

Loneliness, Social Isolation, and Their Connection to Overall Health Across the Lifespan

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A Senior Thesis submitted in partial fulfillment
of the requirements for graduation
in the Honors Program
Liberty University
Fall 2021

Acceptance of Senior Honors Thesis

This Senior Honors Thesis is accepted in partial fulfillment of the requirements for graduation from the Honors Program of Liberty University.

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Abstract

Due to recent circumstances, the incidence of loneliness and social isolation has skyrocketed. Fortunately, there have already been countless studies examining the longer-term implications of these two factors on health. Loneliness and social isolation have been found to impact cardiovascular health, stress response, immune function, resilience, mental health, attachment, spiritual health, and many other determinants of health. A variety of research was examined outlining the psychological implications of loneliness and social isolation. These factors also influence physiological processes and can exacerbate a variety of diseases. After presentation of this evidence, a collection of possible interventions will be discussed, and their efficacy will be reviewed.

Loneliness, Social Isolation and Their Connection to Overall Health

The factors and dimensions of overall well-being include physical, emotional, social, spiritual, and intellectual health. While each of these are individually important, if one dimension is unhealthy, this can lead to a plethora of concerns in a person. One area of well-being is a person's socialization. Two specific areas of socialization which each negatively affect overall health include social isolation and loneliness. Social isolation is an objectively quantifiable variable which can be characterized by living alone, having limited social ties, and being limited in social contact. Loneliness, on the other hand, is a subjective emotional state which may or may not be present with social isolation. Loneliness can be described as perceived social isolation or the difference between the quality of social ties which are desired and what is actually present. It is important to understand and acknowledge the difference between these two because they are not always fully connected. For example, decreasing social isolation by increasing human interaction may not have any effect on an individual's perceptions of the interactions. Ultimately, while a person may increase his or her social interactions, they may still feel incredibly lonely. The same is true the other way. Altering one's thoughts regarding loneliness may not change the amount of interaction an individual's experiences (Holt-Lunstad et al., 2015).

Many complex factors play into how humans respond to social relationships. These factors can either promote or impede the presence of strong social relationships in one's life. Several risk factors for the development of loneliness and social isolation include health problems, disability, gender discrimination, grief, living alone, poverty, and aging. Many of these seem obvious but are often ignored as areas of concern in an individual's social life. Countless studies have examined the physical, mental, emotional, and spiritual repercussions of

social isolation and loneliness. Affected areas include physical activity, ability to use effective judgment with habit formation, cardiovascular disease, depression and anxiety, cognitive ability, endocrine function, and chronic inflammation (Bhatti & Haq, 2017). While this list is not comprehensive, it can be used to identify the importance of social and relational health.

Stress

In order to understand many of the effects of chronic social-isolation and loneliness, one must first understand the mechanisms and physiological implications of stress on the body. Stress, whether caused by physical factors or external factors, require the affected individual to learn to adjust to life changes caused by the stressor. When the stress is negative, it has created demands that are higher than usual demands in a person's life, therefore putting strain on that individual (Rateau, 2020). One of the biggest determinants of an individual's ability to cope with any kind of negative stress is a social support system. While daily social support is not always recognized, typically once a support system is aware of a loved one's stress or trauma, the network becomes more intentionally focused on assisting in changing the situation and feelings. Whether or not these changes are successful, the network of genuine support and care often helps to reduce the implications of the stressors on the individual. Conversely, if an individual does not have a network from which to receive support when under significant stress, he or she may be quick to become resentful or depressed (Thoits, 2011).

Another determinant of the quality of coping with stress is the emotional sustenance provided by the support system. Thoits (2011) discusses the differences between the support offered by a loosely associated social network and the care, sympathy, and comforting presence offered by a significant other or close family member. This study shows that this presence and comfort offered by a closer relationship often confirms the individual's sense of worth in others'

lives and supports the individual's belief that he or she is accepted into a group of people. These psychological and psychosocial mechanisms of comfort will often lead to reduced psychological distress (Thoits, 2011).

Mortality Risk Factors

Many studies have examined the relationship between isolation and mortality. One of these is a meta-analytic review which looks at previous research studies to determine the conclusiveness of these studies. This review utilized research studies between 1980 and 2014 which study the same subjects over time through a prospective design. Criteria for inclusion in this review consisted of a prospective design which followed subjects over time, studies that did not include mortality due to suicide or accident, studies with outcomes other than mortality, and all quantitative designs that were not a single-case study. After the exclusion of the studies that did not meet these criteria, 70 independent studies remained to be analyzed. A majority of the studies used involved adults between the ages of 66 and 71 from a randomized community sample. Data was compiled from each study to evaluate a total of over 3 million participants which were followed over an average of 7 years. This data then underwent a series of multivariate statistical models in order to account for the confounding variables of age and pre-existing health status. These studies found that the risk of mortality significantly increased by approximately 30% in the presence of chronic social isolation, loneliness, and living alone. While correlation rather than causation is all that can be gathered from this analysis, studies showed statistically significant data that those who reported being socially isolated, lonely, or living alone at the beginning of the study had a much higher likelihood of being deceased at the follow-up survey. This was found regardless of socioeconomic status, participants' age, and length of time before the follow-up (Holt-Lunstad et al., 2015).

One important finding of this meta-analysis involves the variable of aging and its effect on mortality in this context. Although older adults have typically been the subjects of study when it comes to isolation and physical health, this analysis called into question the middle-age population as well. Several studies found that the older population was found to experience greater levels of loneliness and/or isolation; however, in the majority of subjects, this primarily affected mental health rather than physical health. In middle-aged adults, the increased risk for mortality due to physical implications of isolation may be due to increased engagement in risky health behaviors. Additionally, many older adults experience social isolation as a complication of aging. While this still has negative implications on mental and cognitive function, it may not be as detrimental to an individual's physical health as the presence of chronic social isolation or loneliness from a younger age. The older adult who is experiencing social challenges has likely developed some form of resilience and healthier coping than the middle-adult who is struggling with the same thing. As a result, the older adult may fare better in the studies which compared the two. Although this meta-analysis provides valuable insight to the social and physical health of adults, further research is needed on the middle-aged population, as well as the complexities of social interactions (Holt-Lunstad et al., 2015).

Lifestyle

One clear source of these health concerns is the lifestyle choices that loneliness can lead to. Countless studies have found that loneliness increases the prevalence of smoking, alcohol abuse, obesity, and lack of physical activity (Bu et al., 2020). Along with older adults, children and young adults are also negatively impacted by loneliness. With perceived social isolation, children are at an increased risk of depression, inadequate sleep, and decreased executive functioning and development. With each of these lifestyle stressors and choices come many

potential disease processes, including depression, cardiovascular disease, and inflammation (Bhatti & Haq, 2017).

Cardiovascular Effects

While several prominent risk factors for the development of cardiