease is also the leading cause of death in the United States across racial and ethnic groups, including Hispanic, African American, American Indian, Native Alaska, and White men; for women of Hispanic, Asian American, American Indian, and Alaskan origin, heart disease is second behind cancer (CDC, 2020a). CVDs involve the heart and blood vessels, and include coronary heart disease (CHD), congestive heart failure, stroke/hypertension, and other forms of heart disease (WHO, 2021). CVDs are often characterized by a process called atherosclerosis—the accretion of fatty deposits called plaque in arteries (National Heart, Lung, and Blood Institute, 2022a). In congestive heart failure, the heart's ability to pump blood is impaired, and insufficient blood is available to meet the body's needs (National Heart, Lung, and Blood Institute, 2022b). The specific cause of

atherosclerosis is unknown, but certain traits or conditions increase the risk, including low levels of good (high-density lipoprotein cholesterol), high triglyceride levels, increased blood pressure, high blood sugar levels indicating insulin resistance, smoking, obesity—particularly excess fat around the waist, and low levels of physical activity (CDC, 2020a). These risk factors are generally modifiable by behavior and are among the major risk factors for CVDs generally; other modifiable risk factors include alcohol use, low socioeconomic status, psychosocial stressors, and psychological disorders (WHO, 2021). The WHO (2021) listed nonmodifiable risk factors as age, gender, hereditary, ethnicity, and more recently, inflammation, and excess homocysteine in the blood. The WHO (2018b) attributed 41% of global CVD deaths to CHD.

Davidson et al. (2018) pointed to a long history of interest in the interrelationships between mind, body, and heart disease, dating back to ancient Greece. They conducted a selective review of patients with CHD comorbid with depression, anxiety, stress, and insomnia, and found that psychological disorders are associated with poor prognosis for CHD patients. A basic premise of the research was that the presence of comorbidities creates behavioral and biologic processes that exacerbate the disease. Multiple potential pathways between the comorbidities were examined; one such example suggests that the increased plaque burden in atherosclerosis causes a reduction in blood flow to the brain, resulting in depression and further damage to the heart (Davidson et al., 2018). Davidson et al. (2018) also pointed to a confounding factor in the use of certain classes of antidepressant medications; although now less commonly used, monoamine oxidase inhibitors and tricyclic antidepressants both have side effects that can cause cardiac toxicities.

Research over the past decade supports Davidson et al.'s (2018) study. Severe mental illnesses such as depression and bipolar disorder are associated with a higher risk of developing

CVDs (Correll et al., 2017); CVD patients' symptoms extend beyond physical symptoms to include depression, anxiety, and stress disorders (Davidson et al., 2018). Depression has a comorbidity rate with CHD 2 to 3 times higher than in the general population (Vaccarino et al., 2020). De Hert et al. (2018) hypothesized that a reciprocal relationship exists between CHD and mental illness, noting that CHD patients had a high rate of comorbid mental illnesses; conversely, patients with mental illnesses were at a higher risk of contracting CHD. Woodhead et al. (2016) noted suboptimal treatment of CVDs for patients with comorbid mental illnesses, which may be the result of interactions with psychiatric and cardiac medications.

A common pathophysiological pathway may link CHD with mental illness. De Hert et al. (2018) examined the epidemiological and physiopathological pathways between CHD and mental illness. Song et al. (2019) summarized existing evidence on PTSD and its effect on CVD, finding an elevated occurrence of CVDs in PTSD patients. However, they pointed out that the studies in their review often had small sample sizes and their review did not include other stress disorders and their role in CVDs. A further limitation identified is that any genetic predisposition, other comorbidities, and psychosocial risk factors were not adequately accounted for. An analysis of data gathered using the Hospital Anxiety and Depression Scale from patients discharged from five heart centers in Denmark found that patients with comorbid heart disease with depression and anxiety are more likely to have cardiac risk factors such as obesity, smoking, overuse of alcohol, and noncompliance with medications than cardiac patients without mental illness (Berg et al., 2018).

Diabetes

The WHO (2020) estimated that 422 million people suffer from diabetes worldwide. China leads the world in prevalence, followed by India, the United States, Indonesia, and Mexico

(Lin et al., 2020). Data from the WHO show that the number of people contracting the disease is increasing worldwide but rising more rapidly in low- and middle-income countries. In addition to the quality of life and socioeconomic impacts of this disease, diabetes also increases the risk of other health complications, even when patients are following a diabetes management protocol (International Diabetes Federation, 2019). According to the National Diabetes Statistics Report published by the CDC (2020b), approximately 34 million people in the United States suffer from diabetes, and another 88 million are prediabetic.

Diabetes is a chronic, metabolic disease that results either from insufficient production of insulin by the pancreas or the body's inability to use the insulin effectively (WHO, 2020). Insulin is a hormone produced by the pancreas to regulate the amount of glucose in the blood. When glucose in the blood is not regulated, serious damage occurs to the organs, including the heart, kidneys, eyes, nerves, and blood vessels. There are three kinds of diabetes: type 1, type 2, and gestational diabetes. type 1, formerly called juvenile diabetes, is a chronic condition caused by no or insufficient production of insulin by the pancreas. Type 2, formerly called adult-onset diabetes, is caused by the body's ineffective use of the insulin hormone (WHO, 2020). Type 2 diabetes is the most prevalent and is generally caused by obesity and physical inactivity. Gestational diabetes occurs during pregnancy and is characterized by blood glucose numbers lower than those of diabetics but above the normal range (WHO, 2020). Diabetes is a significant risk factor for other conditions; it increases the risk of heart attacks and stroke by a factor of 2 or 3 (Sarwar et al., 2010); it can cause neuropathy in the feet, which in turns can result in infection, ulcers, and amputation (Pop-Busui et al., 2017); it affects eyes by damaging the retinal blood vessels, resulting in a condition called diabetic retinopathy,which can lead to blindness (Smith-Morris et al., et al., 2020); and it is one of the leading causes of kidney failure (United States

Renal Data System, 2019). Common physical comorbidities include hypertension, obesity, chronic kidney disease, CVDs, and hyperlipidemia (Iglay et al., 2016).

Diabetes results in biopsychosocial stressors that put patients at risk for psychological disorders; research studies have outlined reciprocal relationships between diabetes and mental illness (Holt & Mitchell, 2015; de Groot et al., 2016; Guerrero Fernández de Alba et al., 2020). The most common mental illness associated with diabetes is depression; depression is 3 times more prevalent in diabetic patients than in the general population (Kreider, 2017). The bidirectional relationship between diabetes and depression is well established, although the precise mechanisms are not fully understood; several variables, including dysfunction of the HPA axis, shared inflammatory pathways, common metabolic effectors, together with common genetic, environmental, and behavioral risk factors are implicated (Alzoubi et al., 2018). It is likely that the common risk factors interact with several possible biological mechanisms; Sartorius (2018) offered the example that ACEs prepare the brain for depressive disorders, and lead to cell-mediated cytokine production, which can be a precursor to insulin resistance and type 2 diabetes, while at the same time having a negative effect on the HPA and other disorders related to endothelial dysfunction. Several studies support the hypothesis that depression increases the risk for progressive insulin resistance, which can lead to type 2 diabetes (Silva et al., 2019; Webb et al., 2017). Joseph and Golden (2017) reviewed the effects of stress on the depression–diabetes interaction and proposed that disrupted stress processes across several systems together with increased stress levels associated with the disease and the burden of self-management protocols for diabetics is a contributing factor to type 2 diabetes.

Disease Comorbidities

The comorbidity of chronic psychological and physiological disorders is widespread (Šprah et al., 2017) and presents significant complications for health care treatment (Sharma, 2016). The most common chronic physical conditions are CVDs, diabetes, and respiratory disease, which are frequently comorbid with serious mental illnesses such as depression and anxiety; both mental and physical diseases share common risk factors (Stein et al., 2019). Causal mechanisms for mental and physical comorbidity occur at the individual and the socioenvironmental levels and share some pathways (Stein et al., 2019). The failure of the Western model of healthcare to accommodate effective and integrated treatment of these comorbidities presents further complications. The biomedical reductionism model of Western medicine rests upon the view that all illness is ultimately the result of discrete biological problems in the body; consequently, treatment of chronic disease is centered around targeted biological solutions, primarily pharmacology (Ghaemi, 2016). Considerable research indicates that the pathways between mental and physical illness are reciprocal and not fully understood (Ohrnberger et al., 2017). Mental health disorders, such as depression and anxiety, appear to increase the risk of chronic disease (Daré et al., 2019; Scott et al., 2016); although the onset of chronic disease can, in turn, increase the risk of mental health disorders (National Institute of Mental Health, 2021a; Sporinova et al., 2019). Comorbidity complicates diagnosis and treatment of both medical and psychological conditions (Sporinova et al., 2019). Li et al. (2019) found evidence suggesting a common biological mechanism is shared between chronic disease and depression. Raghupathi and Raghupathi (2018) suggested that the trajectory of chronic disease can be mitigated by timely diagnosis and treatment of mental health disorders; conversely, untreated mental health comorbidities can exacerbate chronic disease (Scott et al., 2016).

Chronic Disease Outcomes

Outcomes for chronic physical diseases in the United States are poor, resulting in approximately 75% of deaths (Harris, 2019). Improving outcomes for chronic disease is complicated by the high rate of comorbidity; 40% of adults in the United States have two or more chronic illnesses (CDC, 2019), more than 50% have three or more, and these rates increase with age (Tinker, 2017). Mortality rates in patients with serious mental illnesses are also higher than in the general population. Walker et al. (2015) conducted a systematic review and meta-analysis of mortality in people with mental disorders and determined that the risk of death was 2.22% for individuals with mental illness and determined that the mortality rate was significantly higher than in the general populations. In the mortality rate, 67.3% of deaths in individuals with mental illness were the result of natural causes, 17.5% were due to unnatural causes, with the remaining approximately 15% attributed to other or unknown causes (Walker et al., 2015). Without interventions, the outcome of chronic diseases is generally poor and can even lead to death, particularly when the aging process further exacerbates the underlying biological impairments (Prasad et al., 2012). With interventions, outcomes from chronic disease include occasional reversals of the disease process and a return to health, decreased symptomology, a relatively steady state when symptoms neither increase nor diminish for a period, and increased levels of severity and mortality, particularly in people over 65.

Outcomes for chronic diseases are heavily influenced by medical models of treatment, health care policy, and delivery systems. The presence of two or more comorbidities has been shown to have a negative impact on outcomes, which is in part due to reciprocal pathways between disease types, complicating both diagnosis and treatment (Valderas et al., 2009). Polypharmacy drug interactions can also be a factor (Almodóvar & Nahata, 2019). Health care

today for comorbid chronic medical and mental diseases is generally delivered in silos of specialized care. The lack of integration even at the medical record level, together with poor care and pharmaceutical coordination, siloed risk management, and inadequate communication between physicians can have negative impacts on health outcomes via adverse drug interactions, and conflicting treatment plans (Clarke et al., 2017). Interventions to improve outcomes include mono- or polypharmacy, surgery, lifestyle changes, health behavioral change education such as a diabetes nutrition and education program, and stress management practices such as mindful meditation.

Reynolds et al. (2018) explored the elements used in the chronic care model developed in the 1990s to determine efficacy of the different elements of chronic care. They concluded that positive outcomes, such as physiological measures of disease, and improvements in risk behavior most frequently depend on two variables: the quality of proactive patient care and patient activation. In the Wagner model, proactive patient care is enabled at the health policy level, with concomitant resources, and enacted at the physician level by the design of an effective health care delivery system. This model enables a physician to provide self-management support to patients with chronic diseases, which can lead to patient activation and better adherence to medication and health behavior regimens and improved outcomes (Reynolds et al.,).

Using mobile health applications to change patient health behaviors has been shown to improve outcomes (Lee et al., 2018), as has the use of remote patient monitoring technology (Noah et al., 2018). Remote patient monitoring traditionally uses home use medical devices to collect vital signs, which are connected to a mobile patient device via Bluetooth wireless technology and sent to a database in the cloud and made available via a web application for clinician monitoring. Assessment questions are also provided to patients to give the clinician a

more complete picture of the patient's health. Depending on the vital sign results and answers to questions, educational material is also provided to patients to promote changing problematic health behaviors. Remote patient monitoring is also used for mental illnesses such as depression, anxiety, bipolar disorder, and PTSD and takes the form of assessment questions, medication reminders, and disease-specific education. In both cases, daily monitoring of critical disease parameters enables early intervention to prevent emergency department visits and disease exacerbations, and assessment questions and education are intended to assist patients with health behavior change with a goal of eventual self-management.

One last significant aspect of managing chronic disease outcomes is the need to address stress reduction conjointly with other interventions. Chronic stress, particularly when activated in early childhood, has emerged as a major risk factor for a significant number of physiological and psychological disorders (Wang et al., 2019). Overactivation of the stress response system results in high levels of cortisol, which can lead to structural and functional neuroplasticity and dysregulation of neural circuitry, creating psychological disorders such as anxiety and mood disruption and physiopathology, particularly in neuroendocrine, immune, and related systems (McEwen, 2017). The importance of stress reduction in treatment programs was recognized by Kabat-Zinn (2003) in his now widely used mindfulness-based stress reduction program, initially implemented at the University of Massachusetts for cancer patients. Considerable research since that time has confirmed that stress reduction improves outcomes and should be a standard component of treatment for all chronic diseases (Alsubaie et al., 2017; Creswell et al., 2019; Scott-Sheldon et al., 2019).

Discussion

Over the past decades, multiple causes have been identified for chronic diseases. Egger et al. (2019) conducted a narrative review of determinants and developed a model of distal, medial, and proximal variables, and the resulting risk factors or markers for chronic disease. In this model distal determinants are environmental and include physical, cultural, economic, and political factors, leading to the medial determinants of stress, interpersonal relationships, jobs, and social injustice. Ultimately these factors may manifest in proximal determinants such as nutrition, inactivity, and substance use. This progression of determinants has the potential to create risk factors for chronic disease such as high levels of blood pressure, weight, and cholesterol. Kanbay et al. (2019) identified the process of metaflammation as the final conversion of of a chronic low-grade inflammation into risk factors for chronic disease. Egger et al. also noted that distal factors often lead to a loss of identity, sense of meaninglessness, or alienation and introduced the role of ACEs as significant determinants linked to adult chronic diseases.

Many treatment models for chronic disease today are narrowly focused. The last 3 decades have seen a trend in patient education and a focus on health behavior change. The underlying processes and causative factors, however, have largely gone unrecognized. The bidirectional nature of the complex interrelationships between brain, nervous system, immune system, human behaviors, and chronic physiological and psychological diseases is slowly percolating through the healthcare system in the United States but as yet has had little overall impact to the statistics. The concept of integrated mind–body medicine offers hope for a more successful path forward, creating a wrap-around approach to treatment that involves practitioners of many disciplines, including physicians, psychologists, mind–body specialists, nutritionist, and

yoga teachers (Moss et al., 2022). In the mind–body model, the patient ceases to be identified as a diabetic or a person with bipolar disorder and treated in a silo for a specific disease only. This view is replaced by a holistic view of the totality of the patient and encompasses the broad spectrum of bidirectional factors of disruptions to the normal range of function of body and mind. With the continued linear progression in chronic disease numbers, it is essential that modern medicine embrace a mind–body approach to treatment of chronic disease, acknowledging that treating either mental or physical health diseases individually often has little efficacy.

Psychoneuroimmunology

The term *PNI* was introduced by Ader (1980) in a Presidential Address to the American Psychosomatic Society in 1980 to describe the context of an integrated adaptive system of different processes, including immune processes, regulated by the central nervous system (CNS). PNI is a tool to study the reciprocal relationships between human psychological processes, the immune system, and the nervous system (Moraes et al., 2018). Its origins lie in research on psycho-neuroendocrine-immune pathways conducted nearly 60 years ago by Treadwell and Rasmussen (Moraes et al., 2018), who examined the role of cortisol release by the HPA in stress and immunosuppression during an anaphylactic reaction. Later studies have demonstrated multiple associations between psychological, neural, and immunological processes (Moraes et al., 2018).

The field of PNI has been enriched over the past two decades by researchers in psychology, neuroscience, immunology, physiology, pharmacology, behavior science, infectious disease, endocrinology, rheumatology, and others (Opp, 2016). Psychoneuroimmunology is a tool for understanding the mechanisms whereby neurotransmitters, hormones, and neuropeptides

create a bidirectional interaction with the immune system and psychological processes. Interactions of the brain and immune system through the ANS and neuroendocrine activity signal the immune system cells. Conversely, an activated immune system generates cytokines, which are identified by the ANS; this creates the reciprocal pathways connecting the immune system and brain, which enables behavioral influences on the functions of the immune system (Dantzer, 2018). The immune-system-to-brain interaction targets regions associated with emotions and psychological well-being (Nusslock & Miller, 2016). The prefrontal cortex is also an important target for immune-system-to-brain signaling. These interactions result in susceptibility to immune system diseases and stress-induced changes in immune function. The behavioral interactions between the CNS and the immune system result from the effects of conditioning and stressful experiences on the function of the immune system; immune processes also affect emotions, activity levels, appetite, and sleep (Godoy et al., 2018). Other studies have identified associations between PNI factors and cancer (Lissoni et al., 2017), depression and schizophrenia (Muller, 2017), anxiety (Ray et al., 2017), and autoimmune diseases (Honeyman, 2016).

Stress Response

Recent research in PNI (PNI) has amplified the importance of stress and how it affects activities of the nervous, immune, and endocrine systems. The normal steady state of the physiology of the human body is called homeostasis, a condition maintained via several pathways, including the HPA, the sympathetic nervous system, and the fight-flight-freeze behavioral response (Chu et al., 2021). Conditions that disrupt homeostasis result in a stress response, which results in physiological and behavioral changes that involve the ANS and HPA axis (Tsigos et al., 2020). Simply stated, stress results in activation of the amygdala, which in turn signals brain stem cells and the hypothalamus to activate the sympathetic nervous

system, which creates proinflammatory phenotypes in the bone marrow, which is released to the peripheral nervous system (Nusslock & Miller, 2016).

The stress response system is a complex adaptation shaped by natural selection to adjust physiology and behavior to changing circumstances involving real or perceived threats (Nesse et al., 2016). Stress-related pathways and mechanisms originated early in human existence. They were critical to providing an immediate survival response to life-threatening stressors (Nesse et al., 2016). From an evolutionary viewpoint, the stress response system is a complex system shaped by natural selection to create immediate changes in physiology and behavior in the face of perceived or actual threats (Nesse et al., 2016). In early man, stressors are presumed to have been threats to survival. In response, the stress system activated the body for immediate action in the form of fight or flight. In the modern world, the stress response system is often activated in prolonged non-life-threatening situations (Agorastos et al., 2019). When stress becomes chronic, particularly during early child development, the stress system may not be able to manage physiological, environmental, or emotional needs (Godoy et al., 2018). Thayer et al. (2021) studied the normative changes of aging and the effect of stress on the aging processes and concluded that negative stress could create premature aging and accelerate physiological aging.

Brosschot et al. (2018) introduced a neurobiological and evolution theoretical approach to stress response. They proposed that the body's stress response is a default response that is always "on" but inhibited by the prefrontal cortex when the brain perceives safety. When the brain detects a shift to an unsafe situation in the form of a stressor, the stress response returns to uninhibited, and chronic stress responses result from generalized unsafety. Evidence can be seen in the symptoms of generalized anxiety disorder, in which homeostatic anxiety is present. Prefrontal cortex inhibition of the stress response system is the normal state; disinhibition has a

significant impact on the body, causing dysregulation of several systems and somatic problems (Brosschot et al., 2018).

Stressors include physiological, psychological, environmental, and emotional factors. The stress response increases the body's ability to address and survive events perceived by the brain as real or potential threats (Nesse et al., 2016). Once initiated, the stress response attempts to mediate the physiological effects on central and peripheral systems (Godoy et al., 2018). Stress causes structural and functional changes to the amygdala that persist through the lifespan and facilitate stress biology in the peripheral nervous system (Miller, 2016). The acute response to stress occurs via two pathways. The first is the activation of the sympathetic nervous system by the amygdala, causing the release of the catecholamines noradrenaline and adrenaline, which prepare the body for fight or flight (Becker & Rohleder, 2019) by redirecting resources in the body away from nonessential functions, such as digestive activity, towards increased heart rate and respiration as the body prepares for action (van der Kolk, 2014). Catecholamines are not able to cross the blood–brain barrier but they can cause cognitive impairment via indirect pathways (Becker & Rohleder, 2019). The second pathway of the stress response, occurring when the stressor is prolonged, is activation of the HPA axis; this causes the adrenal cortex to release the primary stress hormone, cortisol (Herman et al., 2016). Cortisol increases glucose in the bloodstream, preparing the body for action, and increases availability of substances needed for tissue repair. Cortisol also curbs nonessential functions or functions that would hinder fight-or-flight needs and can cross the blood–brain barrier to impair cognitive activity (Becker & Rohleder, 2019). A systematic review of studies on the effect of stress found consistent evidence for the effects of psychosocial stressors on microglial activity in the hippocampus, and likely in other regions of the brain (Calcia et al., 2016).

Another variable in the examination of trauma and the stress response is the impact of maternal stress on child maltreatment. Räikkönen et al. (2015) hypothesized that maternal stress may change glucocorticoid action in the placenta, subsequently impacting the HPA axis and modifying a child's behavior. Maternal stress after birth can contribute to child maltreatment and affect a young child's cortisol regulation and stress response (Hibel et al., 2019; Whitson & Kaufman, 2017). Khoury et al. (2021) examined how maternal child maltreatment influences the cortisol responses of mothers and their 4-month-old infants and found that maltreatment moderated cortisol patterns in several ways. Where a low level of child maltreatment was present, mother and infant had strong positive associations in cortisol levels measured synchronously. In the case of higher maternal-child maltreatment, no association between mothers and infants was detected. Infants of mothers who exhibited higher levels of child maltreatment had cortisol levels that were moderately high and remained elevated over time in contrast to infants of lower maternal maltreatment, whose cortisol levels decreased over time. Khoury et al. concluded that higher maternal child maltreatment was one contributor to the dysregulation of the child's stress response system.

Hibel et al. (2019) explored how child maltreatment affects diurnal cortisol regulation of mother and child and found a significant difference in cortisol attunement between maltreating mother–child and nonmaltreating dyads. In the control group of mothers with no apparent child maltreatment, cortisol attunement between mother and child occurred around midday, whereas maltreating mothers transmitted cortisol to their children at first waking. Although the implications of this difference in transmission are not fully understood, they are another indicator of the effects of the maternal stress response on the young child. Speidel et al. (2020) determined that developmental mechanisms of the family can mediate the effects of stress dysregulation.

They identified four process variables—positive parenting, positive and negative family expressiveness, and maternal sensitivity guidance during reminiscing as potential mediators of the maltreatment-stress response and determined that overall these interventions resulted in steeper positive change in emotional regulation. More research is needed to enhance the identification of opportunities to mitigate the effects of chronic childhood trauma.

Long-term Adverse Psychological and Physiological Effects of Childhood Trauma

Chronic childhood trauma can have negative long-term consequences throughout the lifespan (Dye, 2018). The effects of chronic stress on the child's stress response system can result in changes in the affecting molecular and genetic makeup, with the potential to create lifelong deficiencies that alter the developmental paths and functions of neurological, endocrine, and immune systems (Boullier & Blair, 2018). The resulting cognitive, metabolic, and immune function impairments are linked to chronic mental and physical illnesses, including anxiety, depression, heart disease, and cognitive problems (Agorastos et al., 2019; Burke et al., 2017; Chu et al., 2021; Danese & Lewis, 2017; Russell & Lightman, 2019). Jiang et al. (2019) found that differential long-term health outcomes induced by childhood trauma can be associated with multiple factors, including genetic, epigenetic, environmental, and variables such as vulnerability versus resilience. This variability can be observed across neurobiological stress response systems, and it has been linked to differential health behaviors and outcomes (Smith & Pollak, 2020).

Understanding how the systems involved in the body's response to stress interoperate has further informed analysis of the long-term effects of chronic stressors. Dr. Nusslock, collaborating with colleagues from the University of Los Angeles Cousins Center for Psychoneuroimmunology, conducted recent research expanding the understanding of PNI's

applicability to long-term mental and physical effects of childhood trauma. The mission of the researchers at the University of Los Angeles Cousins Center (2021) is to investigate interactions between the brain and body, the effects of stressors on the brain and immune system, and the role of psychological well-being to promote health and recovery, and ultimately how to translate this information into effective behavioral strategies for disease prevention and healing across the lifespan. Most previous research had focused on single disease or organ systems; Nusslock and Miller (2016) sought to understand how stress created by the response to adverse situations influences the physiology and anatomy of a developing child and to identify the mechanisms that render a child vulnerable to a wide range of health challenges across the lifespan, even those that appear decades later. They made the argument that a multisystem, multidirectional approach was needed to learn more about the common mental and physical health problems that are associated with childhood trauma. During their research. they reviewed previous PNI studies to look for multidirectional transactions amongst biological systems of the body. They proposed a neuroimmune network that organizes the data, based on the hypothesis that adverse experiences in early life increase the bidirectional signaling between neural circuitries and peripheral inflammation, affecting executive control-, threat-, and reward-related processes.

Adversity can influence the gene expression pathway of inflammatory genes. Childhood trauma sensitizes immune cells, which communicate with the peripheral nervous system, initiating proinflammatory phenotypes stimulated by cytokines to initiate tissue repair (Nusslock & Miller, 2016). This process is adaptive in the short-term. Longer-term, the chronic, low-grade inflammatory response interacts with genetics, lifestyle, health behaviors, and other variables, which can lead to obesity, insulin resistance, and other subclinical disease states. The bidirectional pathways involved create circuitries that predispose individuals to self-soothing

behaviors, including substance use, fast food addictions, and smoking (Hostinar et al., 2018). These unhealthy behaviors partner with low-grade inflammation to lay the foundation for long-term physical and emotional disorders. Research continues to explore the crosstalk between neurocircuitries and peripheral inflammation (Hostinar et al., 2018). Recent research in the field of PNI has found that traumatic life events lead to health problems through dysregulation of the inflammatory response; childhood trauma dysregulates the inflammatory response system so that it becomes more reactive to life stressors, and the resulting elevation in inflammation plays a significant etiologic role in many chronic illnesses (Zhong & Shi, 2019).

Although there is a strong body of evidence of the short- and long-term negative effects of chronic childhood trauma, recent research has demonstrated a physiological variability in children's response to adverse events (Smith & Pollak, 2020). Clinical studies continue to explore why some individuals with childhood trauma develop multiple long-term comorbidities during the lifespan, whereas others fare better. Miller et al. (2020) applied the neuroimmune network hypothesis to explore, at least in part, the variable responses to stress exhibited by children focusing on poverty as the stressor. Their findings confirmed that poverty status and neural responsivity interacted in a statistically significant way to predict the development of inflammation. Children in the study who lived in poverty had a positive association of amygdala threat responsivity with inflammation. The brain–immune system associations decreased as the children's socioeconomic conditions improved. Their findings held up under sensitivity analyses; however, the study had some limitations: it was cross-sectional, so longitudinal studies are needed to address causality. Miller et al.'s references to the occurrence of neural–immunological crosstalk were indirect and inferential, given the lack of technology to make directional

measurements of these exchanges. It is also likely that measuring poverty alone as a stressor is an oversimplification of real-world situations of chronic childhood stress.

Miller et al. (2020) examined the effects of amygdala activity and concluded that it can moderate the effects of early adversity, such as poverty, on inflammation. Miller et al. (2021) assessed the role of the central executive network (CEN) in providing resilience against a higher inflammatory response associated with neighborhood violence and concluded that heightened CEN activity may protect children from long-term inflammatory consequences of traumatic stress. These studies deepen the understanding of the variability in immunological responses to stress in children and suggest that the CEN appears to be a neurobiological factor in resilience (Miller et al., 2021).

Numbing is a biological process that blocks the experience of emotions, and it is a traumatic stress reaction (Substance Abuse and Mental Health Services Administration, 2014). It is possible that the brain directs attention away from emotions and towards physical pain as a mechanism for downregulation of the intense distress of difficult emotions. Understanding this mechanism offers a possible intervention: exposing the psychological distress could potentially diminish the physical pain because it would be no longer needed (Lane et al., 2018).

Impact of Trauma on Aging

Across the globe, life expectancy has generally been increasing over the past decades. The number of people worldwide who are over the age of 65 is growing rapidly and is projected to reach 1.6 billion by 2050 (Ferrucci et al., 2019). Healthy life expectancy is lower than overall life expectancy; in the United States, health in the over 65 population has been deteriorating (Flatt & Partridge, 2018). There is an evolutionary aspect to the association between increased disease in aging. Infectious diseases used to pose the greatest threats to humans reaching

reproductive age; as a result, a strong immune system was necessary in early life to ensure survival of the species (Miller et al., 2021; Toda et al., 2021). Once reproductive age was passed, there was no longer any evolutionary pressure to maintain a strong immune response, which leaves the immune system susceptible to increasing dysregulation with age.

In developed countries, three out of four aging adults are diagnosed with multiple chronic conditions (Hajat & Stein, 2018). Geroscience, a field that studies aging, has been expanded to merge research on aging with ongoing research on chronic disease and inflammation. The geroscience hypothesis posits that because aging and chronic diseases share risk factors, advances in slowing down aging processes may also slow down the progression of many chronic diseases (Sierra & Kohanski, 2017). Research by the trans-NIH Geroscience Interest Group has explored the relationship between the biology of aging and the biology of chronic diseases and in particular how aging can be a modifiable risk factor for chronic diseases (Sierra & Kohanski, 2017). The aging process exacerbates cellular and molecular malfunctions, leading to the onset or exacerbation of chronic diseases, and many of the immunological changes associated with aging are also observed following long-term or chronic stress exposure (Nusslock & Miller, 2016). Findings of the mechanisms, pathways, and biomarkers associated with chronic disease and aging provide valuable insights in the development of a model of psychotherapy that addresses the PNI of adult victims of childhood trauma with comorbid chronic diseases.

As chronic disease has become more prevalent, the percentage of adults reporting ACEs is also increasing. According to the CDC (2019a), approximately 61% of adults in the United States reported at least one adverse childhood experience, and nearly 16% experienced four or more. Childhood traumatic experiences are linked to both mental and physical chronic diseases, further exacerbating the effects of aging (Bellis et al., 2019; Karatekin, 2019; Nusslock & Miller,

2016). Research has linked traumatic stress to the acceleration of biological aging and medical morbidity via pathways implicated in immune function, oxidative stress, inflammation, and the stress response (Wolf & Morrison, 2017). Merz and Turner (2021) proposed that early childhood adversity can result in changes in the molecular and genetic makeup of a child that affect the developing neurological, immune, and endocrine systems irreversibly, resulting in acceleration of immunosenescence and chronic inflammation.

Bidirectional pathways involved in a trauma stress response also extend to processes of aging (Thayer et al., 2021). Trauma triggers a stress response, leading to inflammation, which in turn can lead to chronic diseases via the nervous, immune, and endocrine systems, resulting in immunosenescence and aging. Chronic diseases create oxidative stress, further exacerbating aging processes. Oxidative stress has been shown to have a negative effect on tissue functioning (Cabello-Verrugio et al., 2017). Thayer et al. (2021) concluded that aging causes significant structural and functional changes to the brain, leading to cortical thinning and lower brain volume. They postulated bidirectional connections between these changes and dendritic function and structure and emphasized the role of stress in the physiological processes. They concluded that learning to cope with stress and building resilience to inhibit some of the physiological consequences of stress requires emotional regulation and stress management responses both in the heart and brain.

Trauma, Aging, and Immune function

Immunosenescence (the aging of the immune system) has been proposed as the underlying process associating early life adversity and lifetime health (Elwenspoek et al., 2017). Early life trauma drives biological changes resulting from overactivation of the stress response system, leading to physiological, psychological, and behavioral changes that may accelerate the

rate at which the immune system ages (Reed, 2019). Danese and Lewis (2017) identified an association between childhood trauma and a later-life increase in immune system activation. In addition, exaggerated immune responses to stress can occur in older adults, further challenging an immune system weakened through aging processes (Casaletto et al., 2018). Telomere biology has been identified as a potential mechanism for immunosenescence, linking stress and cellular aging (de Punder et al., 2019). ACEs have been linked to telomere shortening, identified as a biomarker of cellular aging and an indicator of health risk (Dagan et al., 2018). Telomere shortening is associated with cellular senescence: an irreversible cell cycle arrest in which proliferating cells become resistant to growth-promoting stimuli (Campisi & d'Adda di Fagagna, 2007). Recent research in geroscience indicates that targeting cellular senescence can alter the healthspan of mice (Kaur & Farr, 2020). Kaur and Farr (2020) found a strong correlation between the shortening rate of telomeres and life spans.

Trauma, Aging and Inflammageing

Inflammageing is a condition of chronic, low-grade sterile inflammation characterized by an age-related increase in the levels of proinflammatory markers that result in higher vulnerability for accelerated aging and premature death (Ferrucci & Fabbri, 2018). Chronic inflammation can accelerate cell damage and malfunction, causing or exacerbating chronic diseases (Nusslock & Miller, 2016). Chronic inflammation is believed to be one biological pathway through which early life adversity may affect health and aging (Merz & Turner, 2021). Current and recent research supports the hypothesis that accelerated aging of the immune system links early-life adversity to the lifelong health trajectory that results in poor aging (Höltge et al., 2019; Merz & Turner, 2021).

Discussion

The body of research on childhood trauma has demonstrated that both short-term developmental consequences are often followed by longer-term physiological and psychological changes that may have a profound effect on an individual's well-being through the life span and are often implicated in the widespread chronic disease in the United States population. The study of PNI, addressing as it does all related systems of the body, offers an innovative and promising framework for new insights into the body's potential responses to childhood trauma and the links to physical and mental comorbidities. It holds much promise for future improvements in understanding and treatment of adult victims of childhood trauma with chronic diseases.

Theoretical Frameworks

In this section, several theoretical models are reviewed and discussed. The models were selected to form a theoretical framework applicable to treatment of adults with childhood trauma and comorbid physiological and psychological disorders. The term *theoretical framework* refers to the structure of concepts, assumptions, expectations, beliefs, and theories used to construct the research design and approach (Creswell & Creswell, 2018). The framework comprises theories that create the context for the selected topic and research questions and that the researcher believes apply to the planning, review, research, and discussion. Ultimately the theoretical framework provides the perspective through which the study is examined. In the context of this dissertation, the complex nature of adult presentation of the interrelatedness of chronic trauma physiology and psychology and concomitant treatment challenges has not been fully satisfied by any single theoretical model in use today. The selected research is limited to currently available treatment models for adults with childhood trauma, acknowledging the paucity of comprehensive studies that include comorbid chronic diseases in the conceptual model, and adjacent theories

believed to be of value. The review also examines the potential application of the research to an integrated therapeutic approach that, although not directly treating any medical conditions, incorporates the presence of physiological comorbidities into a trauma-informed treatment. An example of this incorporation is the inclusion of stress reduction and stress management techniques into treatment considerations; many adults with childhood trauma have overactive and easily primed stress response systems.

The foundational theoretical framework for treatment of mental health disorders is individual psychotherapy. The APA (2017) listed psychotherapy in its practice guidelines as an empirically supported treatment recommendation for the treatment of PTSD in adults; evidence-based research supports the effectiveness of psychological treatment of PTSD (Lewis et al., 2020b). The second framework is polyvagal theory; its relevance in a treatment approach is reviewed and discussed. The last two models are explored to understand complex trauma treatment with comorbidities in the context of successful aging and the impact of the environment. Research explored here is current, with the exception of seminal studies that were conducted in earlier decades.

Current Psychotherapeutic Treatment Modalities

The APA (2017) described psychotherapy as a process of communication between therapist and patient with the goal of helping people improve their mental health. Locher et al. (2019) and Miller et al. (2021) noted that psychotherapy is an effective psychological intervention for a broad range of mental health issues, including psychological, behavioral, and somatic problems, symptoms, and disorders. *The Encyclopedia of Psychology* described five broad categories of psychotherapy: psychoanalysis and psychodynamic models, behavior therapy, cognitive therapy, humanistic therapy, and integrative therapy (Kazdin, 2000). In these

categories are many other modalities, including cognitive processing therapy, dialectic behavioral therapy, mindfulness-based stress reduction, and EMDR (Boterhoven de Haan et al., 2020). Psychotherapeutic models for trauma are typically centered on the classic PTSD etiology and symptom clusters, although some do include C-PTSD and childhood trauma symptomology (Herman & van der Kolk, 2020). There are several APA Clinical Practice Guidelines for treatment of PTSD in adults; these remain specific to the symptoms of classic PTSD, although some of them reference C-PTSD but without any treatment guidance (APA, 2017). No single psychotherapeutic treatment framework today specifically addresses adults with the complex symptomology of chronic childhood trauma and comorbid chronic physical and mental health illnesses, and very few encompass the additional stressors of aging on mind and body. For the purpose of this study, several psychotherapy treatment models were selected for applicability to the theoretical framework based on a subjective assessment of research evidence. The models are psychodynamic, somatic experiencing (SE), cognitive-behavioral, mindfulness-based cognitive-behavioral, neuropsychotherapy, EMDR, and a trauma-informed therapy model.

Psychodynamic Therapy

Psychodynamic therapy is an effective evidence-based treatment for PTSD (Kaminer & Eagle, 2017; Levi, 2020; Sharpless, 2019). Psychodynamic treatment is grounded in Freudian psychoanalysis, object relations, ego psychology, and self-psychology (Alessi & Kahn, 2017). The theoretical foundation of psychodynamic psychotherapy is well supported in neurobiology (Fulmer, 2018). It is primarily a talk therapy with an experiential component that involves discovery and exploration of aspects of the self buried in the unconscious mind in the context of the therapeutic alliance. The process brings maladaptive emotional and mental processes of the

unconscious that continue to manifest in present moment thoughts, beliefs, and behaviors into conscious awareness (Fulmer, 2018). Repressed material brought into consciousness allows interpretation and processing of old, distorted schemas and feelings hitherto hidden that have sourced current thoughts, emotions, and behaviors (Fulmer, 2018). Jung (1959/1979) identified this model when he stated that "the psychological rule says that when an inner situation is not made conscious it happens outside, as fate" (pp. 70–71). Fulmer (2018) pointed to the term *dynamic*, indicating that the mind is a dynamic system, with complex multidirectional interactions. Trauma disrupts a steady state of mind, causing chemical and anatomical changes in the brain (Lazaratou, 2017). The psychodynamic framework and its neurobiological underpinnings accommodate the volatile nature of trauma presentation, providing context and enabling exploration of the chaotic personality structure (Fulmer, 2018). Also inherent in the psychodynamic approach is its multicultural applicability; the underlying neurobiology of trauma is generally the same regardless of the culture and environment, and similar patterns of trauma response have been identified across different cultures (Berzoff et al., 2021; Fulmer, 2018).

The therapeutic relationship is of primary importance in psychodynamic theory; in fact, early alliance has been shown to be a robust predictor of outcome in psychotherapy, enabling the relationship to act as a container for disruptive thoughts and feelings of the client (McCarthy et al., 2019). Essential elements of the therapeutic alliance include the relationship itself, transference, countertransference, and conflict (McCarthy et al., 2019; Stigler et al., 2007; Yotsidi & Kounenou, 2021). Given the underlying relational disruptions often associated with trauma, this provides a safe framework for the client to experience relational conflict with a more positive outcome. Fulmer (2018) identified at least five major objectives of psychodynamic treatment. These are the development of insight, expansion of choice by finding one's voice,

liberation from the unconscious maladaptive drives developed during trauma, improvement in interpersonal relationships, and corrective emotional experiences. Others, including Stigler et al. (2007) and van Nieuwenhove et al. (2020), included the experience of conflict in the therapeutic relationship. Van Nieuwenhove et al. proposed that interpersonal difficulties are one of the most severe consequences of childhood trauma exposure. They conducted a case study to explore the nature of interpersonal patterns at the start of, during, and at the end of therapy, to provide more insight into the processes involved. Their findings demonstrated that early in therapy the client distrusted authentic self-expression due to a perception that others were judgmental and rejecting, a pattern that originated in early childhood traumatic relational experiences with the caregiver. The therapist's empathetic and empowering presence in therapy allows the client to form a new relational experience, through which interpersonal change could be accomplished. As a case study, their research was very specific and not generalizable across populations; however, it did provide evidence to support the underlying premise that the therapeutic relationship has the potential to serve as a new and healthy relational model.

The value of the psychodynamic model is sometimes diminished by inadequate training of psychotherapists; many master's degree counseling programs often fall short in training on the neurobiology and physiology of trauma and processes underlying the therapeutic alliance, and they largely ignore the presence and impact of chronic medical diseases in adults who experienced childhood trauma. Nor do they adequately typically promote stress management techniques including bodywork, such as yoga. When working with a client with childhood trauma, it is optimal to be aware of how their neurobiology is primed for stress, and address this as part of the treatment program.

Somatic Experiencing

One of the more recent approaches to the treatment of trauma was introduced by van der Kolk in his seminal work on the effects of trauma on the body and the brain. Van der Kolk (2014) proposed that trauma often causes an individual's body and brain to interpret the world as a dangerous place, leading to a more physical experience of trauma, engaging the brain's survival response in the amygdala. Van der Kolk (2019) emphasized the significance of the brain stem and limbic system; working directly with these more primitive subcortical brain levels allows treatment to progress to higher cortical systems. In this context, successful repair of the mind–body connection, leading to trauma healing, can occur by working with body sensations and the more primitive brain functions directly rather than via cognition and stored memories. The amygdala, which is the part of the brain involved in the survival instinct, often retains traumatic experience and heightens threat levels by reactivating the ANS for fight, flight, or freeze, depending on the original trauma response (Palmer et al., 2020), leaving the trauma sufferer with the belief that these responses are beyond their control. Not surprisingly, against this neurophysiological backdrop, and despite the broad range of treatment options for PTSD, an estimated 50% of trauma patients do not respond to the evidence-based treatments of cognitive behavioral therapy (CBT), EMDR, and psychodynamic (Sripada et al., 2019). Levine et al. (2018) argued that these modalities are less effective for individuals with chronic childhood trauma resulting in C-PTSD, whose resulting emotionally activated dysregulated physiological and affective states dominate their response to treatment.

SE is a model of psychotherapy integrating body awareness into the psychotherapeutic process to treat trauma and other stress-related disorders (Levine, 2010). It was formally developed by Peter A. Levine, but he attributed its origins to the work of an Austrian medical doctor and psychoanalyst, Wilhelm Reich, on blocked emotion and how it is released from the

body (Levine, 2010). SE is a body-oriented, “bottom-up” approach grounded in physiology and body memory, emphasizing the importance of the brain stem and limbic system. It starts with the neurological manifestation of the trauma response and progresses gradually towards the higher cortical systems to change the way the body responds to stored trauma (van der Kolk, 2019). The client is directed towards the experience of internal sensations in the body, rather than focusing on cognitive and emotional experiences associated with the trauma (Kuhfuß et al., 2021). Schroder (2017) described SE as a process that enables discharge of the physiological stress response, releasing the activated trauma reaction evinced in the form of posttraumatic stress symptoms and defensive reactions through tears, bodily sensations, or breathing, to return the ANS to its normal state. The process may also reinforce the client’s innate capacity for self-regulation. SE has a much lower propensity than many other trauma interventions for retraumatizing a victim (Brom et al., 2017). The client is required to engage in the present moment with body feelings from traumatic memories that cause physiological arousal, but an extensive revisiting or retelling of the traumatic events is unnecessary. By working with the present moment experience of these sensations, the client is able not only to process the related emotions but also gradually learns how to reduce the arousal associated with the traumatic experiences by increasingly tolerating and accepting the inner physical sensations and related emotions (Brom et al., 2017; Kuhfuß et al., 2021).

In a scoping review, Kuhfuß et al. (2021) examined 83 SE studies conducted prior to August 2020, looking at the model’s efficacy and key methods used. Of the original 83 studies, 16 were determined to meet the inclusion criteria. Their analysis determined that overall the studies demonstrated strong heterogeneity in both the nature of the SE interventions as well as the type of sample. Kuhfuß et al. concluded that their results demonstrated promising if limited

evidence of the efficacy of an SE model for treatment of PTSD. This conclusion is consistent with other studies on body-oriented approaches for treatment of PTSD (Andersen et al., 2017; Brom et al., 2017).

SE has also shown promise in treating adults with comorbid trauma and chronic disease (Andersen et al., 2017). Despite the proven link between PTSD and chronic pain (Kind & Otis, 2019), very few intervention studies have examined individuals with these comorbidities. Andersen et al. (2017) conducted a randomized controlled trial (RCT), assessing the outcome of adding an SE intervention to an existing chronic pain treatment regimen. They found a reduction in PTSD symptoms compared with the control group, who received standard pain treatment. They concluded, however, that the overall effect of the SE intervention was less than anticipated, which they attributed in part to the structure of the trial. The primary outcome of the study was pain-related disability, and to test the efficacy of SE would require that a control group be added also targeting PTSD symptoms.

Cognitive Behavioral Theory

The term *cognitive behavioral therapy* is derived from two models of psychotherapy: a cognitive approach and behavioral theory. Behaviorism owes much to the work of John B. Watson and was enhanced in the 1950s by the work of Albert Ellis, who developed rational emotive behavior therapy. A decade later, Aaron Beck incorporated behavioral theory into his cognitive therapy clinical practice and research, evolving his cognitive model into cognitive and behavior therapy. He became widely regarded as the father of CBT (Beck & Fleming, 2021), and has spent his professional life in research and practice expanding its value. CBT is used to include a broad range of cognitive-behaviorally based therapies that aim to change distorted cognitions and concomitant behaviors, and it has dominated psychotherapy treatment for several

decades (Pietrzak et al., 2018). APA (2017) clinical practice guidelines for PTSD strongly support the use of CBT for trauma patients. The therapy is based on the construct that behavior is learned and that individuals have interpretations of themselves and others, based on early childhood experiences that influence their emotional, behavioral, and physiological reactions to the world. Psychopathology is present when these interpretations are distorted or inaccurate. The distortions often manifest as automatic thoughts with negative and maladaptive content. Beck (2019) found that when he worked with his patients to identify and adapt their distorted schemas, their beliefs and thoughts improved; learning and practicing new, more adaptive thoughts led to beneficial behavior changes. CBT interventions can help individuals to identify and adapt their emotional and cognitive responses to traumatic triggers and develop more adaptive, less stressful, thoughts and beliefs, leading to new behaviors that replace avoidance behaviors and other defense mechanisms (Sockol, 2015).

Unlike SE, which is a physiologically oriented bottom-up model anchored in the body and body memory and focused on the significance of the brain stem and limbic system, CBT is an evidence-based top-down model, targeting cognitive processes in the frontal region of the brain to achieve change. Top-down treatment models prioritize conceptual representations of psychopathologies such as PTSD and are thus more likely to improve outcomes for clients with a highly cognitive presentation with little emotional involvement. The top-down model does not generally involve the body and the central CNS, which may account for the failure of CBT to effect change in some trauma patients. Cognitive-based interventions require cognitive processing, which is problematic for trauma sufferers with impaired cognitive functioning and for those whose thoughts and behaviors are driven by high emotional engagement and dysregulation (Kuhfuß et al., 2021). A systematic look at top-down and bottom-up processes

suggests that neural integration and disintegration is critical to a more informed understanding of mental health and recovery; neural networks collaborate to integrate sensory experiences with thoughts, emotions, and behaviors (Rossouw, 2012; Sporns, 2012). Sporns' (2012) work pointed to the difficulty at a neural level of a one-sided cognitive approach that addresses symptoms to change emotions and behaviors through cognitive processes. The neurobiological consequences of chronic childhood trauma often pose a challenge in traditional CBT; an estimated 50% of trauma patients fail to improve to the evidence-based treatments of CBT, EMDR, and psychodynamic therapies (Sripada et al., 2019).

With increased insight into childhood trauma, the use of CBT for trauma treatment has evolved to introduce trauma-focused CBT (CBT-T). A CBT-T approach has been identified as one of the most effective treatments for many trauma patients, driving symptom improvements (Ehlers et al., 2021). Lewis et al. (2020b) conducted a systematic review of literature and meta-analyses of random controlled trials of psychological treatments for PTSD to evaluate the relative efficacy of different theories. Studies published between 2008 and May 2018 were considered for inclusion based on search terms related to trauma. Of these studies, only seven directly involved childhood trauma. Lewis et al. concluded that of all the modalities included, CBT-T appeared to have the strongest evidence of clinical value, specifically exposure therapy, cognitive processing therapy, and cognitive therapy. The review was used to inform the 2018 update to the International Society for Traumatic Stress Studies (ISTSS, 2018) treatment guidelines. Lewis et al. noted that CBT-T relies heavily on revisiting trauma imagery, which may account for dropout rates.

Mindfulness-Based Interventions

Over the past 2 decades, the practice of mindfulness has gradually emerged as an evidence-based modality in mental health research and clinical practice (Guendelman et al., 2017), demonstrating great relevance to cognition, emotion, and motivation. Mindfulness is defined as "the awareness that arises out of intentionally attending in an open and discerning way to whatever is arising in the present moment" (Shapiro, 2009). As trauma research and clinical practice has evolved, one fruitful avenue of exploration has been the integration of mindfulness into psychotherapeutic models. Bessel van Der Volk, medical director of the Trauma Center at the Justice Resource Institute in Brookline, Massachusetts, integrated mindfulness with neuroscience and other therapies in his innovative work on treatment of trauma. His work has demonstrated how mindfulness, with other interventions, can reactivate parts of the brain that have been deactivated through traumatic stress (Courtois & Ford, 2009). In some ways, mindfulness, grounded in present moment awareness, resembles Gestalt theory, which examines the present moment experience. Mindfulness training quiets the mind, reducing negative automatic thinking and rumination; it also reduces emotional dysregulation and negative emotions (Dumarkaite et al., 2021; Jasbi et al., 2018; Kabat-Zinn, 1994).

The addition of mindfulness to traditional CBT offers an alternative framework to treatment models for mental health disorders, including PTSD and C-PTSD (Dumarkaite et al., 2021). Research on the inclusion of mindfulness-based interventions in trauma treatment has demonstrated positive changes in PTSD patients, which include alleviating some of the more challenging symptoms of repetitive flashbacks, intrusive thoughts, avoidance behaviors, hypervigilance, and emotional dysregulation; and positive changes in cognition and concentration (Roychowdhury, 2017). Mindfulness-based CBT focuses on changing awareness

of, and relationship with, thoughts, leading to an understanding that thoughts are not facts (Boyd et al., 2018). Mindfulness-based stress reduction is another effective intervention for trauma clients whose symptomology includes hypervigilance and a heightened stress response (Boyd et al., 2018). In a review of study literature, Guendelman et al. (2017) examined the neurobiological effects of mindfulness-based interventions in psychotherapy. They found that an 8-week mindfulness-based stress reduction program might result in neuroplastic changes in areas associated with emotional reactivity, arousal regulations, interoception and exteroception, self-consciousness, mood, and memory systems. Guendelman et al. also reported that none of the studies identified changes in prefrontal cortex areas or any of the regions of the brain linked to top-down emotion regulation and suggest that the beneficial effects of mindfulness-based stress reduction may occur mainly via a bottom-up or nonemotion regulation related cortical and subcortical systems. They concluded that more research was needed to increase understanding of the mechanisms of emotion regulation that underlie mindfulness and its use in psychotherapy, from clinical and biological perspectives. New insights into emotional disturbances will enable improvements in therapeutic interventions for mental health disorders characterized by emotional dysregulation, such as PTSD.

Dumarkaite et al. (2021) conducted an RCT to investigate the effects of a CBT-structured mindfulness-based intervention for PTSD and C-PTSD symptoms conducted via an internet delivery model. The results supported the hypothesis that mindfulness-based internet interventions can reduce C-PTSD symptoms and improve mental health and well-being. Specifically, for C-PTSD symptoms, statistically significant improvements were identified in disturbances in self-organization symptoms (DSO): negative self-concept, relationship disturbances, and sense of threat. Symptoms of DSO are not included in the diagnostic criteria

for PTSD, which explains why improvements were not seen in PTSD symptoms. Dumarkaite et al. concluded that there is still a need for trauma-focused therapies that explicitly address traumatic memories and experiences for PTSD patients. Other studies conducted recently confirmed this finding (APA, 2017; ISTSS, 2018; Lewis, et al., 2020b). Dumarkaite et al. proposed that because mindfulness-based cognitive-behavioral interventions emphasize experience of the present moment, traumatic experiences can be avoided, which, in conjunction with the physiological and psychological benefits of mindfulness, may be more effective for C-PTSD but not for the classic PTSD presentation. However, Kabat-Zinn (2012) pointed out that mindfulness can help to integrate all dimensions of human experience—emotional, somatic, cognitive, and social. It seems probable that in the case of severe trauma, mindfulness-based interventions may be reserved for a later phase of treatment, after a patient has made some gains in DSO symptoms, enabling further symptom resolution through present moment awareness. Findings from Dumarkaite et al. support the concept of a phased treatment approach, using different modalities as treatment progress through different stages of integration.

Eye Movement Desensitization and Reprocessing

EMDR is a psychotherapeutic treatment developed by Francine Shapiro in the 1990s. It was intended to lessen or alleviate the stressful symptoms associated with memories of traumatic experiences (Shapiro, 2001). EMDR is conducted in eight phases in a framework of adaptive information processing of memories of past trauma, identifying and working with current situations that trigger disturbance, and the skills that will enable the individual to form positive memory templates. EMDR is targeted at the brain's information processing processes on the premise that trauma symptoms are due to memories of disturbing experiences that have not been appropriately processed. The unprocessed memories include emotions, beliefs, perceptions, and

physical sensations that an individual experienced during the traumatic event(s) (Shapiro, 2001). In PTSD, traumatic memories are unable to link with other memory networks where memories of adaptive life experiences are stored, which prevents learning from taking place, which constitutes a failure of episodic memory to be integrated into the semantic memory system. (Shapiro, 2001). Direct processing of the unprocessed traumatic memories seems to facilitate the neuralization of nonadaptive perceptions affects, and sensations through linkage to the adaptive memory networks and transforming the memories by reprocessing them (Hase et al., 2017). Although EMDR brings traumatic memories into the present, it does not involve any detailed cognitive examination or experiencing of the trauma, or prolonged exposure to the memories.

Treatment includes focusing simultaneously on awareness and presence of spontaneous associations of trauma imagery, thoughts, emotions, and physiological sensations, while underdoing bilateral stimulation of the brain, usually via eye movements (EMDR Institute, 2020). The bilateral stimulation engages the brain's information processing system, which makes internal connections that enable assimilation of the traumatic memory into the adaptive memory networks of the brain. As this process unfolds, multiple changes may occur, including positive emotions, new insights and beliefs, and other physical reactions. In this way the traumatic aspect of the memory becomes integrated and disarmed (Landin-Romero et al., 2018).

EMDR has become a widely used evidence-based first-line treatment for PTSD, sometimes in conjunction with CBT (ISTSS, 2018) or other therapeutic models such as a somatic approach (Schwartz & Maiberger, 2018). A SLR of studies on EMDR including adults and children diagnosed with C-PTSD associated with chronic childhood trauma found that the six included studies showed favorable outcomes of EMDR treatments across the age groups (Chen et al., 2018) compared to other treatment modalities, including CBT and medication. Wilson et

al. (2018) conducted a systematic narrative review from RCTs to examine evidence for the efficacy of EMDR for trauma. Their findings indicated improvements in PTSD through reduced trauma symptoms. Shapiro (2001) proposed the use of EMDR for chronic pain and chronic health conditions, but little research information is currently available on this topic, although it could be of considerable interest in the context of treatment of adults with childhood trauma and chronic disease.

Neuropsychotherapy

The work of Klaus Grawe and others led to the emergence of a new field in psychology known as neuropsychotherapy, integrating findings from the new field of neuroscience with clinical psychology. Neuropsychotherapy provides a neurobiological meta-framework for psychotherapy, enabling learnings from neurobiology to enhance psychotherapeutic treatment models (Dahlitz, 2015). It has also driven a paradigm shift in psychotherapeutic treatment models from the previous focus on higher cortical and cognitive processes towards the incorporation of affective phenomena in the understanding of behavior change. Neuroscience research has demonstrated that bottom-up, left-hemisphere neural processes play a key role in behavior (Dahlitz, 2015). Insight into the biological activity of a neutral network involved in a specific emotion, combined with a psychological understanding of an individual's interpersonal relationships and environment, enables an integrated, mind–body approach to treatment (Navalta et al., 2018). Simply put, the neuropsychotherapeutic model aligns brain functions with therapeutic interventions. The psychotherapist intentionally helps the client to engage in the processes of neuroplasticity; research has demonstrated that the therapist-client alliance itself is responsible for creating neuroplasticity for clients (Roussow & Kobie, 2014).

This approach is of potential value for adult with ACES. Trauma can be viewed as a disruption of neural substrates associated with different executive functions. Ward et al. (2017) suggested that therapeutic work on a mental representation can help to transform a primitive, sensory, fear-arousing traumatic memory into a more comprehensive, verbally encoded, assimilable neural representation. They discussed a theory introduced by Brewin in 2001 postulating a dual representation system in memory; the first system includes the conscious, and well elaborated memories that can be retrieved actively and which do not carry traumatic physiological charge. The second system is linked to traumatic experiences and the amygdala-driven fear response; these traumatic memories are formed very rapidly in the moment of the perceived or actual threat, include relevant sensations and emotions from the trauma, and are not subject to conscious, extensive elaboration. Ward et al. discussed how a neuropsychotherapeutic approach can help to transform a primitive, near sensory, and fear arousing memory of an event into a more elaborated, verbally encoded, and emotionally more neutral representation, enabling integration into the main conscious memory system. A neuropsychotherapist can help a patient slow down their hyperresponsive amygdala via neurobiological empathy, and reduce hyperactive responses (Grawe, 2017).

The role of attachment rupture in trauma benefits from a neuropsychotherapeutic framework. The full impact of childhood interpersonal trauma becomes clearer with an understanding that the development of trauma symptomology in stress systems and affect regulation takes place to a great extent in the context of the young child's early attachment relationships (van Assche et al., 2020). The attachment rupture is a differentiating variable for childhood trauma versus adult trauma, occurring as it does during early development processes and affecting critical parts of cognitive and subconscious processing. When a child's attachment

needs are not met, secondary maladaptive attachment strategies develop that become habituated as well-documented different attachment styles. When young children and their caregivers experience chronic interpersonal trauma, the natural neural process of attachment can be ruptured, interfering with developmental tasks such as autonomy, regulation of emotions, prosocial skills, perceptions, and other skills (Chambers, 2017; Spinazzola et al., 2018). The disorganized attachment response affects the structure and function of the developing right brain (Schore, 2017). The neuropsychotherapeutic framework can provide a heuristic framework for assessment, conceptualization, and treatment of attachment issues in adults with childhood trauma (Navalta et al., 2018). No studies have yet been identified on the use of neuropsychotherapy for adult victims of childhood trauma with comorbid chronic disease.

Trauma-Informed Psychotherapy

Over the past 2 decades, neuroscience and experiences with treatment of veterans returning from the Vietnam War together with research on ACES have driven the conceptual framework of trauma treatment into new fields. A traumatic disorder more severe than PTSD was identified, described as C-PTSD, which was introduced into the ICD-11 (2018). C-PTSD is a clinical syndrome is usually associated with early life chronic traumatic events of an interpersonal nature, such as child abuse or neglect (Giourou et al., 2018; Hyland et al., 2018). The emergence of a more complex presentation of trauma symptoms drove new treatment paradigms, with trauma-informed care emerging in the forefront. Trauma-informed care was developed in the early 2000s to improve treatment of patients with complex trauma who were nonrespondent to traditional psychotherapy models (Alessi & Kahn, 2017). For trauma-informed psychotherapy to have meaning, it needs to be grounded in the neurobiology of trauma and

recognize and address the impact of the widespread effects of traumatic experiences on the individual at cognitive and affective levels, together with the underlying neurobiological effects.

The trauma-informed psychotherapist must be well-versed in trauma and its consequences, be familiar with appropriate screening tools, comprehend the underlying neural substrates and the effects of different interventions, develop an integrative approach to treatment that takes advantage of strengths and resilience, and minimize or remove opportunities for retraumatization and secondary trauma (Center for Substance Abuse Treatment, 2014). Fisher (2014, as cited in Pretak, 2018), described trauma-informed care as helping patients to find the present moment and noted that a mindfulness-based approach to trauma treatment can keep patients anchored in present reality as they work through the processes of healing. Trauma-informed care is relevant in psychotherapeutic treatment of adults with C-PTSD and comorbidities because the model can be incorporated into treatment for chronic disease in family medicine (Purkey et al., 2018). The use of a common trauma-informed treatment framework for the care of adults whose traumatic childhood experiences have worked their way from psychological effects into physiology can provide a platform for a fully integrated treatment model.

Trauma-informed care includes several key principles in common with an integrated model of care for trauma and chronic disease. The first is an awareness on the part of the healthcare provider, whether medical or mental health, of trauma and its medical and psychological effects, not only in terms of presentation and symptomology but also of the underlying neurobiology. The second principle is the concept of safety, which is a critical impairment in trauma victims (Brosschot et al., 2018). Safety in the context of the interpersonal relationship can be achieved by various actions on the part of the provider and relies to a large

extent on a trust that can be built over time as the clinician strives to develop a safe, predictable relationship with the patient. Examples include consideration of patient symptoms such as anxiety in public spaces and scheduling the patient for a time of day when a waiting room is least full, not rescheduling appointments regularly (an unfortunate circumstance that occurs more and more frequently into today's healthcare environment), displaying empathy and validation, and making sure the patient feels heard during an office visit or therapy session. Safety in the healthcare relationship, through neuroplasticity, can help to rewire the brain to perceive the world as a safer, less hostile environment (Purkey et al., 2018). A third principle is a shift in the clinician's treatment of a patient from a victim to an empowered and resilient being who has the capacity to thrive even in illness. This shift replaces a vital part of the mirroring of early childhood experience, imbuing a patient with a belief in their self-identity and self-efficacy in a way that can be internalized.

Another principle, well-defined in psychotherapy treatment but barely mentioned in mainstream medical care, is alliance with the patient. As with the self-concepts of strength and resilience, a strong alliance between a healthcare provider and a patient can rescript the interpersonal relationships of childhood, through a degree of attachment which, although it clearly does not replace an infant–caregiver bond, does provide a new, healthier lens for relationships. The last principle involves recognition and comprehension of cultural, religious, and gender differences. A clinician's ability to demonstrate a sensitivity to racial and gender marginalization provides another positive, interpersonal experience (Purkey et al., 2018).

An approach that embraces the cognitive, affective, and neurobiological aspects of chronic childhood trauma moves healthcare closer to a mind–body approach and has the

potential to evolve into a unifying integrated framework for medical and psychological treatment.

Polyvagal Theory

The second major theoretical framework reviewed is polyvagal theory. Stephen Porges (2011) introduced polyvagal theory as a model of neural regulation of the ANS by the vagus nerve in response to signals from the brain and body and the surrounding environment. Polyvagal theory explains the mechanisms by which stress responses can retune the ANS to remain in defensive states, and provides a neuropsychological framework to view trauma. Actions can be automatic and adaptive at a neurobiological level rather than a cognitive level and are generated at a level of awareness below the consciousness of daily life. The polyvagal nerve is contained in the ANS. The role of the ANS is to manage survival in response to signals and sensations, which it does through three branches (Dana, 2018): the sympathetic nervous system (the parasympathetic nervous system), and the enteric nervous system; the latter is mainly confined in action to the gastrointestinal tract. The sympathetic nervous system responds to cues of danger by preparing the body for action—the fight or flight response—by signaling for the release of adrenaline. The parasympathetic branch of the ANS contains the vagal nerve, which has two components: the ventral vagal branch and the dorsal branch. The ventral vagal circuity responds to cues that enable feelings of safety and connection. The dorsal pathway responds to cues of danger, breaking connection with others, and effectively “freezing” the individual. In a normally functioning ANS—without the changes resulting from trauma—the nervous system constantly detects and evaluates risk. However, in a trauma patient, personal perception of the trauma victim can override the ANS risk assessment and create a trauma response.

Porges (2018) introduced the term *neuroception* to identify the neural processes, existing separately from perception, that can identify and assess environmental and other risks beneath the cognitive layer of consciousness. If the process of neuroception results in a determination that the environment is safe, the autonomic state is regulated to dampen activation of the ventral vagus branch, inhibiting the defensive circuity, and enabling a return to feelings of safety and connection. In individuals without significant psychological or neurological impairments, the ANS assesses risk and matches the neurobiological state to the actual level of environmental risk perceived by the individual. In the case of a trauma victim, perceptions of danger can be triggered by small, everyday events; this mismatch triggers the flight, fight, or freeze responses despite of the absence of danger and inhibits social engagement behaviors and feelings of safety (Porges, 2018).

Polyvagal theory proposes that it is these mechanisms of the ANS that provide the neurobiological substrates for adaptive behavioral strategies. Polyvagal theory explains the mechanisms by which stress responses can retune the ANS to remain in defensive states. In this framework, the therapeutic goal is to engage the ventral vagus to trigger the circuits primed to support social engagement (Porges, 2018). Porges proposed that the ventral vagal state and the neuroception of safety promote connection and change. A polyvagal approach to treatment includes a recognition of the autonomic state and of the adaptive survival response, regulation of the survival response into a ventral vagal state, and a rescripting (Dana, 2018). It is important therefore that trauma-informed psychotherapists understand the need to cultivate safety in the therapeutic environment, including the use of their own facial expresses, cues, vocal tones, any other body movements that suggest concern and support. Doing so requires self-awareness on the

part of the psychotherapist to monitor their own body and nervous systems because their emotional and neural stability is critical in the process.

There has been recent criticism of the underlying anatomical and physiological constructs of polyvagal theory (Liem & Neuhuber, 2021). According to the critics, the theory has failed to consider the unique structural and functional changes in the regulation of the ANS during the evolution from asocial reptiles to social mammals. Liem acknowledged the usefulness of the social engagement system as a treatment model but disagreed with the validity of mapping the model to the ANS and pointed out that there is little scientific empirical evidence to support it. It seems likely that the overlay of medical model evidence is not always directly applicable in the field of psychology, where traditional talk therapy based purely on psychoanalytic theory has proven positive results. Porges (2021) issued a response in defense of his theory in which he took each criticism and addressed it, pointing out that the opposition was tangential to the fundamental principle of the theory. In his counterargument, Porges concluded that from a functional viewpoint, polyvagal theory offers an understanding of the role of the ventral vagus and social engagement model to calm ANS defensive circuitry in mammalian social behavior. Applying polyvagal theory to psychotherapeutic treatment by emphasizing safety and connection seems inarguable for C-PTSD, where these basic human needs have been disrupted in early childhood.

Successful Aging Theory

The third theoretical approach is the successful aging theory, first developed by Rowe and Kahn (1998) and primarily focused on high-income populations. The increase in lifespan over the past century has brought with it increased susceptibility to chronic diseases due to lifestyle issues including diet and lack of exercise, and to cellular aging after childbearing years

(Whitley et al., 2016). In conjunction an added stressor to aging physiology has been the alarming increase in environmental toxins such as mold and heavy metals (Vriens et al., 2019; Zolnikov, 2015). For many years an overall decline in health was considered a normal, and even immutable, function of aging. Towards the last decades of the 20th century this view began to change. The concept of successful aging gained popularity, gradually dispelling the former generally held belief that the aging process was unalterable. Rowe and Kahn (1998, 2015) distinguished between the usual course of aging versus successful aging, and this concept became the subject of gerontological research, with subsequent researchers offering criticism and expansions (Martinson & Berridge, 2015). Interest and research on the biological, behavioral, and social variables affecting aging grew, and a new more optimistic approach to aging became more prevalent, in which the aging individual has some tools at hand to improve well-being during the inevitable process.

Rowe and Kahn's (1998, 2015) successful aging paradigm focuses on three important elements of well-being as individuals age: low probability of disease and disability, good cognitive and physical capacity, and active engagement in life. The original model might better be described as a desired condition for aging. In the medical model of healthcare more prevalent 2 or more decades ago, patients were accorded little self-efficacy in treatment and management of diseases of old age and were almost entirely at the mercy of the flawed U.S. healthcare system. McLaughlin et al. (2010, as cited in Martinson & Berridge 2015), applied Rowe and Kahn's criteria for successful aging to data drawn from the Health and Retirement Study (HRS) for adults aged 65 years and over. The HRS, first conducted in 1992, is a nationally representative longitudinal survey of work, aging and retirement in nearly 40,000 adults over the age of 50 in the USA. It has been fielded every 2 years since inception, and the resulting dataset

is widely used for research informing public policy in these areas. McLaughlin et al. findings indicated that only about 11% of adults in the dataset used aged successfully in any year, per Rowe and Kahn's model. This and related work led to a general concern that the criteria used in the original model are too narrow to be of value for public health purposes. Further criticism suggests there is clear evidence for a genetic factor in cell biology, mediated by many complex cell biological processes that are linked and regulated across a wide range of molecular and cellular scales (DiLoreto & Murphy, 2015).

Zolnikov (2015) modified the successful aging model to extend its applicability to low- and middle-income populations by incorporating considerations of the environment in the aging process, as well as access to health care. The original model was designed primarily for high-income populations, and not therefore generalizable across all levels of society. Zolnikov noted that several adaptations have been made to the early model to address the significance of access to health care, and healthy activities, but environmental issues were ignored. Exposure to environmental toxins such as mold, heavy metals, and other chemicals in used everyday life pose a further challenge for aging adults with cellular and molecular aging.

Another aspect of aging that has been largely overlooked until more recently is the impact of childhood trauma. Exposure to chronic early life adversity is associated with higher risk for many physical and mental health problems (Colich et al., 2020; Rowe & Kahn, 1998). More recent research supports a further association between childhood trauma and accelerated aging (Chen et al., 2018; Colich et al., 2020). Research has produced conflicting results for some of the potential markers for biological aging, including age of onset of puberty; cellular aging, including telomere length; advanced DNA methylation age in relation to chronological age; and amygdala–prefrontal cortex connectivity leading to cortical thinning (Colich et al., 2020). Colich

et al. (2020) conducted a systematic review and meta-analysis to evaluate whether the effects of childhood trauma on biological aging are dependent on the nature of the trauma. They concluded that there is some evidence for the association between different ACEs and accelerated biological aging in the form of timing for onset of puberty, cellular aging, and cortical thinning in childhood and adolescence. Colich et al. pointed to several limitations of the study, including the unknown variable of genetics, the relatively small number of studies reviewed, and effects on different cell types. Belsky (2019, as cited in Colich et al., 2020) pointed out that early onset of puberty is probably an adaptive response to the environment, accelerating child-bearing age. Other studies have identified delayed onset of puberty after early childhood adversity, rather than early onset (Colich et al., 2020). There is a clear need for more research needed to evaluate how an understanding of the effects of accelerated aging after childhood trauma can inform interventions for mind and body.

Many psychological factors are relevant to aging—chronic diseases, loss of full function of body and often mind, retirement and the end of a career, the shrinking of an individual's world, the reality of death with the death of friends, and others. These problems are often compounded in Western culture by the stigma associated with aging. Older adults are often cast aside, losing authority and autonomy even over their personal lives, often regarded as a burden, and frequently discriminated against by employers, directly or through staffing and hiring practices and policies. When life begins with chronic trauma, maintaining Erikson and Erikson's eighth developmental goal of integrity in old age can be challenging (Orenstein & Lewis, 2020), and the elderly can fall into despair. Erikson's wife Joan added a ninth stage to the original eight stages of psychosocial development, occurring around the age of 80 years and above, incorporating the experiences of the previous psychosocial stages and adding a final stage

(Erikson & Erikson, 1998). Erikson promoted Lars Tornstam's theory of geotranscendence in the final stage of life in which the basis is a feeling of connectedness with the universe, an internalized comprehension that the future is limited, a clear sense of the shrinking of their physical world due to limitations of aging, and a comprehension that death is the natural way of all living things. Knight (2017) proposed a model of psychodynamic psychotherapy linked to the Eriksons' stages of development, in which each stage brings the opportunity for resolution of the developmental process, culminating in successful navigation of the aging process. Knight's model has merits, providing some insight, structure, and purpose around the lifespan, but it does not address the lifespan consequences of trauma or their impact on developmental stages throughout life. Psychotherapeutic treatment for aging adults must find a way to integrates the above in a model that also comprehends the long-term consequences physical and mental consequences of ACEs.

Older adults often face new traumas and stressors, including life transitions, emotional adjustments, loss of friend or relatives, loss of physical and sometimes mental abilities, elder abuse, and often loss of independence. Unresolved childhood trauma, with a history of dysfunctional interpersonal relationships and experiences, increases an individual's susceptibility to elder abuse. Trauma informed care in successful aging calls for an understanding on the part of the mental and physical health care providers to comprehend the significance of past childhood trauma as well as current traumatic experiences. Van Aasche et al. (2020) discussed the evidence for the role of childhood trauma on older adults, associating early adverse experiences with anxiety and depression later in life. They proposed that in part this association is indirect, mediated by insecure attachment and high levels of attachment anxiety. They conducted a study to explore the association between childhood interpersonal trauma,

attachment, and depression and anxiety in later life, and concluded that early life trauma can lead to lifelong attachment issues, with a compounding effect in the elderly. Van Assche et al.'s findings should inform the development of a psychotherapeutic treatment modality for this population. The psychotherapeutic alliance has the potential to repair attachment ruptures, having features of an attachment relationship, and it can serve as the basis for change (Slade & Holmes, 2019).

Summary

The prevalence and persistence of mental and physical diseases in adults with childhood trauma reflects a failure of the current medical and psychological models of treatment. This prevalence and persistence is due in some part to the lack of systematic integration of the two approaches, as well as the lack of training in the interrelatedness on the part of many psychotherapist and medical practitioners. In a qualitative study, Roberge et al. (2016) explored the perceived needs, barriers and facilitating factors to providing psychotherapy for patients with comorbid mental health diagnoses and chronic diseases, through interviews with patients and clinicians. Both groups of interviewees agreed on the lack of whole-person or integrated medical and psychological, care. The lack of integration between medical and psychological providers is particularly concerning in polypharmacy (Mair et al., 2020). The interrelatedness of physiology and psychology, a subject of much current research, must be comprehended in treatment models. If an adult with childhood trauma is in treatment for depression and anxiety, for example, and has comorbid diabetes and hypertension, the biological and psychological interactions between body and mind add a layer of complexity and challenge to treatment. The additional stressors of chronic childhood trauma with no relief often result not only in attachment and developmental ruptures, but also disruption of the development of a coherent and sense of authentic self and

identity. These symptoms are generally associated with C-PTSD (Herman & van der Kolk, 2020).

Although evidence-based research supports the general efficacy of various psychotherapeutic models in the treatment of childhood trauma in adults (Nemeroff et al., 2003) these models may be less applicable to elderly patients with unresolved childhood trauma for whom it is important to have an opportunity to process the past abuse and minimize the negative effects (Palmer et al., 2020). It is often assumed that childhood trauma is so distant that it is no longer a factor, but a significant percentage of older individuals are not successfully treated or find only short- whose improvement. There is little to no research on psychotherapy for adults with chronic childhood trauma and comorbid chronic physical and mental health illnesses. Some trauma-informed psychotherapy today does include various forms of bodywork such as yoga, but there is still no conceptual accommodation for comorbid chronic physical disease and its significance in the overall healing of mind and body; nor is there any significant incorporation of findings and implications of PNI into traditional psychotherapeutic models. In summary, concepts of successful aging in a theoretical model of trauma-informed psychotherapy for adults with ACEs and comorbid chronic disease may be of great value in determining how to build well-being and resilience. These theories are of relevance to the research questions by focusing on elements that promote successful aging in a trauma-informed setting. This information is important and can ultimately be used to shed more light on the magnitude of adverse development that contributes to poor growth across the lifespan and how best to treat and improve it. Current treatment approaches would benefit from an evolution towards a phased, developmentally responsive, personalized, and integrative model of care which can more

effectively mitigate the significant problems of chronic physical and mental illnesses and thereby improve well-being and reduce the economic costs of trauma.

CHAPTER THREE

Methodology

The problem of childhood trauma, particularly during critical early developmental stages, has been identified as a severe and rapidly growing concern in the United States (Houry, 2019). The long-term effects can continue through the lifespan, leading to chronic mental and physical illnesses (Chang et al., 2019). Researchers has identified several bidirectional pathways between physiological, neural, and psychological systems and continue to seek a better understanding. The relatively new field of PNI is focused on identifying and understanding the bidirectional interactions between physiological processes, the immune system, and psychological processes (Dantzer, 2018; Nusslock & Miller, 2016). Despite recent research studies in the field of PNI, no theoretical psychotherapeutic framework exists today for an integrated treatment approach for adults with chronic comorbid physical and mental illnesses and a history of childhood trauma. Findings from this research, together with research on various treatment models for adults with chronic childhood trauma, could inform a new conceptual model that integrates physiology with psychology.

Psychology is a field focused on understanding mental processes and behaviors; it is generally described as a social science. Research psychologists use scientific methods to determine questions and test hypotheses to add to the body of knowledge about human and sometimes animal thought and behavior. In the scientific method, research methodology is essential for the validity and reliability of the findings. Methodology bring rigor to data collection, analysis, and interpretation to prevent researchers from skewing results (Creswell & Creswell, 2018). Four primary research approaches were available for this study: qualitative,

quantitative, mixed methods, and a SLR. Each method has distinct processes for data collection, organization, and presentation.

Qualitative Methodology

Qualitative research is generally concerned with understanding human experience and behavior; it differs from quantitative methods, which tend to assume fixed and measurable realities. The qualitative approach to research is interpretative and ethnographic. Human experience is not always readily measurable; the qualitative method of research gathers nonnumeric data such as text, audio, or video recordings from a wide range of sources: narrative, theoretical, ethnographic, phenomenological, and case studies. Information includes diaries, interviews, focus groups, and relevant documents. The objective is to deepen the understanding of experiences of the participants by identifying key themes (Mohajan, 2018) that contribute to the body of knowledge in an area. Qualitative research is by its nature subjective, both in the data presented to a researcher, and in the researcher's interpretation; researchers must be aware of their own biases to maintain rigor both in the design of the research, selection of participants, and conclusions drawn.

The quantitative method of research also studies human behavior but relies on numbers. Quantitative approach measures phenomena related to human experience and behavior. The underlying assumptions are that the world of human behavior can be measured objectively and that the observations can lead to conclusions about the human experience. Quantitative data are gathered by various means, including surveys, observations, and archives, to test an objective hypothesis. Statistical analysis is used to seek causal relationships between the variables measured (Creswell & Creswell, 2018). Quantitative research methods rely on researchers' expertise in statistical analyses for the accuracy of results. With more recent increased insight

into the physiology underlying mental health, quantitative methods can prove useful in measuring physiological responses, such as activity in different parts of the brain, for example, during exposure to different stimuli. Although they may be useful in identifying outcomes of current treatment models, they are not easily applicable to research questions related to identifying new conceptual treatment frameworks.

A mixed methods study uses a combination of quantitative and qualitative research methods. The use of two approaches, although more complex in design, execution, and interpretation can provide a deeper and more comprehensive understanding of the area under study. In a mixed methods study, data are collected in support of research questions and hypotheses, in the form required for each method; both forms of data are integrated into the findings with the goal of generating new insights (Creswell, 2015, as cited in Levitt et al., 2018). Often, one approach is used to improve an understanding of findings from the other method. Although a mixed methods study can deepen a knowledge area, it is more complex, time-consuming, and requires rigor in execution to maintain reliability and validity.

An SLR offers a different research question approach, requiring a comprehensive, structured search of published data relevant to the topic of study. The goal of a systematic review of the literature is to identify and critically assesses the relevant research to reach new conclusions and explore future implications. The data collected are assessed and synthesized and findings are applied to the research questions (Siddaway et al., 2019). Systematic reviews provide a methodical, repeatable, and transparent research methodology to understand the current body of knowledge about a subject, organizing information from multiple research studies (Johnson & Hennessy, 2019). They can be used to develop a new theory, evaluate existing ones, or highlight gaps in evidence in existing research, and they have the potential to

inform public policy and practice when a rigorous selection and assessment approach is implemented (Creswell & Creswell, 2018). SLRs also introduce a higher layer abstraction from the raw data, thus avoiding statistical oddities or faulty thinking, facilitates the integration of many studies conducted on childhood trauma, and enables an assessment of meaning from the collective data. As with any research method, systematic reviews require structure; for example, literature selection inclusion and exclusion criteria must be consistently applied, reducing subjectivity in the findings.

Research Method

A systematic review of published literature has been selected for this study for several reasons, including recent advances in PNI research, the difficulty of conducting a meaningful quantitative study without longitudinal data, and a perceived gap in psychotherapeutic treatment models for adults with childhood trauma and comorbid mental and physical illnesses. Childhood trauma has been the subject of a significant amount of research since Felitti et al.'s (1998) landmark study on ACES, which concluded that the effects of childhood trauma last long into the lifespan and are cumulative. Since that time, more recent research has identified not only the interpersonal neurobiological changes caused by childhood trauma but also the linkages to other adult mental health disease such as mood and psychotic disorders. Although the PNI research on adults with childhood trauma is increasing, there appear to be very few studies that link childhood trauma with comorbid chronic disease in the theoretical conceptualization; the few that exist are generally about chronic pain.

This study is theoretical, intended to examine, assess, and analyze existing findings to identify gaps, recent research in PNI and related fields, and look for new themes and opportunities. A theoretical study does not provide original data, nor does it require experimental

methods or the manipulation of variables. A theoretical study may be conducted using the classic approach of reviewing data in the published literature without any new statistical analysis. A theoretical study may also use a meta-analysis to analyze the accumulated data of the literature review; this approach relies on some assumed degree of homogeneity in the various studies. (Boland et al., 2017).

The SLR methodology was chosen because it lends itself to suggesting new interpretations of scholarly research (Creswell & Creswell, 2018); this information can highlight opportunities for further research on new enhanced treatment models. The approach taken aims to expand existing knowledge, in particular the gap in the literature on the presence of chronic disease comorbidities and bring awareness and development to the treatment of this population. Treatment of childhood trauma has improved over the past decade with the acknowledgement of the C-PTSD symptom cluster, and the use of nontraditional interventions such as mindfulness and bodywork. The research questions presented in this study require an extensive analysis of current and past research to evaluate current treatment models and to assess the need for a more integrative PNI framework for provision of mental health services to adults with childhood trauma and chronic diseases. The SLR approach is well-suited to the research questions addressed in this dissertation because it includes research studies across a range of physiological and psychological topics, enabling a broader view of physical and mental comorbidities in the targeted population.

Research Questions

RQ1. How efficacious are current psychotherapeutic treatment modalities in the treatment of adults with adverse childhood experiences and comorbid physical and mental illness?

RQ2. How has recent research into psychoneuroimmunology and related fields informed the treatment of comorbid mental and physical disease?

RQ3. What model of psychotherapy can be developed that addresses the interrelatedness of physiology and psychology across the lifespan, using a basis of trauma-informed care, and adjusted to address the underlying impairments of chronic disease?

Participants and Location

This systematic literature review did not directly involve human participation. Studies included in the literature review were primarily conducted in the United States and Europe, with a few exceptions including Singapore. The unifying requirement for the majority of studies selected was the participation of adults with childhood trauma and chronic mental health disease. Where available, comorbid mental and physical conditions were also included, although these were very sparsely represented in the literature. Outcome studies were preferred to gain an assessment of efficacy of the current treatment models available. In each study selected for review, the model of healthcare was primarily the biomedical model, although a few alternative health care modalities are included where available. The research questions of this study addressed psychotherapeutic treatment of adults, so trial participants were mainly adult and senior, ranging from 18 through 70 years old. Studies of children and teenagers with childhood trauma were excluded, with one exception: a study on the effects of mothers' parenting stress on mother-to-child brain synchrony was included. Studies of populations in non-Western, cultures were largely excluded due to differences in models of care, including cultural and religious practices. Other studies were used to support relevant discussion.

Instrumentation

Instrumentation refers to the tools or ways used by investigators to identify and gather potential study data, and addresses the design, selection, construction, and assessment of the data collection processes; the term is also used in relation to internal validity of the research. There are two levels of instrumentation in this dissertation; the first is that applied to the different studies reviewed; the second applies to the SLR of those studies. Instrumentation in the studies reviewed varies widely and includes interviews, observations, questionnaires, group discussions, focus groups, and other sources of patient data. The research questions formed the basis for identifying relevant prior published research. Instrumentation for this study is based on systematic review methods guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and checklist. The PRISMA guidelines were developed in 2009 and include a predefined data collection flow and checklist for implementation (Selçuk, 2019). The PRISMA protocol used in this section includes the following items from the PRISMA checklist: define the protocol; define eligibility criteria (characteristics, dates of publication, publication status); define information sources used; define search strategy used; outline how studies were selected; define the data collection process; describe risk of bias at the study and/or outcome levels; and describe methods of synthesizing study results (Moher et al., 2009). The PRISMA protocol included the use of a flow diagram to clearly illustrate the application of the tool to the literature review.

Two main aspects of this study were considered in the identification of key search terms: the research questions posed and the theoretical frameworks used for the study. Some primary key terms directly relevant to the research questions were identified, and various adjunct key terms were identified to support specific conclusions stated. Several generally applicable were

used throughout the study identification process. Key terms of childhood trauma, chronic mental and physical diseases, and aging were used to gather background information of the problem under review. The first research question addressed the efficacy of current psychotherapeutic treatment modalities in treatment of adults with ACEs and comorbid physical and mental illness. The primary considerations for this question were outcomes of existing psychotherapy treatment for adults with childhood trauma and comorbid chronic mental and physical diseases and supporting information. The primary key search term was *childhood trauma*; the search was expanded to include *PTSD, C-PTSD*, and *ACEs*. Secondary terms related to this question include psychotherapy treatment modalities, outcomes, mental health, chronic disease, and comorbidities.

The primary key terms for the second question were related to current research to inform potential treatment modalities that relied more heavily on a deeper understanding of the biological, physiological, and neurological underpinnings of childhood trauma. Terms used include *IPNB* and *PNI*. Where possible, outcomes data were also included. The third question was used to identify a new model of psychotherapy to address the interrelatedness of physiology and psychology, using a basis of trauma-informed care, and incorporating the underlying impairments of chronic disease treatments; key search terms included psychotherapy model, framework,

Key terms associated with the theoretical frameworks used were also selected. Key terms included current psychotherapeutic treatment models and conceptual frameworks, including psychodynamic, cognitive-behavioral, mindfulness-based, and other modalities. The second theoretical framework was polyvagal theory, which was included in the key terms list. The final framework was the successful aging theory proposed by Rowe and Kahn (1998) and the

expansion of that theory by Zolnikov (2015). This framework allows exploration of the underlying issues associated with the effects of childhood trauma across the lifespan, the intersection between childhood trauma and aging. Keywords were *aging* and *lifespan*, which were secondary to *trauma* and *treatment*.

Most of the studies reviewed were published between 2017 and 2022 with the exception of key contributory studies such as Felitti et al.'s (1998) ACEs study. Where possible, preference was given to studies between 2019 and 2021 to capture the latest research findings in IPNB and PNI. Literature searches were conducted via electronic search of peer-review published articles from a variety of sources, including PubMed, PsychInfo, ProQuest, PsycArticles, EBSCO, Google Scholar, and APA PsychNet.

Data Collection

Data collection was accomplished via a thorough electronic search of the keyword search terms identified in peer-reviewed published articles from a variety of sources, including online databases such as PubMed, PsychInfo, ProQuest, PsycArticles, EBSCO host, and APA PsychNet. Additional background information was retrieved from other online sources including Google Scholar and national and international websites such as the CDC and the WHO. The majority of studies reviewed were published between 2017 and 2022 with the exception of foundational studies that remain relevant today such as Felitti et al.'s (1998) ACEs study of 1998. Where possible, preference was given to studies between 2019 and 2021 to capture the latest research findings in IPNB and PNI.

The database search identified 445 records matching the keyword search terms. Of these most of the records were primary or secondary literature: empirical studies or SLRs, meta-analyses, review articles and other summaries. Databases provided 372 records, and 73 came

from other websites. Approximately half the records were informational, including fact sheets, conference proceedings, and other relevant reference data in chapter one. All studies selected for initial review were written in English, although some were conducted in Europe and other locations. A search for duplicate records identified six, which were removed, leaving 439. Where multiple articles on a given topic were identified, the most recent were selected unless there was a unique aspect of an older one that was relevant.

The next screening involved an assessment of relevance using the abstracts. An additional 23 records were removed based on the abstracts because of applicability (quality of the review, type of trauma, location, population, and age), relevance to research questions, date of research (superseded by more recent information), and quality considerations. At this point, 416 records remained, several of which were used primarily as reference data for background information and context. These records underwent a full review for eligibility, and a further 14 records were excluded again based on additional information about type of trauma, population, age, and direct relevance to the research questions. The final number of records included in the full literature review was 402. The search was conducted originally in late 2018 and early 2019, and then further refined in December 2021 and January of 2022. The large number of records reflects the broad-ranging and complex factors to be considered in treating adult victims of childhood trauma with chronic comorbid mental and physical diseases. Key facts were recorded for each article selected for the review, including title, location, and methodology of the study, population, research methods, key findings, inclusion and exclusion criteria, limitations, source, and section of the literature review supported by the study. See Figure one for the PRISMA flow diagram.

Data Analysis

Through the PRISMA methods described above, 402 records were identified for this literature review. The large number of records is due in part to the breadth of the topics within the scope of the study, which covers a broad field of research. The subjects contributing to the topic of the review include the prevalence and effects of chronic childhood trauma, particularly in early childhood; chronic adult psychological and physiological adult disorders and their etiologies; neurobiological and PNI underpinnings of mental and physical disease; the complications of comorbidities across physical and mental diagnoses; several key psychotherapeutic treatment modalities; and how the effects of childhood trauma continue across the lifespan, often accelerating cellular aging in body and brain. Where relevant, outcome studies were preferred to gain an assessment of efficacy of the current treatment models available. In each study selected for review, the model of healthcare is primarily the biomedical model, although a few alternative health care modalities are included where available.

The articles selected during data collection were assessed in the context of the three research questions and the theoretical frameworks applied. The purpose of this study was to collect and analyze information relevant to the treatment of adults with mental health disorders who have experienced ACEs, also described as childhood trauma or early life stress, and who have comorbid chronic physiological diseases such as diabetes or heart disease. The research questions are posed in the context of the identified population. The first question concerns the efficacy of current psychotherapeutic treatment modalities for this segment of the population; the second explores recent research in PNI and related fields; and the third raises the possibility of development of a model of psychotherapy that addresses the bidirectional interrelatedness of physiology and psychology, using a foundation of trauma-informed care, and addressing the

underlying impairments of chronic disease and associated treatments. Three theoretical frameworks were applied: current psychotherapeutic treatments for adults with childhood trauma, polyvagal theory, and the successful aging model.

The PRISMA method and guidelines were applied in data identification, evaluation, synthesis of findings, and limitations encountered in the selected literature to improve the validity and reliability of the SLR, and to reduce the potential for bias in study selection (Creswell & Creswell, 2018; Moher, 2009). The records in the final analysis were analyzed further to identify the applicable section(s) of the current SLR. Many of the studies had relevance in multiple sections; 335 records comprising articles and fact sheets were used in chapter one and chapter two to provide the background to the problem, the study overview, and to explain the significance of the study. Nineteen studies were used to answer the first research question, 43 for the second research question, and 48 for the third research question. The remaining studies provided information for chapters one, two, and five, ranging across key topics such as childhood trauma and ACEs, chronic diseases and comorbidities, and psychotherapeutic treatment modalities. See Table 6 for sources for each research question.

Validity, Reliability, and Bias

The primary goal of SLRs is to identify, evaluate, and synthesize empirical and other evidence on a selected topic. SLRs, when designed and executed with rigor and repeatability, often provide valuable input to policy decisions in healthcare. The value of the research conducted in an SLR is dependent on validity, reliability, and bias. Validity refers to the extent to which a study adds value to a body of knowledge, which is a factor of bias and reliability. Internal validity addresses how the study is constructed and executed and the extent to which bias is minimized, although external validity addresses the extent to which the findings and

conclusions are generalizable, for example across other populations and locations. Use of the PRISMA method provided internal validity to the review, and the selection process used provided content validity. External validity is somewhat limited because the studies selected focused primarily on Western populations and healthcare models and because only the major comorbid physiological and psychological diseases were included in the review. The inclusion criteria resulted in a broad sweep of human subjects and diseases without much regard to differentiating factors that would be relevant in healthcare. Given that one of the goals of this study was to create an integrated treatment framework for a segment of the population, it can be argued that the generalization is provided with the framework construct, which would need be broad enough to address the many different presentations of the population under study.

Reliability is closely aligned with quality. The quality and reliability of an SLR is both direct and indirect. The quality of the methodology used to produce the review and the quality of the included studies are both necessary. The PRISMA methodology used to construct and execute the review is intended to render the SLR reliable. In a systematic review, the selected articles should include quality criteria and a description of the reliability of the instruments used (Greco et al., 2013). A systematic review of adherence to methodological or reporting quality of studies on evidence-based healthcare found that although quality assessment tools and reporting guidelines exist, their implementation is inconsistent and improved adherence should be a goal (Pussegoda et al., 2017). Quality of the studies was an important criterion applied during the full-text review of articles. Each full-text article reviewed was assessed for use of quality measures; any that did not incorporate some mechanism for quality were rejected during the application of the PRISMA method. Key points and observations of the literature reviewed were identified and recorded based on their methods, findings, and conclusions.

Error and bias are potential problems for validity of a systematic review. Although bias can be explored and accounted for using methods such as the PRISMA method, errors can result in quality problems and incorrect findings and threaten internal validity of studies. One of the major limitations to a systematic review is the potential for bias in data collection and analysis. The use of the PRISMA method is intended to reduce bias in literature selection. This literature review did not have direct human participants, so the potential for bias in human subjects was indirect, existing in the studies reviewed. In the studies with human subjects, the issue of bias was generally acknowledged and addressed. The research questions were open ended to enable conclusions to be reached based on the findings; however, I had a strong bias in the search for data to support the need for an integrated psychotherapeutic treatment approach of adults with comorbid mental and physical illness, which may have affected the selection of keywords and subsequent selection criteria. The PRISMA method was used to counter this tendency and provide improved quality and transparency by inclusion of opposing findings.

Limitations

One limiting factor of consideration is the heterogenous nature of the different studies included in the literature review. Because several of the studies were SLRs or secondary analysis of multiple prior studies, this resulted in inconsistencies in methodology, measures, population, and location. As a result there is an inherent risk in generalization of results that is not fully mitigated by statistical and quality methods employed by the researchers. Another area of note was the difficulty of different diagnoses; although 18 of the 19 studies targeted one or more of childhood trauma, PTSD, and C-PTSD, there was little consistency in interventions used with one exception. In several studies the well-accepted treatments of CBT, PE, and EMDR and other trauma-informed therapies for PTSD were used, but the inconsistency in contrasting treatments

made it challenging to draw more granular conclusions beyond the generally evidenced significant reduction in trauma symptoms. Drawing inferences from the studies required a higher-level directional view of the problem area rather than providing obvious solutions. There was also a notable lack of endpoints associated with the process of aging, Rowe and Kahn's (1998, 2015) aging model, and how it affects psychotherapy treatment. The effect of Erikson's developmental challenges of aging is not well comprehended in current psychotherapeutic models, and older people form a meaningful percentage of the population engaged in, or seeking, mental health treatment. This literature review was also limited by the availability of applicable studies in the relatively new field of PNI). The scope of PNI is pivotal in any research aimed at integrating physiology, psychology, etiology, symptomology, diagnosis, and treatment across mental and physical illnesses.

Delimitations

There were several delimitations of the study intended to narrow the focus to the research questions. One delimitation of this study was the target population of the studies reviewed. This SLR is focused on treatment of adults with childhood trauma. Childhood trauma studies were reviewed and cited for information on the effects of childhood trauma, especially through the lifespan and for other background information. Studies related to chronic diseases, PNI, and theoretical frameworks were restricted to those with adult participants, adult being defined as 18 years or over. Given the potential differences in cultural healthcare practices, most of the studies included were from the United States and Western European countries, although one or two others were included because their findings were more generally applicable regardless of healthcare practices.

I made another delimitation subjectively in selecting the psychotherapeutic modalities included in this review. The selection was made based on two factors: the availability of literature for different types of psychotherapy and outcomes; and their relevance to trauma and/or to an integrated mind–body approach. There are undoubtedly many more modalities that may prove valuable in an integrated treatment approach, but the availability of literature was one indicator of the relevance of the treatment methods selected. Further delimitations include the use of meta-analyses and other studies that used data collected through various large-scale survey instruments such as the WHO Mental Health Survey. With these reviews, human participant bias existed indirectly.

The primary limitation of the current research study is that it introduced no new empirical data. However, by providing a review of existing empirical and other studies, it did enable a broad assessment of the prevalence and etiology of physiological and psychological comorbidities associated with childhood trauma, and current state of treatment, and provided the opportunity for avenues for future empirical research in this important field.

CHAPTER FOUR

Results

The convergence of problems resulting from childhood trauma, chronic disease, and a rapidly increasing aging population presents a major challenge to health and well-being in the United States. Previous research has adequately demonstrated the probability of lifelong effects of early life stress (Copeland et al., 2018; Curran et al., 2018; Dye, 2018; Kaiser et al., 2018; Smith & Pollak, 2020; van Assche et al., 2020). Children exposed to childhood trauma may suffer from the deleterious effects of chronic stress on health and well-being throughout the lifespan (Agorastos et al., 2019; Chang et al., 2019; Copeland et al., 2018; Smith & Pollak, 2020; Sonu et al., 2019; van Assche et al., 2020). The problem of adequate psychotherapeutic treatment for adults with childhood trauma and chronic disease is further exacerbated by the fact that mental and physical comorbidities present significant problems in diagnosis and treatment (Sartorius et al., 2013). Testimony presented to the U.S. Government House Oversight and Reform Committee identified childhood trauma as a critical and growing problem in the U.S. population (Houry, 2019). Yet the reality and long-term consequences of ACEs and the relationship to chronic disease and accelerated aging are still not well established in the context of the U.S. healthcare system. The current U.S. healthcare policy and legislative horizons offer no suggestion of a path to integrated care; Western medicine lacks a systematic integrative view of chronic disease; pharmaceuticals now form the backbone of modern medical practice. In the U.S. healthcare system, physiological and psychological diseases are generally treated independently by noncollaborating care providers; there is often little collaboration between primary care providers and disease specialists.

Although there is a growing body of research on treatment of childhood trauma when it presents as mental health issues (van Nieuwenhove & Meganck, 2017), there is a remarkable lack of attention to effective treatment methods directly targeting adult survivors of childhood trauma who suffer from comorbid chronic disease. Current treatment approaches generally fail to incorporate the full scope of significant findings of the past 2 decades in the fields of PNI and IPNB. Psychological disorders in adult populations are typically treated by mental health clinicians using traditional and some newer models of psychotherapy, such as Eye Movement Desensitization and Reprocessing (EMDR); chronic physiological diseases are treated by family physicians and disease specialists. It is unusual for mental and physical healthcare providers to collaborate; the leader in this field in the United States is the Veterans' Administration, who, while stating a direction towards a complementary and integrated approach to veterans' health, currently focus largely on mental health and chronic pain (Taylor et al., 2019).

This literature review explored the underlying PNI of childhood trauma, the neurobiopsychological and physiological consequences through the lifespan, and available treatment models to contextualize and address the challenge of effective psychotherapeutic treatment of adults with childhood trauma and comorbid chronic disease. A total of 402 studies were reviewed after using the PRISMA approach; of these, 19 were used to answer Research Question 1, 43 for Research Question 2, and 48 for Research Question 3. The remaining records were used to provide general supporting background information. See Table 6 for literature sources by research question.

Three research questions guided this theoretical study:

RQ1. How efficacious are current psychotherapeutic treatment modalities in the treatment of adults with adverse childhood experiences and comorbid physical and mental illness?

RQ2. How has recent research into psychoneuroimmunology and related fields informed the treatment of comorbid mental and physical disease?

RQ3. What model of psychotherapy can be developed that addresses the interrelatedness of physiology and psychology across the lifespan, using a basis of trauma-informed care, and adjusted to address the underlying impairments of chronic disease treatment?

Participants and Location

This literature review is a systematic review; it did not directly involve human participation therefore no direct recruitment, communication, screening, or other human subjects research criteria were used. However, most of the studies reviewed included human subjects, and an overview of the participant data are presented here. Studies included in the literature review include psychotherapy treatment outcomes, as well as supporting studies addressing the theoretical constructs. These studies were empirical studies, meta-analyses, and systematic or narrative literature reviews. Other literature used to inform this review presented information relevant to the underlying complexity of the adult effects of childhood trauma, including neurobiological and other physiological implications in adulthood.

Research Question 1 addresses the efficacy of current psychotherapeutic treatment for trauma, and where possible childhood trauma and comorbid physical and mental illness. Nineteen studies with human participants were reviewed. Studies included were primarily conducted in the United States and the United Kingdom, with a few exceptions including China and Israel. Participants of studies reviewed for the first research question were mainly adults and seniors ranging from 18 to 70 years old with a self-reported or documented history of trauma. For the purpose of this review, studies exclusively on posttraumatic stress in veterans were excluded. Although the veteran population is likely to include victims of childhood trauma,

subsequent military trauma would have been a confounding factor in interpretation of the results. No inclusion or exclusion criteria were applied for gender; studies typically identified male and female participation; one study investigated female college students only (Bosch et al., 2013). It was interesting to note that even recent studies did not address nonbinary genders. The number of study participants varied widely based on the nature of the study. Some secondary data analyses used datasets containing thousands of patient records, other empirical studies had much smaller sample sizes. Studies of children and teenagers with childhood trauma were excluded, with one exception: a study on the effects of mothers' parenting stress on mother-to-child brain synchrony was included. Studies of other non-Western populations were largely excluded due to differences in models of care, as well as cultural and religious practices.

The unifying requirement selection of studies was the participation of adults with childhood trauma and chronic mental health disease. Where available, comorbid mental and physical conditions were also included, although these are very sparsely represented in the literature. Participants in the studies that met the criteria for this review had a mental health diagnosis, a chronic physical disease diagnosis, or both; generally, the study participants had a clinical diagnosis of PTSD or, more rarely, C-PTSD. Studies with participants with other mental health disorders, including mood and anxiety disorders, were used to explore the relationship between mental health disorders and comorbid chronic physical diseases. The recent introduction of C-PTSD in the ICD-11 (WHO, 2018b) was adopted in the United States only as of January of 2022 and few qualifying outcome studies are available for C-PTSD. This availability is significant in the context of this literature review, because C-PTSD is now believed to be a more accurate diagnosis for adults with chronic childhood trauma (National Child Traumatic Stress Network, 2017).

Results Research Question 1

Research Question 1 was used to determine the efficacy of current psychotherapeutic treatment modalities in the treatment of adults with ACEs and comorbid physical and mental illness. Psychotherapy is generally considered an effective psychological intervention for a wide range of mental health issues, including psychological, behavioral, and somatic problems, symptoms, and disorders. Psychotherapy models used in the studies selected included psychodynamic, SE, cognitive-behavioral, mindfulness-based CBTs, neuropsychotherapy, EMDR, and a trauma-informed model of therapy. These are only a subset of all available modalities but are the most widely used and supported in the literature. Some studies contrasted different modalities, and others focused on one model. RCTs and SLRs of these trials are generally regarded as the best studies to judge the benefits of treatments (Pollock & Berge, 2017). Nineteen studies were reviewed to explore the current state of psychotherapeutic treatment outcomes for trauma and, where possible, childhood trauma. Because childhood trauma is not in itself a clinical diagnosis, and its presentation follows closely the C-PTSD diagnostic criteria, which are not yet instantiated in DSM-5, there were relatively few studies available with outcomes.

Study Type and Selection Criteria

The key search terms for study selection to answer Research Question 1 were *childhood trauma, PTSD, C-PTSD,* and *chronic disease*; studies selected had to have at least one of these key terms. After reviewing the literature, an additional key term was included in combination with chronic disease (physical comorbidities): *psychological distress*. Using the literature review selection criteria, a total of 19 primary or secondary outcome studies were reviewed to answer the first research question, which included six RCT studies with primary data analyses, three

studies with secondary data analyses of RCTs, eight SLRs, a summary review, and one empirical feasibility study without a control group.

Table 1

Research Question 1: Summary of Study Selection Criteria and Study Type

Source	Date	Childhood trauma	C-PTSD	PTSD	Physical comorbidity	Psychological distress	Psychotherapy treatment outcomes	Study type
Andersen et al.	2017			X	X		X	RCT
Bosch et al.	2013	X					X	2ndary RCT
Boterhoven de Haan et al.	2020	X		X			X	RCT
Brom et al.	2017			X			X	RCT
Chen et al.	2018	X	X				X	SLR
Dumarkaite et al.	2020		X	X			X	RCT
Jasbi et al.	2018			X			X	RCT
Karatzias & Cloitre	2019	X	X	X			X	SLR
Lewis et al.	2020b			X			X	SLR
Mavranezouli et al.	2020			X			X	SLR
Moraes et al.	2018			X	X		X	SLR
Nemeroff et al.	2003	X					X	2ndary RCT
Niles et al.	2018			X			X	SLR
Scott-Sheldon et al.	2019				X	X	X	SLR
Valenstein-Mah et al.	2019			X			X	RCT
Voorendonk et al.	2020		X	X			X	Empirical
Watkins et al.	2018			X			X	Summary
Wiedermann et al.	2020	X		X			X	2ndary RCT
Wilson et al.	2018			X			X	SLR

Study Measures

Most of the studies reviewed for Research Question 1 included baseline and end-of-treatment measures; a few included posttreatment follow up. Table 2 includes the study type and measures. Where information about measures was not available in the study reviewed, it as coded as not specified (NS). The measures were classified in two ways: clinician administered, or self-report. The clinician-administered measures were carried through clinician interview of

participants using trauma-specific measures. The self-report measures were completed by study participants in a variety of ways, including in-person at study centers, by mail, and online.

Table 2

Study Measures

Sources	Study type	Baseline measures clinician-administered	Baseline measures self-report
Andersen et al., 2017	RCT	Harvard Trauma Questionnaire Part IV for PTSD	NS
Bosch et al., 2013	2ndary RCT	Clinician-Administered PTSD	Life Stressors Checklist-Revised; QoL inventory; Beck Depression Inventory-II
Boterhoven de Haan et al., 2020	RCT	Clinician-Administered PTSD Scale for DSM-5 (CAPS-5); Imagery Interview.	Impact of Events Scale-Revised (IES-R) self-report questionnaire for symptomatic responses over last 7 days for specified trauma event—guilt, anger, disgust, and shame; Beck Depression Inventory-II; Posttraumatic Cognitions Inventory; Trauma-Related Guilt Inventory; T-R Shame Inventory; Anger Expression and Control Scale; Hostility subscale of the Symptom Checklist-90-R SCL-90-R; Dissociative Experiences Scale-Taxon; Happiness Questionnaire; Remoralization Questionnaire; Schema Mode Inventory
Brom et al., 2017	RCT	CAPS-5	Center for Epidemiological Studies Depression Scale; Posttraumatic Diagnostics Scale (PDS)
Chen et al., 2018	SLR	NS	Impact of Events Scale; State Trait Anxiety Inventory; Beck Depression Inventory.
Dumarkaite et al., 2021	RCT	Clinician assessment of C-PTSD, PTSD or DSO symptom severity; Reliable Change Index	NS
Jasbi et al., 2018	RCT	NS	Baseline self-report questionnaires on PTSD, depression, anxiety, and stress
Karatzias & Cloitre, 2019	SLR	Clinician assessment of PTSD & DSO symptom severity	NS
Lewis et al., 2020b	SLR	NS	NS

Mavranezouli et al., 2020	SLR	DSM–IV (CAPS) or DSM-V (CAPS-5); PTSD Symptom Scale—Interview Version; Structured Clinical Interview for DSM-IV	Anxiety Disorders Interview Schedule for DSM-IV: Lifetime version or DSM-5—Adult and Lifetime Version; Self-report instruments of PTSD symptoms; PTSD Checklist, including all versions (PCL-5, PCL-M, PCL-C and PCL-S); PTSD Symptom Scale—Self Report; Life Events Checklist for DSM-5; ; Symptoms of Trauma Scale; Trauma Screening Questionnaire; Primary Care PTSD Screen; Davidson Trauma Scale; Posttraumatic Diagnostic Scale; Impact of Event Scale /Impact of Event Scale Revised
Moraes et al., 2018	SLR	Multiple assessor-rated PTSD symptom scales not individually identified	NS
Nemeroff et al., 2003	2ndary RCT	CAPS (DSM-IV) or CAPS-5 (DSM-V)	Childhood Trauma Scale; Hamilton Rating Scale for Depression
Niles et al., 2018	SLR	NS	Anxiety Disorders Interview Schedule for DSM-IV: Lifetime version (ADIS-IV-L) or DSM-5 (ADIS-5)—Adult and Lifetime Version
Scott-Sheldon et al., 2019	SLR	NS	Various validated self-report measures eg Hospital Anxiety and Depression Scale,
Valenstein-Mah et al., 2019	RCT	Structured Clinical Interview for DSM-IV	Life Events Checklist for the DSM-5
Voorendonk et al., 2020	Empirical	Clinician-Administered PTSD Scale for DSM-5	NS
Watkins et al., 2018	Summary	Clinician assessment of DSM-5 PTSD criteria	International Trauma Questionnaire
Wiedermann et al., 2020	2ndary RCT	Structured Clinical Interview for DSM-IV	NS
Wilson et al., 2018	SLR	Clinician assessment of PTSD symptomology	NS

Interventions

A wide range of psychotherapeutic interventions were included; the unifying factor was their use in treatment of trauma, in most cases. Table 3 presents the interventions used in each study.

Table 3

Psychotherapeutic Interventions by Study

	Trad-itional	Trauma focused cognitive IVs					PNI IVs						
Source	CBT	CPT	CBT-T	TF-CT	PE	CB-ASP	EMDR	ImRs	SE	MB	MBCT	LKM	Other mind–body
Andersen et al. 2017													X
Bosch et al. 2013		X											
Boterhoven de Haan 2020							X	X					
Brom et al., 2017									X				
Chen et al., 2018							X						
Dumarkaite et al., 2021										X			
Jasbi et al., 2018											X		
Karatzias & Cloitre, 2019	X				X		X						X
Lewis et al., 2020b	X	X		X	X								
Mavranezouli et al., 2020			X		X		X		X				
Moraes et al., 2018							X						
Nemeroff et al., 2003						X							
Niles et al., 2018													X
Scott-Sheldon et al., 2019										X			

Valenstein-Mah et al., 2019						X
Voorendonk et al., 2020		X		X	X	
Watkins et al., 2018	X	X		X		
Wiedermann et al., 2020			X			
Wilson et al., 2018					X	

Key to Table 3

- Cognitive processing therapy (CBT)
- Cognitive-behavioral therapy for trauma (CB-T)
- Trauma-focused cognitive therapy (TF-CT)
- Prolonged exposure (PE)
- Cognitive-behavioral analysis of system psychotherapy (CB-ASP)
- Eye movement desensitization and reprocessing (EMDR)
- Imagery rescripting (ImRs)
- Somatic experiencing (SE)
- Mindfulness-based therapy (MBT)
- Mindfulness-based cognitive therapy (MBCT)
- Loving kindness meditation (LKM)
- Multiple other mind–body interventions including mindfulness practice, yoga, meditation, tai-chi, qigong, breathing exercises, spiritual practices, and relaxation techniques (Other Mind Body)

Some of the studies referenced additional interventions but did not report out on the outcomes data so these interventions are omitted here. The interventions used are consistent with traditional psychotherapy practice and current emerging understanding of trauma and PNI. CBT has been one of the gold standards for treatment of PTSD over the past few decades; the other psychological methods used are specifically trauma-focused.

Outcomes

Outcome endpoints varied in specificity across the studies, but the unifying theme was reduction in trauma symptomology in most cases. The reductions were achieved against baseline

measures achieved through clinician-administered instruments or participant self-report. The interventions were grouped into traditional, trauma-focused cognitive, and PNI. Table 4 maps outcomes to intervention group by study and identifies where follow-up beyond the end of treatment occurred. Longitudinal outcome data was notably lacking in the outcome studies; only five studies included follow-up outcome assessment beyond 2 months, leaving the persistence of identified symptom reductions in question.

Table 4

Interventions, Outcome Measures and Follow-Up by Study

Sources	Intervention type	Outcomes	Longitudinal follow-up	Outcomes sustained at follow-up
Andersen et al., 2017	PNI	Reduction in PTSD symptomology	Posttreatment and 12 months later	Effects persisted at 12-month follow-up
Bosch et al., 2013	Trauma-focused cognitive psychotherapy	Childhood trauma/C-PTSD symptom reduction; small QoL improvements; women with more types of trauma reported less symptom reduction	Posttreatment	None
Boterhoven de Haan et al., 2020	PNI	Reduction in symptoms of childhood trauma in both models	1. Posttreatment, 8 weeks later and 1 year.	NS
Brom et al., 2017	PNI	Significant reduction in PTSD symptoms; 44% of patients lost the diagnosis of PTSD	Posttreatment, 15 weeks later, and another 15 weeks	NS
Chen et al., 2018	PNI vs traditional psychotherapy	C-PTSD symptom improvements present at treatment end, but no significant difference detected between EMDR and routine individual psychotherapy. At 3-month follow-up, greater improvement in symptoms for EMDR	Posttreatment and 3 months later	NS

Dumarkaite et al., 2021	PNI	52% had significant decrease in C-PTSD symptoms; significant reduction in DSO symptoms; small reduction in PTSD sense of threat.	Posttreatment	NS
Jasbi et al., 2018	PNI	Small improvement in PTSD scores	Posttreatment	NS
Karatzias & Cloitre, 2019	Traditional and trauma-focused cognitive psychotherapy and PNI	Childhood trauma and C-PTSD symptom improvements. CBT: moderate to large improvement on disturbances in relationships but lower than other interventions. Prolonged Exposure: moderate effect on DSO symptoms; no evidence of benefit over other therapies used. EMDR: moderate improvement on self-concept; moderate to large on disturbances in relationships; large on affect dysregulation and PTSD symptoms. CBT v PE v EMDR: limited evidence of small to moderate advantage over CBT for PTSD symptoms; no differences between the 3 for other outcomes.	Posttreatment	NS
Lewis et al., 2020b	Traditional and trauma-focused cognitive psychotherapy, and PNI	Strongest evidence of effects on PTSD in CBT-T(CPT, CT, and PE) and EMDR. CBT also had some effects.	Posttreatment	NS
Mavranezouli et al., 2020	Traditional and trauma-focused cognitive psychotherapy, and PNI	Moderate to low effects on PTSD symptoms; efficacy order: EMDR, combined SE/CT, TF-CBT, and supported self-help.	Posttreatment and 1 to 4 months later	EMDR and TF-CBT effects persisted at 1–4-month follow-up
Moraes et al., 2018	Traditional psychotherapy and PNI	Decreased levels of stress-related hormones were found for mind–body interventions like yoga, meditation, tai-chi, mindfulness, and CBT.	Posttreatment	NS

Nemeroff et al., 2003	Trauma-focused cognitive psychotherapy	Childhood trauma patients given psychotherapy alone experienced greater improvements than those on antidepressants, and remission rate was twice as high than those on drugs alone.	Posttreatment	NS
Niles et al., 2018	PNI	Varied but generally improvements in PTSD symptoms of hyperarousal reduction and improved distress tolerance.	Multiple but not itemized	Some effects persisted but not specified
Scott-Sheldon et al., 2019	PNI	Favorable effects on psychological and physiological outcomes	Posttreatment. Others used but not specified	Effects not maintained over time if not practiced regularly
Valenstein-Mah et al., 2019	PNI	Low to moderate feasibility and acceptance among participating students. PTSD symptoms and drinking frequency and quantity decreased for LKM participants but no significant difference than control group.	Posttreatment and 1 month later	Reported as variable but not specified
Voorendonk et al., 2020	Trauma-focused cognitive psychotherapy and PNI	Combination of PE & CBT-T & EMDR: 79% showed reliable symptom improvement for PTSD and C-PTSD. No participant showed symptom worsening.	9 days after last treatment session only	NS
Watkins et al., 2018	Trauma-focused cognitive psychotherapy	Strong evidence of efficacy for PTSD treatment for all 3 intervention types (PE, CPT, and TF-CBT).	Posttreatment	No data
Wiedermann et al., 2020	Trauma-focused cognitive psychotherapy	PTSD patients who received CT-PTSD treatment showed large improvements.	At last treatment session and some additional follow-up but no details provided	NS

Wilson et al., 2018	PNI	EMDR effective with range of presenting symptoms of PTSD. It improved PTSD symptomology and reduced other trauma-related symptoms. Results were consistent across cultures. It was well-tolerated with low drop-out rate;	At last treatment session. Additional follow-ups not specified	NS

The results from studies for this research question suggest that the psychotherapeutic interventions in the studies are somewhat effective in reducing trauma symptomology. Most of the results referenced improvements in PTSD symptoms, but only one third addressed C-PTSD and/or DSO symptoms commonly found in adults with childhood trauma. One study targeted reduction of stress hormones (Moraes et al., 2018) and another various physiological and psychological measures (Scott-Sheldon et al., 2019).

The relationship between early life trauma, adult mental illness, and comorbid chronic physical diseases is complex and multidirectional between the brain, the nervous system, and the immune system, still not fully understood, and not well instantiated in psychotherapy treatment models. One reason is the absence until more recently of a diagnosis that accurately captures the symptomology of early relational trauma and attachment failure or rupture. The result is that clinical diagnoses fall back instead on symptom diagnosis, the most common of which appear to be mood or anxiety disorders when a patient's presenting symptoms do not easily comply with a PTSD diagnosis. Even with the recent introduction of C-PTSD into ICD-11, other challenges remain. The definitive symptomology that differentiates C-PTSD from PTSD is the DSO cluster; individuals with childhood trauma often experience more severe impairments in social and psychosomatic functioning compared with PTSD symptoms (Karatzias et al., 2017). Research also suggests that adults with C-PTSD are easily retriggered by processing of traumatic

memories because of the dysfunctional storage of trauma memories (Knipe, 2018). Processing of traumatic memories is a mainstay of traditional PTSD treatment. When, in addition to these and other challenges, the psychological and physiological impairments of chronic physical disease are also present, it is easy to understand why so many adult victims of childhood trauma who receive traditional psychotherapy treatments do not always progress well.

The last couple of decades have seen an increase in nontraditional psychotherapeutic interventions targeted to bridge the deficiencies of other treatments, with some degrees of success, as evidenced with EMDR. However, it seems likely that a solution must consider the use of multiple modalities and a phased approach. Recent years have seen research in the underlying neurobiology of trauma and the connection to chronic disease (Cross et al., 2017; Purkey et al., 2018), but this is not systematically addressed in any current psychotherapy model. Although actual numbers are not available because of the impracticalities of identifying this population effectively, some—maybe more than some—people affected by the multiple challenges of childhood trauma and comorbid mental and physical disease suffer from significant impairments and can end up as homeless, as their symptomology alienates them from others and often prevents them from succeeding in the workplace. The goal of the first research question was to understand what psychotherapeutic interventions work today for childhood trauma for adults, C-PTSD, and PTSD, to provide a baseline to explore when considering the processes of chronic disease and aging.

Tabulation of the results of the studies reviewed demonstrated the emergence of three thematic patterns: the relative efficacy of included psychotherapy models for C-PTSD and PTSD; the sparsity of published treatment research on childhood trauma, mental illness, and

chronic physical comorbidities in adults with childhood trauma; and efficacy of PNI interventions for C-PTSD and in particular, the DSO symptom cluster.

Efficacy of Psychotherapy Treatment for Trauma

Reported outcomes in 16 of the 17 studies that targeted childhood trauma, PTSD, and C-PTSD showed varying degrees of significant improvement of baseline trauma symptomology in all groups regardless of psychotherapeutic model employed. The loving kindness meditation (LKM) study (Valenstein-Mah et al., 2019) was the exception; participants were college students of both genders aged 18 through 29 years of age. The LKM study included a control group and a group that participated in a 4-week LKM practice, Participants receiving the LKM interventions showed a decrease in PTSD symptoms but with no significant difference than in the control group who completed the baseline measure at study start and received treatment as usual without LKM interventions (Valenstein-Mah et al., 2019). Participants in this study reported perceived and actual barriers to treatment and it appeared that there were a few, including conflicting class schedules. Seven of the other studies reported improvements in childhood trauma and/or C-PTSD symptoms; 11 studies reported decreased PTSD symptoms. The Voorendonk et al. (2020) study found that 79% of participants showed reliable symptom improvement for both PSTSD and C-PTSD. Although the positive outcomes for studies targeting childhood trauma and C-PTSD show strong results, none of these studies mentioned follow up assessments and therefore persistence of symptom reduction is not demonstrated. None of the studies included chronic comorbid physical and mental illness with a history of childhood trauma. This lack of inclusion led to the second theme. Corrigan and Hull (2015) conducted a literature review of psychotherapy treatment for posttraumatic presentations to understand why it is sometimes ineffective; they concluded that some of the single mode approaches that yield high effect sizes

for treatment often involve noncomplex symptomology and are not generalizable for those with complex trauma presentation.

Treatment Gap for Targeted Population

Although 16 of the 17 studies on trauma outcomes demonstrated efficacy of psychotherapy treatment for a range of trauma symptoms, there is clearly a treatment gap for adults with childhood trauma and comorbid mental and physical diseases. No study specifically addressed all these criteria. A few studies included comorbid mental and physical diseases without reference to the presence or absence of childhood trauma; other studies targeted childhood trauma without reference to chronic disease. Psychotherapy treatment modalities that have been shown to be efficacious for PTSD and C-PTSD may not have similar outcomes for adults who are also struggling with chronic diseases and the lifelong effects of early life stress.

Trauma-focused psychotherapies and PNI interventions both address mind–body pathways in different ways but do not fully incorporate the physiological and psychological complexity that accompanies childhood trauma and adult comorbid chronic physical and mental illness. The experience of childhood trauma and a chronically hostile, neglectful, or chaotic environment, together with an adult trauma diagnosis of PTSD or C-PTSD, other chronic mental illness, chronic physical disease, and eventually aging, creates a significant imbalance in neurobiopsychological systems that cannot be fully addressed with existing treatment models. The goal of this research would be to understand if the addition challenges of chronic physiological disease and aging change the outcomes measures for psychotherapy, and in what ways. With that data, new models of psychotherapy can be explored to incorporate findings from the fields of PNI and IPNB, taking into consideration the presence and effects of comorbid physiological diseases across the adult lifespan.

Efficacy of Psychoneuroimmunological Interventions

PNI interventions, which include a wide range of therapeutic methods—eye-movement desensitization and reprocessing, imagery rescripting, somatic experiencing, mindfulness-based cognitive therapy, mindfulness-based interventions, meditation, yoga, tai-chi or qigong, relaxation practices, breathing exercises, spiritual practices, loving kindness meditation—were used in 15 studies to improve trauma symptoms across baseline diagnoses of PTSD, C-PTSD, or childhood trauma. Of these, 10 studies were on PTSD, four each on C-PTSD and childhood trauma, and three studies included PTSD, C-PTSD, and childhood trauma. Five studies contrasted PNI interventions with a mixture of traditional psychotherapy in the form of CBT, and trauma-focused cognitive methods as described in Table 3. One study used a combination of PE and CBT-T.

Generally, PNI interventions achieved significant reduction in symptoms in PTSD, C-PTSD, and childhood trauma as measured in the studies, and outperformed traditional and trauma-focused treatments in almost all cases. Two studies did not include trauma symptom outcomes as endpoints but used PNI interventions to achieve other gains. In one, PNI interventions resulted in decreased levels of stress-related hormones (cortisol, epinephrine, and norepinephrine) as well as significant associations with other neurological and immunological variables such as Interleukin-6, which regulates immune response, and tumor necrosis factor-alpha, an inflammatory cytokine produced during acute inflammation (Moraes et al., 2018). In the second study, use of PNI led to improvements in symptoms of common mental health disorders of anxiety, depression, distress, and perceived stress as well as in physiological markers for CVD (Scott-Sheldon et al., 2019).

One of the PNI studies targeted a wide range of conditions including psychological and physiological variables (Moraes et al., 2018). Moraes et al. (2018) provided inclusion criteria for their psychoneuroimmunology study, which is presented here as reference for the potential value of PNI treatment for adults with comorbid chronic physical and mental illness.

1. Job burnout
2. HIV
3. Cancer
4. Wounds
5. Healing
6. Herpes
7. Lupus
8. Autoimmune disease
9. Sleep
10. Stress
11. Pain
12. Physical activity
13. Psychotherapy
14. Psychoanalysis
15. Behavioral therapy
16. Complementary medicine
17. Depression
18. Anxiety
19. Schizophrenia

20. Posttraumatic stress
21. Spirituality
22. Religion
23. Psychosocial issues
24. Cytomegalovirus
25. Natural killer cell
26. Positive emotions
27. Mindfulness
28. Coping
29. Cognitive therapy
30. Cytokines
31. CVD
32. Interventions
33. Sickness behavior
34. Mood

One of the most well-established PNI treatments is EMDR, which was evidenced in the review findings; EMDR was used in several studies either alone, in conjunction with, or in contrast to several other modalities including trauma-focused therapies, and one traditional model (CBT). In one study it was found to be effective with a range of presenting PTSD symptoms (Wilson et al., 2018); when used in conjunction with PE and CBT-T 79% of participants showed reliable symptom improvement for PTSD and C-PTSD (Voorendonk et al., 2020). A large body of evidence supported the use of EMDR for trauma, and when combined with other trauma-informed treatments, symptoms may be improved further. The only study

using a PNI intervention that did not achieve significant improvement was one that used LKM as an intervention (Valenstein-Mah et al., 2019). In that instance findings showed no significant difference in PTSD symptoms after 4 weeks of LKM than for the control group. Valenstein-Mah et al. offered a variety of reasons for this, including class schedules; however, it seems possible that LKM alone is insufficient to introduce significant shifts in neurobiophysiology. Although it is a meditative practice, it lacks the broader impact of mindfulness-based interventions such as daily mindfulness practices, mindfulness-based CBT, and others. No physiological data points were collected in the LKM study; these might have informed the findings further.

Discussion Research Question 1

Generally the literature review supports a reasonable degree of efficacy in psychotherapeutic treatment of general trauma, particularly PTSD. There is less support for efficacy of treatment of complex trauma or childhood trauma, in part because a diagnostic category for complex trauma has only recently been added to the ICD-11 and was not in use at the time of the studies. There is very little outcomes research on psychotherapeutic treatment models for adult victims of childhood trauma with comorbid physical and mental illness. A meta-view of the literature clearly indicates that treatment models for the unique challenges of the targeted population have scarcely been articulated, far less developed and tested in RCTs. Given the exponentially rising costs of healthcare in the United States, the effort to find a more versatile treatment model that encompasses different modalities for different presentations and stages and embraces the underlying neurophysiology becomes more compelling each year.

Results Research Question 2

Literature for Research Question 2 was selected to gain a deeper understanding of the biological, physiological, and neurological impairments of trauma and chronic disease and the

implications for treatment. The articles examined included information about the PNI and IPNB of childhood trauma and early life stress, and the interrelationship between complex trauma, chronic disease, and aging. I reviewed 43 to explore the psychoneuroimmunological aspects of childhood trauma and adult mental and physical comorbidities (see Table 6). These articles were used in combination with the outcome results of the first research question to identify which mechanisms of treatment identified in recent research have proven to be effective for the target population. The impact of the bidirectional relationships between childhood trauma, chronic physical disease, and the processes of aging were evaluated to inform a potential treatment approach.

Four major themes emerged during the review of literature for the second research question. These were the expanding relationship of science and psychology; the contribution of PNI and related research to an improved understanding of the interconnection between childhood trauma and chronic physical and mental illnesses; the resulting complexity of symptoms resulting from childhood trauma with comorbid diseases; and the deleterious effects of childhood trauma on aging.

Science and Psychology

In the past, psychotherapy has targeted the mind, thoughts, and behaviors. The expansion of psychological theory into the fields of neurological and biological sciences has brought a new dimension to an understanding of psychology and psychotherapy (Moraes et al., 2018). Modern neuroscience used in the field of psychology includes additional variables such as brain chemistry and physiology (Opp, 2016). The literature reviewed indicates that the neurosciences have enabled a more granular understanding of the neurobiological processes associated with childhood trauma (Gonzalez & Berman, 2010). The activity of the mind reflects activity of the

brain; various neuroimaging techniques are available today to reveal both form and function of the brain, revealing neural anatomy, interconnections, chemistry, physiology, and electrical and metabolic activity. The tools used include functional magnetic resonance imaging, positron emission topography scans, diffusion-weighted magnetic resonance imaging, magnetoencephalography, and electroencephalography. In a 2018 SLR of 25 controlled neuroimaging trials on victims of childhood trauma, findings showed evidence of long-term effects on the brain that differed depending on type of trauma. This data allows psychological and neural processes involved in many human functions such as emotion, self-perception, and self-regulation to be identified, shedding more insight into the workings of the human mind (Gonzalez & Berman, 2010). Outcome studies for PNI interventions such as mindfulness often include some form of neuroimaging to provide evidence of the changes brought about by various mindful-based interventions (Moraes et al., 2018). The increased insight into neurobiology informs not only the theoretical field of psychology but also psychotherapy. The ability to examine changes in brain connectivity, structure, and function as outcomes in RCTs of various psychotherapeutic interventions has enabled the efficacy of theoretical understanding to be evaluated empirically.

Contribution of Psychoneuroimmunology

A review of the literature on the broad ranging field of PNI contributes towards a more comprehensive understanding of the physiological mechanisms and pathways affected by early life trauma, and how they cause changes to normal developmental processes of childhood that may persist throughout the lifespan (Bryan, 2019; Burke et al., 2017; Chang et al., 2019; Danese & Lewis, 2017; Dye, 2018). Research in the fields of PNI provides evidence of the potentially lasting effect of chronic childhood trauma on the child's stress response system, identifying

pathways that result in molecular and genetic changes that disrupt normal development and function of neurological, immune, and endocrine systems (Boullier & Blair, 2018). These changes can result in impairments of the immune, cognitive, and metabolic functions (Russell & Lightman, 2019), often leading chronic mental and physical illnesses, including anxiety, depression, heart disease, cognition, autoimmune conditions, and other chronic diseases (Agorastos et al., 2019; Burke et al., 2017; Chu et al., 2021; Danese & Lewis, 2017). The information provided through the study of PNI can be evidenced in neuroimaging data. Several studies have examined the use of neuroimaging data in treatment of PTSD and identified areas of value in neuroimaging data (Marwood et al., 2018; Santos et al., 2019).

Danese and Lewis (2017) conducted a review of PNI research and concluded that experiences early in life establish long-term interaction patterns between neurological and immunological processes; this interaction enables behavioral effects on immune system function (Dantzer, 2018). The interaction from the immune system to the brain targets brain regions associated with psychological well-being and emotions (Alexander et al., 2021). The behavioral interactions between the CNS and the immune system arise from the effects of conditioning and the stress response on the immune system, also affecting emotions, sleep, activity levels, and appetite (Godoy et al., 2018). The PNI mechanisms of early-life stress create the risk of pathologies both psychological and physiological in nature. Danese and Lewis proposed that the PNI of early-life stress can provide a flexible framework to enable a more comprehensive understanding of childhood trauma and of potential psychotherapeutic treatment. Additional research has uncovered links between PNI mechanisms and cancer (Lissoni et al., 2017), depression and schizophrenia (Muller, 2017), anxiety (Ray et al., 2017), and autoimmune diseases (Honeyman, 2016).

Complex Symptomology of Childhood Trauma

Recent research on early life trauma and the corresponding inhibition of neural integration sheds light on the dysfunction that presents via the symptomology of childhood posttraumatic stress, often posing significant challenges to diagnosis and treatment (Giourou et al., 2018). These challenges include dysfunctional storage of traumatic memories, psychological defenses, shame, dissociative tendencies, somatization, and affect regulation that can result from early attachment ruptures.

The incorrect storing of traumatic memories leads to flashbacks, nightmares, hypervigilance, and other symptoms of trauma. Ward et al. (2017) proposed that using a filter of neurobiology in psychotherapy can enable integration of a memory into the conscious memory bank. Unlike earlier etiological concepts of psychopathology, the neurosciences provide more detailed and useful insights into neurobiological impairments which can then inform not only the development of a more sophisticated theoretical framework, but also specific interventions to neutralize some of the symptoms of complex trauma, and how to transition complex trauma patients through stages of treatment effectively (Grawe, 2017). Psychological defenses are developed in childhood as a response to chronic ACEs. These include avoidance, often leading to addictive behaviors; idealization of self or others which can present as narcissism (self) or unhealthy attachments; or inappropriate shame or self-blame for negative events that were outside the control of the child. These defenses serve to block unresolved traumatic memories from the conscious mind, hindering processing and reintegration of the trauma. Dissociation is another dysfunctional defense in trauma; when the suffering and dysfunction is too great to bear, dissociative tendencies can occur, ranging from temporary loss of awareness of the present moment to division of personality into separate identities. The last category addresses the affect

regulation difficulties as an individual experiences triggering events reflecting past experiences rather than present reality. Emotional dysregulation is a widely experienced symptom of any trauma, and it is especially damaging to people who have experienced attachment issues in childhood, as they recreate past relationship ruptures in adult life.

Another factor that affects trauma symptomology is somatization. Somatization is a process that occurs when psychological dysfunction manifests itself as physical bodily symptoms. Early life stress and the dysregulation of physiological systems can lead to somatization problems (Brosschot et al., 2018; van der Kolk, 2019). According to Kroenke (2003, as cited in Victor & van Dyke, 2017), 33% of physical symptoms reported to healthcare providers present no identifiable disease correlates. SE is a nonpsychoanalytic, biophysiological treatment model that adopts a bottoms-up approach, working directly with physiology and body memory, and progressing towards the higher cortical systems to reprogram the way the body responds to stored trauma (van der Kolk, 2019). It provides a way to work with trauma patients who are experiencing generalized unsafety, overwhelming anxiety, panic, agitation, hypervigilance, rage, and other dysregulated emotions (Levit, 2018). SE directs the client inward towards to experience internal bodily sensations, rather than engaging emotions and cognitions associated with trauma (Kuhfuß et al., 2021). This process allows a discharge of physiological stress thereby releasing the activated trauma symptomology, restoring the ANS to normal functioning. The physiological sensations of overwhelm experienced by trauma victims can lead to dissociation. They are mediated by the survival functions of the fight-flight-freeze response of the amygdala (van der Kolk, 2014), which lead to disruption and impairment of hippocampal and cortical functioning, preventing their participation in the processing, recoding, and integration of unbearable experiences (Levit, 2018). SE is beneficial to some adult victims of childhood

trauma, allowing a mechanism for reengagement of the trauma without an extensive retelling of the events. Emotional processing can take place and trauma victims can gradually come to accept sensations and emotions (Brom et al., 2017; Kuhfuß et al., 2021).

The Impact of Childhood Trauma on Aging

Rowe and Kahn's (1998, 2015) successful aging paradigm, modified by Zolnikov (2015), identified several necessary aspects of successful aging, or well-being during the aging process: a low likelihood of disease and disability, good cognitive and physical capacities, active engagement in life, and environmentally favorable conditions. Recent research supports a strong association between childhood trauma and accelerated aging (Chen et al., 2018; Colich et al., 2020). Stress causes structural and functional changes to the amygdala that persist through the lifespan and facilitate stress biology in the peripheral nervous system (Miller, 2016). Thayer et al. (2021) studied the normative changes of aging and the effect of stress on the aging processes. They concluded that negative stress could create premature aging and accelerate physiological aging. Further, the high cortisol levels associated with early life stress create oxidative stress, leading to inflammation and cell damage, leading to high-risk behaviors that exacerbate the progression of chronic diseases and aging (Holter et al., 2021). Older adult victims of unresolved childhood trauma with cognitive and physical decline may not be able to participate effectively in psychotherapy, thereby exacerbating the challenges of successful aging as they struggle with the long-term effects of untreated trauma (Palmer et al., 2020). The results of unresolved trauma together with diminished cognition and memory further contribute to feelings of stress and anxiety about loss of function and freedoms, often leading to despair.

Discussion Research Question 2

The literature review for Research Question 2 validates the findings for Research Question 1: the paucity of research of on treatment of adult victims of childhood trauma and comorbid physical diseases. Although the numbers of adults identified in this population are steadily increasing, a more integrated treatment approach has not emerged in the treatment guidelines yet. Researchers in the fields of PNI have made significant contributions to an understanding of the complex, intertwined interactions of body and brain when a child experiences chronic adverse conditions of neglect, lack of emotional attunement, or sexual or physical abuse. Research in this field has greatly informed comprehension of the mechanisms of trauma in childhood, the interactions with other neurophysiological systems, and the consequences throughout the lifespan. Unfortunately this recent knowledge is not well reflected in current psychotherapeutic models.

Despite this lack of application, the literature reviewed for Research Question 2 supports the fact that the science exists today to provide more person-centric treatment based on neurobiological evidence as well as self-report and symptomology. The value of neuroimaging is underutilized in both diagnosis, treatment planning, and outcome measures for trauma. Neuroimaging technologies are costly; however, the direct costs of psychotherapy are only a small fraction of the costs of psychological impairment; the indirect costs to families and societies are hard to measure but extensive. The use of neuroimaging in prediction is also being studied in chronic diseases (Hall et al., 2018). Although much is still to be learned about the brain systems and biochemistry, the current body of knowledge seems enough to make use of neuroimaging data, just as it is used in physiological diseases and conditions. Varied results in different studies highlight the uniqueness of individual responses to traumatic early life stress

and treatment modalities; what works for one patient often does not work for another. Adding the neurobiological data into the clinical evaluation would provide value to diagnosis and treatment.

Also unresolved is the use of phases and different interventions at different stages of trauma treatment, with inconsistent research findings. There are several factors that suggest that the concept of phased-based treatment should be given consideration in treatment planning. Individual responses of adults with childhood trauma often vary widely; personal circumstances of the trauma, the level of abuse and unsafety, the presence or absence of an attachment figure, and other variables indicate that these factors need consideration when formulating a case conceptualization and treatment plan. Generally, the complexity of the conditions involved, together with their etiology, is not well accommodated in the Western medical model, and patients are correspondingly underserved. Furthermore, findings from PNI research are not generally incorporated into clinical training to enhance the practice of medicine. Although some graduate-level courses in counseling psychology offer one or more classes related to PNI, there exist no evidence-based models of treatment for successful psychotherapy for adults living with the shroud of chronic diseases arising from childhood trauma.

Results Research Question 3

Research Question 3 was used to develop a new psychotherapy treatment model for adult victims of childhood trauma that addresses the interrelatedness of physiology and psychology across the lifespan, using a basis of trauma-informed care, and adjusted to address the underlying impairments of chronic disease. I reviewed 48 records reviewed to understand the context and possibilities for Research Question 3 (see Table 6). Theories and models in psychology provide a framework for understanding complex phenomena of human belief, thought, and behavior; they enable exploration and identification of ways to bring about change where needed. Theories take

the current understanding of a subject area such as human behavior and attempt to provide a probable explanation structured in a way that links to potential causes and effects. Models can then be developed from theories to create schematic representations of the subject matter, instantiating the theoretical understanding into research, which can be used to explore treatment methodologies. Today's models of psychotherapy are derived from theories of psychology developed over many decades. Traditional branches of psychotherapy include psychoanalytic, cognitive-behavioral, and existential-humanistic, and integrative; various models of treatment exist in each area, unified by a common theme. The last decade or more has seen the emergence of new constructs based on the rapidly growing fields of neuroscience including neurobiology and PNI, and their application to psychology. These new theories may fit well into an integrative understanding of human psychology, and it is from this field of research that a new model may be derived.

Findings from Research Question 1 and 2 were combined with additional literature to determine what overarching model of psychotherapy might be developed for consideration in effective treatment in the context of the dynamically changing interrelationship between brain, nervous, endocrine, and immune systems of the body. Four themes were identified: the challenges to effective treatment, the need to explore flexible psychotherapeutic models through the lifespan, the use of trauma-informed care in a phase-based treatment approach, and the role of the psychotherapist in treatment.

Table 5

Sources for Research Question 2

Psychoneuroimmunology	Childhood trauma	Psychotherapy	Aging	Chronic diseases
Ader, 1980	Agorastos et al., 2019	Brom et al., 2017	Rowe & Kahn, 1998	Hall et al., 2018
Alexander et al., 2021	Boullier & Blair, 2018	Chen et al., 2018	Rowe & Kahn, 2015	Holter et al., 2021
Brosschot et al., 2018	Bryan, 2019	Graw, 2017	Thayer et al., 2021	Van der Kolk et al., 2019
Burke et al., 2017	Chang, et al., 2019	Levit, 2018	Zolnikov, 2015	Victor & van Dyke, 2017
Chu et al., 2021	Dye, 2018			
Colich et al., 2020	Giourou et al., 2018			
Danese & Lewis, 2017	Palmer et al., 2020			
Dantzer, 2018	Speidel et al., 2020			
Godoy et al., 2018				
Gonzalez & Berman, 2010				
Honeyman, 2016				
Kuhfuß et al., 2021				
Marwood et al., 2018				
Moraes et al., 2018				
Muller, 2017				
Opp, 2016				
Ray et al., 2017				
Russell & Lightman, 2019				
Santos et al., 2019				
Ward et al., 2017				

Challenges to Treatment

The diverse literature on trauma research reveals the variability of individual presentation, experiences, and consequences of trauma, trial selection processes and methodologies, trauma assessment measures, treatment approaches and plans, outcome measures, and more. Some of these are pose challenges to meaningful and generalizable research. With the individual nature of traumatizing experiences especially when self-reported, the range of neurobiochemical responses, and the diversity of symptom presentation and diagnostic inconsistencies, homogeneity in participant groups in outcome studies may be questionable, making it difficult to identify causative variables in specific outcomes. Another challenge to trauma treatment lies in the potential neurobiological consequences of chronic childhood trauma: trust issues, generalized unsafety, somatization, somatosensory repeats, repressed memories, intrapsychic defenses, traumatic memory processing, hypervigilance and hyperarousal, dissociation, dysregulation of emotions, and altered conceptualization of self and others. Many of the PNI interactions that arise from trauma result in feelings of generalized unsafety, hypervigilance, and trust issues (Brosschot et al., 2018). Chronic early life stress also often leads to multiple impairments of attention, memory, cognitions, somatization, numbing, and others (Nelson et al., 2020), and distorted beliefs about self and others (Danese & Widom, 2020), which can have a negative impact on effective participation in the therapeutic process (Corrigan & Hull, 2015). Traditional psychotherapeutic models such as cognitive or emotionally focused interventions, or exposure therapy, are often not successful in modifying dysregulation of the autonomic nervous response on a daily basis (Fisher, 2019).

The failure of diagnostic categories to address the complexity of symptoms arising from chronic childhood trauma has been a major challenge to research, accurate diagnosis, and treatment. Although early life trauma was recognized in the study over 20 years ago (Felitti et

al., 1998) this has not been reflected in standard diagnostic tools until the recent introduction of complex trauma in the ICD-11 (WHO, 2018a), adopted in the United States in January 2022. The definition found in the DSM-5 (APA, 2013) continues to define trauma as experiences that have the potential for serious harm: “actual or threatened death, serious injury, or sexual violence” (p. 271). This definition excludes psychosocial events and does not directly address the developmental trauma that occurs during ACEs. As a result, a PTSD diagnosis misses the broader symptomology found in so many adult patients with childhood trauma (Ford, 2017a). This failure to address the complex symptomology presented by chronic adversity in early childhood years led to the continuation of the status quo: adults with childhood trauma are regularly diagnosed symptomatically with mood, anxiety and other disorders while ignoring the underlying PNI that results from chronic early life stress.

Traumatic stress often results in feelings of being overwhelmed by, or conversely, numbing out emotions and even dissociation (Greenberg, 2021). Treatment can be compromised by the fact that traditional modalities lack techniques that directly address the autonomic and somatic effects of trauma; sensitivity to trauma stimuli, dysregulation of the ANS, and tendency toward decompensation as stress levels rise can prevent effective treatment (Fisher, 2019). The bidirectional pathways involved in neurobiological changes resulting from trauma lead to the creation of brain circuitry that can tend toward self-soothing addiction behaviors such as substance abuse and overeating (Holter et al., 2021; Hostinar et al., 2018). Addictive behaviors generally pose a problem in psychotherapy, where the pull of the addiction is often too great for consistent participation in trauma treatment.

Lewis et al. (2020b) conducted a systematic review of literature of RCTs and found that dropout rates for patients undergoing individual psychotherapy for trauma are higher than for

patients in treatment for nontrauma-based mental health disorders. Lewis et al. noted that although this data may be an artifact of study methodologies and limitations, the results are consistent with recent studies of treatment specifically targeting childhood trauma or C-PTSD. Psychotherapists also sometimes avoid trauma-based interventions because of concerns about tolerability and dropout (Lewis et al., 2020b). There are conflicting findings on the topic of dropout, however, in part attributed to variability in populations and study methods; dropout data are also misleading because it includes all reasons to leave treatment versus negative experiences to interventions (Lewis et al., 2020b).

Other factors that can impair psychotherapeutic efficacy include the pressure in community health and health insurance companies for goals associated with reducing symptoms, which leads to a lack of clinical focus on affective experience and other critical symptomology of childhood trauma (Corrigan & Hull, 2015); the pressure for time-limited treatment in many insurance plans (Corrigan & Hull, 2015); and the current disagreement and lack of adequate empirical data to understand the value of a phased approach that starts with stabilization. Many patients with childhood trauma have insecure and disorganized attachments (Slade & Holmes, 2019), coupled with generalized unsafety (Brosschot et al., 2018). The psychotherapist can serve as a proxy for some of the requisite components of secure attachment, but this can only happen when trust and a degree of safety are established (Tsai et al., 2019).

The addition of chronic physiological diseases such as diabetes, heart disease, and autoimmune conditions adds another layer of challenges as adult survivors of childhood trauma struggle with physical difficulties; the interaction between impaired psychology and physiology can be overwhelming and can also lead to high-risk behaviors (Garrido et al., 2018). The processes of aging exacerbate the effects of chronic disease, and when trauma

remains untreated, can amplify the mental and physical symptoms. Thayer et al. (2021) conducted a study on aging and the effects of stress and conclude that negative stress can accelerate the processes of physiological aging. Understanding the mechanisms, pathways and biomarkers involved in processes of chronic disease and aging can inform a model of psychotherapy for adult victims of childhood trauma with comorbid mental and physical diseases.

Psychotherapy Across the Lifespan

Psychotherapeutic treatment for traditional PTSD often has positive outcomes (Valenstein-Mah et al., 2019; Voorendonk et al., 2020). The underlying theories do not, however, incorporate the complexities of psychological and physiological changes that may span a lifetime after a traumatized childhood. As the body ages, bidirectional pathways altered through trauma responses extend to processes of aging resulting in functional and structural changes to the brain (Thayer et al., 2021). The impediments to long-term health and functioning and increased vulnerability to mental and physical disease begin to merge with the inevitable processes of aging (Agorastos et al., 2019; Copeland et al., 2018; Sonu et al., 2019; van Assche et al., 2020). The presence of chronic diseases creates oxidative stress, with a negative effect on tissue functioning (Cabello-Verrugio et al., 2017) further exacerbating aging. Thayer et al. (2021) concluded that inhibiting some of the physiological consequences of stress by learning how to manage stress and building resilience requires both emotional regulation and stress management. Many adult victims of childhood trauma do not receive effective trauma treatment; as this population ages, a psychotherapy model that incorporates stress management is even more critical than in younger years, given the trajectories of mind and body associated with growing old. Psychotherapy for aging adults should address the complexity of childhood trauma, chronic

diseases, as well as the developmental challenges of aging, the need for life review, and other more traditional therapies for seniors. It should do so, however, in the context of an understanding of the increased vulnerability of adult victims of childhood trauma and comorbid chronic disease.

Trauma-Informed Care and Phased-Based Treatment

Trauma-informed and *trauma-focused treatment* are terms often heard today in psychotherapy. The concepts can be interpreted in a couple of ways, which are often used without clear definition in the literature. Trauma-informed care typically involves providing the therapist with some level of training in the neurobiopsychological aspects of trauma, symptomology, and trauma-focused interventions. The United States Department of Health and Human Services (2012) suggested that a trauma-informed approach to psychotherapy treatment be guided by safety, empowerment, collaboration, trust, and choice. It shifts the focus from dysfunctional symptomology towards the lived experiences of the trauma victim, and can filter the impact of trauma on emotions, thoughts, behaviors, self-regulation, and sense of self (Sweeney et al., 2018). In this way, a trauma-informed therapist can tailor interventions with an understanding of an individual's personal history of trauma, triggers, and reactions.

Attachment trauma is common in C-PTSD, with significant implications for the therapeutic alliance and for treatment planning (Kinley & Reyno, 2019); a psychotherapist working with childhood trauma needs specific training and strong sensitivity to the neurobiopsychological impacts of the trauma and of interventions. Many therapists who work daily with trauma patients lack the necessary specialized training and run the risk of deepening the psychological wounds of trauma. In addition to trauma training, Racine et al. (2020) proposed the need for a universal approach to identifying and addressing trauma in psychological

and physiological care by administering a more standardized trauma assessment instrument for individuals seeking care; today several are used and may be based on DSM-5, ICD-11, or other self-report or clinician-administered measures. In addition, today in the United States many illnesses of mind and body present as symptoms of underlying trauma but are treated at face value without addressing the traumatic dysfunction that directs an individual's life if left untreated.

The problematic presentation of adults with ACEs may be influenced not only by model of psychotherapy but also by timing and staging of interventions. Franco (2021) advocated for a tripartite approach to treatment of C-PTSD, beginning with coping in the present moment with what presents, followed by working to address root causes of traumatic experiences, and finally learning how to move on with life; all of these require the formation of a successful therapeutic alliance. Coping in the present moment calls for working with the patient to achieve an improved sense of safety, emotional regulation, and generally functioning. The middle stage is about processing trauma, rescripting or reframing the narrative, and integrating the traumatic memories. The last stage involves helping the patient learn to let go of distorted beliefs and building healthy relationships with self and others and improving daily functioning (Franco, 2021).

Cloitre et al. (2010, as cited in van Vliet et al., 2021) conducted an RCT to evaluate the effectiveness of a phase-based treatment approach. The trial comprised three groups who received either skills training followed by prolonged exposure therapy; or supportive therapy followed by exposure therapy; or skills training followed by supportive therapy. The results for the skills/prolonged exposure group were the most favorable, and Cloitre et al. concluded that the phase-based approach was more effective than the trauma-focused approach. This study had

several limitations, however, including the absence of a control group receiving only exposure therapy.

Corrigan and Hull (2015) conducted an SLR on 13 studies on trauma treatment, finding that that there may be efficacy in a phased treatment approach across complex trauma presentations,. Other studies have conflicting findings. Van Vliet et al. (2018) conducted an RCT to reexamine the question of a stabilization phase prior to trauma treatment for individuals with ACEs and possible complex trauma. The study included 122 adults between the ages of 18 to 65 years with trauma symptoms and self-reported history of repeated childhood abuse. Participants were allocated to one of two groups: one group's treatment began with stabilization, in the form of eight sessions of Skills Training in Affect and Interpersonal Regulation (STAIR), followed by 16 sessions of EMDR. The second group received the 16 sessions of EMDR with no preliminary phase. Assessments were conducted prior to treatment, after every eighth session, posttreatment and at 3 and 6 months follow up. Secondary study endpoints were the severity of PTSD symptoms, changes in trauma symptoms, and quality of life. These were assessed using the Clinician-Administered PTSD Scale for DSM-5, the Structured Interview of Disorders of Extreme Stress-Revised, and symptom-specific questionnaires. Both treatment groups showed symptom reduction in the posttreatment assessments, with 68.8% of the combined participants no longer meeting the full criteria for PTSD posttreatment, and 3.3% still met the criteria for C-PTSD compared with 28.9% at baseline. No significant difference was found between the treatment groups on any psychopathology scale. Dropout rates for both groups were similar.

The Role of the Psychotherapist

The role of the therapist is an essential element of psychotherapy; the alliance between psychotherapist and client has the potential to repair attachment ruptures, having features of an

attachment relationship, and it can serve as the basis for change (Slade & Holmes, 2019). The need for a trauma therapist to understand safety, trust, and relational issues in trauma is vital for successful navigation of traumatic experiences (Crits-Christoph et al., 2019). Heinonen and Nissen-Lie (2020) conducted a SLR of how therapist pretreatment characteristics effect patient outcomes. Their findings suggest that the more effective therapists appear to have strong interpersonal skills, which are probably a reflection of their own personal lives and attachment history. Ellis et al. (2018) conducted a systematic review of relevant literature and found several studies establishing a positive association between a reduction in trauma symptomology and relationship variables in the therapeutic relationship.

The therapeutic alliance can create a safe holding environment for the client in which exploration of trauma can take place. One example is in the SE model of psychotherapeutic treatment: the therapist is a coregulator of the tension between danger and safety (Levit, 2018). Coregulation, generally associated with psychoanalytic therapy for trauma, is equally important in SE, where any kind of exploration of bodily stored traumatic events may destabilize the patient to the point of dissociation, as most psychotherapists who work with trauma victims well know. The therapeutic alliance also serves to repair attachment failures and ruptures; with SE, the therapist's ability to attune to the patient's sensory and affective states in a nonjudgmental and safe manner allows the patient to be vulnerable emotionally, physically, and mentally (Levit, 2018). In situations where the therapist may not be able to hold space for the patient in this way, it may be difficult or impossible for SE to succeed in bringing relief. The therapist's skill in SE interventions is a critical factor for successful processing. If the therapist is not sufficiently trained, or has not processed personal trauma successfully, they may unwittingly enact the role of abuser (Levit, 2018). Levit (2018) pointed out that highly charged emotions during SE may be

misinterpreted as dysregulation. Although SE avoids direct confrontation of traumatic memories, processing bodily stored sensations from the trauma could potentially be a form of retraumatization; Levit commented that other parts of the brain, not directly involved in the somatic process, are still active and may mediate cortical function dysregulation because of the experiential process, paralleling the brain processes at work when watching a television show or movie; part of the brain is engrossed in the story unfolding on the screen, whereas other functions of the brain hold awareness of the fictitious nature of the event.

Discussion Research Question 3

The rise in chronic diseases worldwide and the prevalence of mental and physical comorbidities has so far failed to secure enough attention to conduct sufficient research to align psychotherapy treatment modalities with current understanding of the bidirectional relationships between mind and body and the resulting damage to lifelong psychological and physiological processes that can rise when a young child experiences chronic adverse conditions. Learnings from science provide information for a framework of the trauma life cycle and the potential efficacy of different approaches. Additionally, neurobiological data can potentially be used to create an integrative representation of brain connectivity and function as input to a theoretical model of psychopathology that may enhance current models of treatment and introduce new perspectives (Venkadesh & van Horn, 2021). An example is the field of IPNB, which draws from many branches of science and integrates them to improve the understanding of mind and brain. It provides a framework for understanding how brain development shaped by early childhood relationships and relationship ruptures can direct an individual's mental and emotional life (Siegel, 2020). In summary, research data, though insufficient and often not generalizable, is

sufficient to open the way to a new approach to a treatment framework and model of psychotherapy.

CHAPTER FIVE

Discussion

The psychological implications of chronic ACEs are now acknowledged and evidenced in research (Copeland et al., 2018; Dube, 2018; Dye, 2018). The effects of chronic early life stress on physical health and aging are wide-ranging and can persist through the lifespan (Berens et al., 2017; Bryan, 2019; Chang et al., 2019; Sonu et al., 2019). Childhood trauma can result in prolonged activation of the stress response system, causing damage to neural, immunological, and other physiological systems, resulting in vulnerability for a broad spectrum of chronic physical and mental illnesses in adult life (Teicher et al., 2016). Chronic early childhood stress contributes to the increase in comorbid chronic psychological and physiological disease in the United States and other countries. In the United States, chronic diseases are estimated to cause approximately 75% of death (Harris, 2019). According to the CDC (2019b) six out of 10 adults in the United States have been diagnosed from a chronic disease; four adults in 10 have two or more diseases. The burden of healthcare spending and diminished quality of life poses an ever-increasing problem in spite of the advances of modern medicine. The long-term results of childhood trauma may share etiology but lack an integrated treatment approach. Mental health disorders are treated through psychotherapy; chronic physiological diseases and problems of accelerated aging are the purview of general and specialist practitioners of medicine; there is little, if any, coordination of care between the two healthcare disciplines. Findings of research studies on the long-term effects of ACEs have not been well integrated into current clinical psychotherapy models (Berens et al., 2017) despite the widespread nature of the problem; there are few research studies that directly address treatment of adult victims of childhood trauma with comorbid mental and physical illnesses.

The first objective of this literature review was to examine the efficacy of psychotherapeutic treatment modalities for adults with childhood trauma and comorbid mental and physical illnesses. The second was to understand how recent research in PNI and related fields can inform the treatment of adult victims of childhood trauma with comorbid mental and physical illness. The third objective was to develop a model of psychotherapy that addresses the interrelatedness of physiology and psychology, using a basis of trauma-informed care, adjusted to address the underlying impairments of chronic disease.

RQ1. How efficacious are current psychotherapeutic treatment modalities in the treatment of adults with adverse childhood experiences and comorbid physical and mental illness?

RQ2. How has recent research into psychoneuroimmunology and related fields informed the treatment of comorbid mental and physical disease?

RQ3. What model of psychotherapy can be developed that addresses the interrelatedness of physiology and psychology across the lifespan, using a basis of trauma-informed care, and adjusted to address the underlying impairments of chronic disease?

Three theoretical frameworks were used to support this research. The first framework addresses the psychotherapeutic treatment modalities for adults who present with trauma symptoms; relevant models include psychodynamic theory, CBT, mindfulness-based CBT, EMDR, neuropsychotherapy, and trauma-informed care. The second theoretical model was polyvagal theory. A critical goal in trauma treatment is to return the ANS to a healthy state (Porges, 2011). Polyvagal theory provides a framework for understanding the mechanisms by which stress responses reprogram the ANS to remain in a defensive state, leading to physiological changes and dysregulation. The third theoretical framework was Rowe and Kahn's (1998, 2015) successful aging theory, including an adaptation by Zolnikov (2015) to the model

to extend its applicability to low- and middle-income populations by adding considerations of the environment and access to health care to the aging process. The Row and Kahn/Zolnikov model provides a foundation of aging into which the effects of childhood trauma can be incorporated and understood. Using these three theoretical frameworks, this research will focus on navigating trauma-informed care in the successful aging approach.

This study was conducted using systematic review methods guided by the PRISMA guidelines and checklist as a model when searching databases (Higgins et al., 2017; Moher et al., 2009; Li et al., 2019). The breadth of the topics included initially resulted in 445 records; after screening, 402 were used; 19 for Research Question 1, 43 for Research Question 2, 48 for Research Question 3, and 238 for background and educational material of the research areas.

Findings

The word *psychology* derives from psyche, a Greek term for soul or spirit. Today psychology refers to the study of mind and behaviors; in essence, it is about the self as manifested in thoughts and deeds. After birth, an individual is subject to life events that shape their sense of self, others, and the world generally, with corresponding effects on functioning. Individuals react differently to both positive and negative experiences; individual changes influence the anatomy of the brain (Karmiloff-Smith, 2011; Valizadeh et al., 2018). Valizadeh et al. conducted a longitudinal study of 191 healthy older people using magnetic resonance imaging to assess 450 anatomical features. They identified an individual combination of specific brain characteristics for every individual to the degree that each brain could be uniquely identified. Similarly, individual biochemistry varies within the limits of physiological constraints (Schulz, 1994). The unique nature of individual brains and biochemistry is the playing field of the study of psychology. Review of the literature for all three research questions underscored the diverse

nature of the human brain and biochemistry, and the challenges posed to effective diagnosis and treatment of trauma when physiological comorbidities are present. Effective research in psychology needs to recognize human diversity in anatomy, physiology, and psychology, albeit within some limits, and account for it as systematically as is possible given the human subject matter. All research findings should be viewed with the understanding that human minds and behaviors sometimes defy scientific methods.

The goal of treatment for any illness or disorder is to reduce symptoms and ideally to improve functioning in some quantifiable way. Several themes emerged during the review leading to insights into the treatment of adult victims of childhood trauma with comorbid chronic disease. Research studies on outcomes generally include symptom reduction endpoints, and sometimes quality of life assessments, neither of which necessarily provides evidence that the individual has fully integrated the traumatic experiences and achieved a high level of functioning with a coherent and cohesive sense of self. The absence of endpoints assessing integration of trauma became apparent in the literature reviewed for the first research question. Generally results indicated that in many cases current psychotherapeutic treatment can be efficacious for PTSD as measured mainly by symptom reduction versus resolution or change to inherent sense of self and functioning. It is also apparent that the number of variables involved in trauma responses and symptomology, diagnosis, population sample selection, inclusion and exclusion criteria, instrumentation, and application of treatment methods introduce a degree of subjectivity into the process that may lessen the repeatability and generalization of the results. For example, symptom reduction is often an outcomes study endpoint; it is not always the case that symptom reduction leads to well-being and higher functioning. Although current treatment for PTSD has some success in symptom reduction and quality of life improvements, there is little research

examining longitudinal effects of treatment over a lifespan, and to what degree psychological well-being is sustained after treatment ends.

Assessing the efficacy of current psychotherapeutic treatment for childhood trauma is fraught with challenges. Childhood trauma often does not present as PTSD. Individuals seek treatment for symptoms they recognize as mood disturbances or frequent feelings of anxiety. They often complain of sleep or appetite disruption, sometimes nightmares or flashbacks, and occasionally anger. Unfortunately, sometimes psychotherapeutic interventions are focused only on the client's self-report of symptomology, without an in-depth assessment of the underlying etiology of the symptoms. The field of PNI and related research has provided strong evidence for the different pathways that create some of the symptoms experienced, and many are related to chronic adverse experiences in early childhood that constantly activate the stress response. Childhood trauma can result in a more complex presentation of symptoms than PTSD, creating more difficulties in diagnosis and treatment (Giourou et al., 2018). Symptoms very common in childhood trauma are often overlooked and may result in a single disorder diagnosis, such as depression, or even PTSD. The relatively new creation of a C-PTSD diagnostic category which adds a new symptom cluster known as disturbances in self-organization (DSO). The DSO symptom clusters (emotional dysregulation, interpersonal difficulties, and negative self-concept) add a degree of complexity that is not fully addressed in many psychotherapeutic interventions for trauma currently. Many individuals fail to recognize or identify their emotional dysregulation, interpersonal issues, feelings of shame, or an incoherent or disorganized sense of self when they initiate treatment; in fact, it is common for these individuals to ascribe their feelings to the behaviors of others rather than to recognize any inherent dysfunction on their own part.

The diagnosis of C-PTSD, most closely describing the effects of chronic childhood trauma, is relatively new in diagnostic manuals and lacks a significant body of outcomes research. As a result, the most common outcome studies for trauma address PTSD, which, although sharing three symptom clusters with C-PTSD, lacks the critical differentiation of the disturbances in self-organization (DSO) cluster now associated with childhood trauma. There was less support for current psychotherapeutic treatment modalities for C-PTSD, particularly so in the case of reduction of the DSO symptoms (Corrigan & Hull, 2015). Furthermore, the experience of disruption of physiological and psychological processes resulting damage to brain, immune and endocrine systems is so dependent on the nature of the trauma, individual brain anatomy and biochemistry, resilience, and other mitigating factors, that making sense of treatment results is not a simple matter. Almost no studies reviewed here attempt to differentiate in PNI processes, symptoms, and intervention results based on type of childhood trauma; all trauma is not equal. For those studies when an attempt was made to filter on childhood trauma, confounding factors challenge the statistical value of the research: defense mechanisms that repress trauma memories including denial and dissociation, childhood trauma studies with adults often rely on self-report or previous diagnosis by a clinician untrained in trauma, the length and nature of the trauma, possible resilience or vulnerability of the victim: all these and more are significant in assessing efficacy of treatment for childhood trauma victims.

On a broader level, the APA clinical practice guidelines (2017) do not reflect current research on the etiology, progression, and symptomology of PTSD. C-PTSD was not a diagnosis when it was published, but the guidelines have been the subject of much criticism even for PTSD (Dauphin, 2020). Specifically, Dauphin (2020) noted the exclusive use of randomized clinical trials, limited definitions of outcomes, inconsistencies with APA's 2012 resolution of the

recognition of psychotherapy effectiveness, the formulaic connection between diagnosis and treatment, and several other problems. APA (2017) concluded that there was little research to indicate which treatments are most effective for adults with trauma. In 2021 the APA convened a new multidisciplinary panel to examine more current evidence on the treatment of PTSD; results are not yet available, but it is to be hoped that complex trauma is addressed and some of the earlier flaws are lessened.

Another finding that emerged from the literature review for the first two research questions is the treatment gap for adult victims of childhood trauma with comorbid physical illnesses. Chronic comorbid mental and physical illness has not been the subject of much research, nor do most current psychotherapeutic treatment models address the impact and implications of chronic disease with psychological disorders. Adults with childhood trauma, psychological and physiological disease emerged as underserved in current research on the target population (Sartorius, 2018), evidenced by the lack of available published research. Further disparity in treatment arises from the shortcomings of treating childhood trauma via a PTSD diagnosis and related interventions. Other factors include the relative scarcity of trauma-informed models of treatment, and the absence of longitudinal studies on adults with childhood trauma and comorbid physical and mental illness across the lifespan. Timing and sequencing of interventions is also important for complex symptoms; current psychotherapeutic models are generally effective for traditional PTSD, but outcomes for complex PTSD are better when the psychotherapy is phased-based and trauma-focused (Voorendonk et al., 2020).

The Western model of medicine is generally fragmented, in that specialists work with specific organs and processes of the body without taking a systems view of the body in its entirety. This model is heavily reflected in the extensive use of medications purely to treat the

side effects of medications prescribed to minimize symptoms of diseases; the resulting polypharmacy makes it difficult to identify originating symptoms versus side effects. Polypharmacy also affects psychotherapeutic use of medications for mental health disorders; patients often complain of extensive side effects, and diagnostic symptoms become more intertwined and difficult to interpret. Western medicine has evolved into a reductionist approach, with pharmaceutical products as the treatment of choice, administered to minimize symptoms without comprehending the system in which they are applied.

There is a compelling need to adopt a more comprehensive approach to treatment of mind and body; an example is the relatively new field of functional medicine and functional psychiatry. Functional medicine is an interdisciplinary field using proven quantitative analysis methods to identify and understand relationships between neurotransmitters, immune and endocrine functions, nutrition, and psychological symptoms. Functional medicine makes uses of a broad range of physiological laboratory tests to build a more comprehensive view of physical and mental dysfunction. Beidelschies et al. (2019) conducted a study to assess the association between functional medicine and patient reported health-related quality of life (HRQoL) outcomes and concluded that the functional medicine model of care resulted in beneficial associations with patient-reported HRQoL outcomes and that the results were sustained over the following 12-month period. Similarly, functional psychiatry emphasizes a systematic approach to treating disorders as opposed to masking symptoms with prescription drugs, viewing the symptoms and treatment options in the context of the body as a system.

Functional medicine brings into play the merger of pure science and psychology in treatment of illnesses. The underpinnings of this merger lay in the more recent study of PNI and related fields. PNI addresses the multidirectional relationships between psychological process,

the immune system, and the nervous systems (Moraes et al., 2018). In PNI, the approach is not limited to identification of a single symptom or set of symptoms within one physiological system alone; rather it is used to determine the mechanisms whereby hormones, neurotransmitters and neuropeptides interact with psychological processes and the immune system. Zhong and Shi (2019) concluded that childhood trauma dysregulates the inflammatory response system resulting in increased sensitivity to stressors and higher levels of inflammation linked to many chronic diseases. PNI has contributed to a greatly improved neurophysiological understanding of the etiology of trauma, and how chronic early life stress affects developmental stages and primes the body for diseases later in life. Such an understanding, applied through the lens of functional medicine, can bring about greatly improved diagnoses and treatment across mental and physical comorbidities.

PNI complexity found in C-PTSD. Such understanding can provide a foundation for a greatly improved approach to treatment, with interventions that target specific areas of psychological and physiological dysfunction. Examples of effective PNI-based treatments found in the review for Research Question 1 include EMDR and mindfulness-based interventions; both of which have demonstrated some success in treatment of complex trauma (Boterhoven de Haan et al., 2020; Chen et al., 2018; Dumarkaite et al., 2021; Jasbi et al., 2018; Voorendonk et al., 2020).

PNI of childhood trauma and the processes of aging; each exacerbate the other, rendering traditional psychotherapeutic methods ineffective. The APA has clinical practice guidelines for psychotherapeutic treatment for the aging population, but these do not embrace the results of childhood trauma. Research in PNI explores how early life trauma can cause structural and functional changes to the amygdala that persist throughout life (Miller, 2016). Thayer et al.

(2021) concluded that negative stress such as that resulting from childhood trauma can accelerate physiological aging. Untreated childhood trauma, combined with the later life acceleration of chronic disease pathways, can contribute to common feelings of stress and anxiety in the senior population, as they lose function and freedoms, and fall into despair (Palmer et al., 2020). One conclusion from a review of PNI and trauma suggests that treatment models need to be flexible over the lifespan, in response to changing psychological and physiological processes and abilities. Findings from PNI research can inform flexible models of treatment at different stages of the lifespan.

Review of the literature for all three research questions also brought to the forefront the challenges of treatment for the target population. Already discussed here, the problems facing effective treatment can seem overwhelming and can include variability of research methods, individual instantiations and presentations of childhood trauma, cognitive and memory issues, interpersonal, emotional regulation and self-concept disturbances, diagnostic limitations, the broad absence of solid PNI-based trauma training for psychotherapists, the critical need for a psychotherapeutic approach that is also grounded in client-centered, relational constructs to enable a safe holding space for treatment, comorbid physical disease, and the so-called evidence-based symptom goals and time-limited treatment associated with insurance plans. An approach grounded in PNI adequate training of psychotherapists and policy and healthcare implementation changes will also be required.

A consolidation of the study findings was necessary to answer the third research question. Several findings lead to the same conclusion: current psychotherapeutic treatment models do not address the inherent complexity of the problem set. A systematic examination of the etiology and effects of childhood trauma transcends physiological and psychological experiences of trauma; it

includes ecological and socioeconomic considerations, policy and healthcare implementation, profit motives in healthcare, and the relentless oppression of the less fortunate members of society who have been victimized in childhood and are often ill-equipped to advocate for themselves, remaining relentlessly locked in the shroud of childhood trauma. Some of these barriers to healing require societal change on a level unlikely to be acknowledged in a strongly capitalist society, where money has replaced care for individuals and communities of the type found in some other countries such as the Netherlands and some Scandinavian countries, where profit motives are restricted and a more collective culture exists, seeking for equity, health, and wellness for all members of society.

With the backdrop of so many structural and philosophical challenges to the effective treatment of childhood trauma for adults with comorbid physical diseases, it is necessary to identify where changes can be made. One of the major areas of change needed is the development of an integrated model of care that acknowledges and addresses physical and mental illness in the larger framework of PNI. Systematic coordination between primary care doctors, specialist practitioners, and psychotherapists should be the norm now that PNI has provided a framework to comprehend the links between the two. In the United States, collaborative care model has been adapted for use by a small number of healthcare providers in different healthcare contexts. Examples of a successful approach to integrated care models include the Behavioral Health Project in California, Community Mental Health Case Management in Missouri, and the Harris County Community Behavioral Health Program in Texas (Goodrich et al., 2013). Goodrich et al. (2013) concluded that a collaborative care model has proven more effective than standard care models in improving mental health outcomes across several settings and diagnoses, without a concomitant increase in healthcare costs.

The need for trauma-specific PNI-based training of psychotherapists who work with adult childhood trauma victims with comorbid physical diseases also emerged as critical to moving treatment forward towards a more predictable rate of success that can be measured in improved functioning and concept of self. Enough is known today about the negative impact of early childhood attachment rupture and the negative effects on development of self-identity and self-efficacy to surmise that the nature of the therapist-client relationship is pivotal to effective treatment. Therapists who work with this population need strong interpersonal skills to establish a solid therapeutic alliance that can survive the processing of deep trauma. Therapists who treat trauma in conventional treatment modalities are at risk of inflicting more damage than repair, particularly if they are not sufficient client-centered to create a strong alliance and safe holding environment that can enable traumatic memory processing. Without training, therapists can inadvertently appear to pathologize the client, thereby adding to a burden of shame heavily felt by trauma victims. Training is needed in attachment issues, psychological defenses, traumatic memory processing, to name but a few of the skills required to create a safe platform for change. A safe platform can be achieved through coregulation between therapist and client when the exploration of traumatic memories may otherwise destabilize the client to the point of dissociation.

For all the reasons outlined above, a new framework for treatment of adult victims of childhood trauma with comorbid physical diseases should be thoroughly grounded in the science of PNI mental and physical healthcare, with the ability to apply different modalities at different stages of trauma treatment and stages of the lifecycle of the individual. It should also be based on a trauma-informed, phase-based approach that provides the maximum opportunity for safe release and healing. A broad PNI framework allows for multiple trauma-informed models of

care; this multimodal approach can draw from adaptation of a wide range of PNI-based psychotherapeutic treatment models spanning cognitive, physiological, psychological, and emotional interventions as a traumatized individual moves through different stages of treatment. Key findings from the literature support the value of a phase-oriented approach to treatment, enabling degrees of healing and integration in smaller steps and avoiding the hopelessness that can be associated with such complex symptomology. Such adaptations of current models should be evidence based and reflect the underlying PNI processes and resulting dysfunction. Timing of different trauma-informed models should be governed by treatment progression as it moves through various stages of healing. Trauma treatment can be viewed as an unfolding, peeling back layer by layer of the dysfunction caused by early life emotional, physical, and verbal abuse. Trauma-informed treatment models allow for a selection of interventions best suited to a particular stage. The use of trauma-informed treatment runs counter to many psychotherapeutic treatment plans, which are often based on a particular treatment model that considers only one or two aspects of the trauma effects. An example is CBT. An adult trauma victim undoubtedly has distorted models of self and the world, founded in disrupting experiences of childhood. These distorted models lead to maladaptive and often destructive thoughts and behaviors that affect relationship and day-to-day functioning in adult life. CBT can play a vital role later in the treatment cycle. Once sufficient trauma processing, resolution, and integration has taken place, it is vital to revisit dysfunctional beliefs and behaviors, and CBT is an excellent tool for this purpose. It is, however, of little value when the trauma is up front and center, affecting every aspect of an individual's life, and emotional improvement is not yet established.

Implications for Professional Practice

This study has identified several implications for professional practice in treatment of adult victims of childhood trauma with comorbid physical and mental disorders. It has sought to identify and emphasize the fundamental shift that needs to occur in the treatment of childhood trauma—and other disorders—through the incorporation of PNI findings on the etiology and progression of the effects of early life adversity across the lifespan. Childhood trauma is one of the most complex, least understood, and widespread issues of modern life in the United States. It is widely prevalent, underestimated for many reasons, and underlies many societal issues of the modern world, including the horrifying increase in violence, family disruption, and a self-centered mentality of victimhood without personal accountability to self or society to seek change. The problem is only exacerbated by the common presence of medical comorbidities accompanying trauma that interact with the underlying dysfunction in neurobiological systems to exacerbate dysfunction and unhappiness.

The challenges of childhood trauma treatment are difficult to solve on any large scale and can probably only move forward through a series of well-defined efforts to bring about change at governmental, socioeconomic, and health care levels. In the field of psychotherapy, specific implications for practice need to be studied further, and existing learnings through scientific research on PNI and related fields should be implemented through a change in treatment frameworks and models, diagnostic practices, healthcare policy and implementation, therapist training, and education about childhood trauma that builds on the Felitti (1998) ACEs study. Education needs to be incorporated into our overall understanding of childhood trauma so that individual sufferers of the consequences do not bear such a burden of shame associated with their thoughts and behaviors.

Such momentous change cannot be accomplished easily, and some of it, although closely aligned, is outside the scope of therapeutic practice. In terms of professional practice, the most compelling implications of the findings of this study lie in the education of both psychotherapists and medical doctors; PNI should be incorporated as mandatory training for healthcare professionals. Psychotherapists should be trained in the skills mentioned earlier: a client-centered approach to trauma, the need for safety, trust, and interpersonal healing, emotional attunement, and how to provide a secure launching platform for change. In addition to these skills, counseling psychology master's degree programs should be restructured to teach a PNI approach to understanding the psychology of childhood trauma and resulting symptomology. As new research progresses, those learnings should be incorporated into training and certification programs to better equip psychotherapists to serve this population. Concomitantly, training for medical professionals should move towards a systematic approach to human diseases based on the underlying PNI; this would provide for a more holistic and integrated approach to treatment that has the potential to reduce polypharmacy and the reliance on prescription drugs. Specific trauma certification programs can be developed and made available to all psychotherapists who treat childhood (and other) traumas.

The changes of aging are especially significant for adults with childhood trauma, and more training should focus on changes through the lifespan, to better inform treatment methods and goals for older individuals with unresolved childhood trauma. Rowe and Kahn's (1998, 2015) successful aging model, modified by Zolnikov (2015) could also be expanded to include the addition of early and unresolved adverse experiences, addressing what changes can be made to enable an individual who suffered through early life trauma to succeed at the developmental task of aging through generativity rather than despair. The successful aging model can be

incorporated into a new, PNI-based theoretical framework for treatment of adult victims of childhood trauma with comorbid mental and physical disease.

This study highlights the broader deficiencies in treatment of what is a significant and growing percentage of the United States population. Changes in policy and healthcare implementation will also be needed to address an integrated approach to healthcare, and to provide guidelines on related topics such as polypharmacy. Given the huge pharmaceutical lobby, one of the most powerful in the United States, this will be an extremely difficult area in which to effect policy change, but it needs to be done. In the shorter-term, healthcare providers can move towards integrated or collaborative care models such as those implemented in a few isolated systems across the country.

Recommendations for Research

Many changes are necessary to fully address the growing problems to society presented by untreated or inadequately treated childhood trauma in adults. If the spiraling of childhood trauma in the United States is to be slowed down and addressed more effectively, it is critical to seeking funding for several large-scale research efforts. Before changes can be made in healthcare policy and implementation, there is a need for extensive research to provide evidence-based, PNI-based treatment models that address not only symptom complexity in a trauma-informed context and in the presence of comorbid physical diseases, but also the evolution of symptoms across time, bringing the need for flexibility across the treatment window. Such research is equally essential before significant changes are introduced to graduate and postgraduate programs in counseling psychology to introduce new PNI learnings into curricula. The sheer number of variables involved in structuring human subjects research in the target

population is daunting. Such research would benefit from standardization of methods, instruments, and endpoints.

One of the first priorities should be a broad program of research is to develop or adapt models of treatment based on the framework of PNI that incorporate both psychological and physiological diseases and aging. Research in PNI should also examine and identify what a trauma-informed approach to treatment means in a quantifiable and measurable sense, so that studies can be conducted to determine efficacy against non-trauma-informed methods. Research studies into the use of PNI-based interventions should explore not only the PNI aspect of treatment, but also the concept of flexible models across the treatment timeline, adapted to whatever symptomology is most problematic at a given stage. Trauma patients present with complex symptoms that are made more problematic by the fact that some are well-masked consciously or unconsciously; some of the symptoms affect the ability to build a relationship or be self-aware enough to provide a clear picture of the struggles caused by the effects of childhood trauma on brain and body. Developing a better understanding of evidence-based, different models of PNI-based treatment and how they may be used at different stages in the therapeutic process would be beneficial to patients in their journey towards well-being. Research into physiological, ethnographic, and cultural implications of PNI-based models need to be conducted so that these populations can be served in a way that accounts for differences and prevents further traumatization.

Other changes are needed in the structure and process of research itself. Existing assessment instruments, analysis tools, and outcome endpoints for childhood trauma should be enhanced, standardized across childhood trauma research programs, and assessed for efficacy in RCTs. Standardizing on diagnosis across multiple studies allows for greater comparison across

different research efforts and enables meta-analysis and data-mining. Inclusion and exclusion criteria for RCTs should be developed and standardized. Some standardization of endpoints for a limited set of trials would be valuable, although the question of persistence of endpoint improvements after time is still in question; there are few longitudinal studies of more than a year for this population. Studies used in the literature review often had no follow up on outcomes beyond study end; a few did include follow ups at 1 month, or even 6 months, but these were in the minority. When trauma clients are discharged from treatment because they have recovered functioning to a point where they feel ready to end therapy, there may still be unresolved trauma that manifests at a later stage through unexpected triggers, flashbacks, nightmares, or other symptoms. Longitudinal studies would provide insight into which models and interventions result it persistent outcomes. Target populations for studies should span all socioeconomic sectors of society. The effects of unresolved trauma on aging processes should be researched from the same PNI-based framework to inform the use of models of treatment that better support seniors struggling with cognitive and memory issues together with physical limitations. Research can also focus on adult childhood trauma victims with different physiological diseases, to better understand if some physical illnesses are more closely linked to trauma than others. Some limited research has already been done in this area but has focused mainly on depression with comorbidities such as diabetes. Longitudinal quantitative and qualitative randomized controlled trials are needed to measure immediate outcomes of psychoneuroimmunological models, as well as persistency of gains over time. Quantitative measures would be valuable in light of the fact that psychoneuroimmunological data lends itself to quantitative measures; general functioning and quality of life measures require a more qualitative approach.

Research may enable better treatment, better outcomes for patients, and better training of psychotherapists. It can also be used to inform policy and healthcare implementation, a nation-wide effort program should be launched to address systemic issues in healthcare models of care, clinician training, and polypharmacy. The result of these changes will make a significant step forward to effective treatment of childhood trauma and medical comorbidities. It can be argued that untreated and unresolved childhood trauma often results in parenting that replays the traumatic experiences, perpetuating the problem across generations; it is also a potential factor in criminal behavior and addiction. This study has striven to bring together a wide range of information into a proposed framework that can serve the target population. Although implementation of many of the changes suggested here are dependent on evidence-based research for implementation, there are things that can be done today to start effecting change by introducing existing data from the field of PNI into psychological studies.

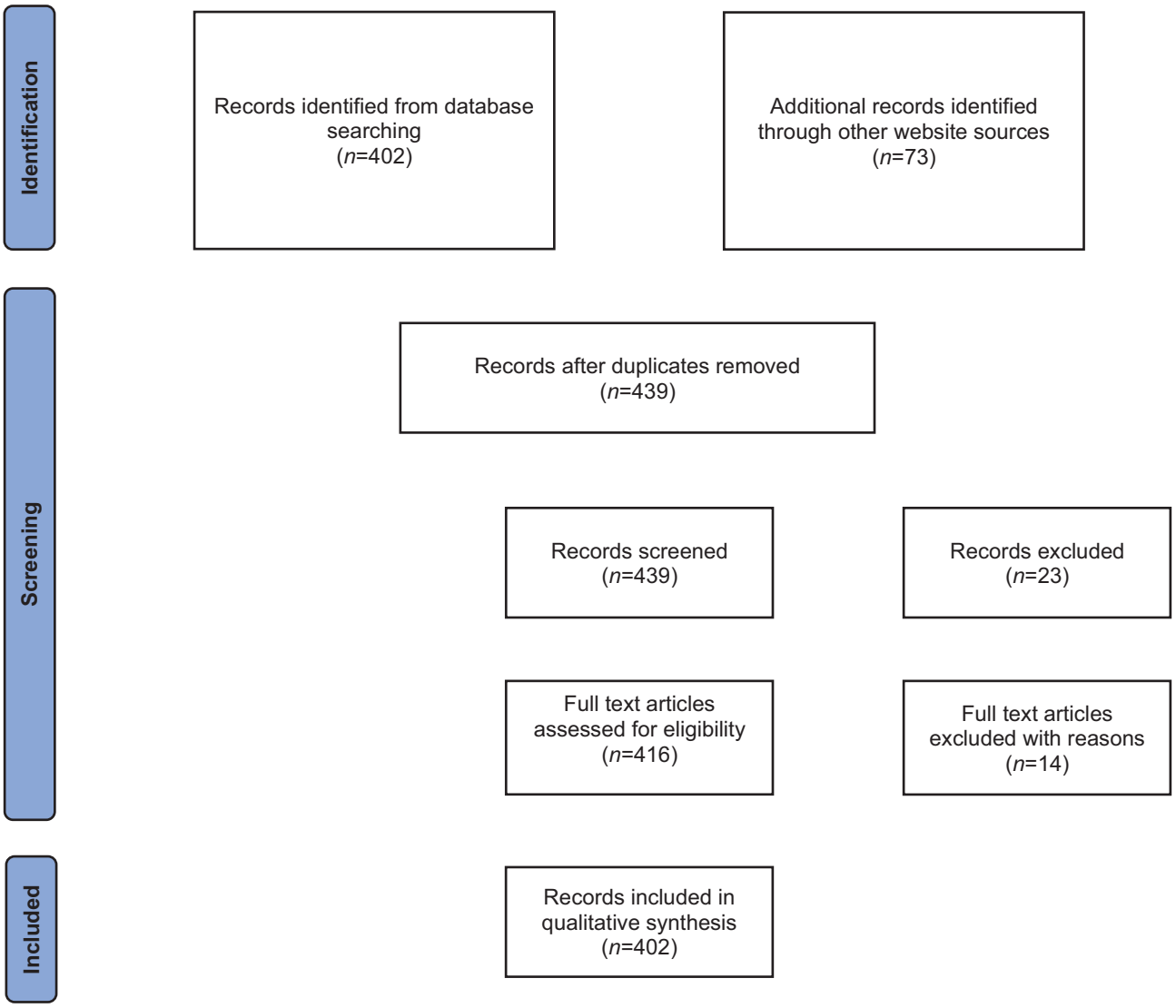
Conclusion

This study has contributed to an understanding of the gamut of mental health problems, applying the filter of PNI from research studies, with the intention of establishing the potential value of a PNI-based framework with flexible, phase-based models of treatment for the target population that can be adapted for the processs of comorbid physical diseases and aging. In doing so, it has contributed to the body of knowledge about treatment of childhood trauma and comorbid chronic disease, clearly demonstrating the treatment gap, and current deficiencies in identification, diagnosis, and effective treatment, of adult victims of childhood trauma with chronic comorbid diseases. The field of PNI has provided sufficient evidence to date to suggest that many mental health disorders have their roots in the neurobiological effects early life stress. The science exists today to provide more person-centric treatment based on neurological imaging

and other relevant diagnostic methods in addition to self-report and clinical evaluation. This is true even for psychotic disorders; research suggests that childhood trauma can be linked to schizophrenia and similar disorders. One of the more prohibitive issues in the application of PNI to childhood trauma and comorbid disease is the cost barrier presented by potentially routine use of neuroimaging methods in diagnosis, treatment planning, and outcome measures. This problem has been overcome in the using of imaging in other areas, for example the use of mammograms in early detection of breast cancer. A full cost-benefit analysis would probably reveal that the use of costly imaging would pay for itself compared to the costs of childhood trauma in society. It is to be hoped that structural changes in the provision of health care in the United States can address the interlinked mental and physical diseases that face a growing percent of the population and in doing so, take advantage of advances in science that introduce PNI data into the subject area.

Figure 1

PRISMA Flow Diagram



Note. Moher (2009).

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Appendix: IRB Approval

CALIFORNIA SOUTHERN UNIVERSITY
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PHONE: 714.480.0800 | TOLL FREE: 800.477.2254 | WEB: WWW.CALSOUTHERN.EDU

Institutional Review Board Decision

Applicant's Name: Maureen Glynn

Date of Submission: 02/16/2022

Date of Review: 02/21/2022

Determination of Review:

☑ **Meta-analysis/Substantive Literature Review Approved [Study meets requirements. Study meets criteria in 45 CFR 46 where applicable.]: You can begin your Meta-analysis/Substantive Literature Review.** Please see IRB Approval below.

☐ **Deferred: You cannot begin your Meta-analysis/Substantive Literature Review.** The review has some questions about procedures, some procedures need to be changed, and/or several changes are needed to forms. Please answer the reviewer's questions and submit a revised application and supplemental forms. If you are a student, please submit through your dissertation chair.

Resubmission Instructions:

Please indicate changes completed or ask any questions in the "Response to Reviewer Comments".
Please revise the original information in each section of the application as required.

Please also revise the check boxes as needed, and include updated materials with your next submission.
Please do not submit a partial application.

Approval from Chair, Institutional Review Board

The signature of the Chair of the Institutional Review Board, when affixed below, indicates that the activity identified in the enclosed application has been approved with the conditions and restrictions noted here.

Restrictions and Conditions:

Brett A. Gordon, Ph.D., FSA Scot 02/21/2022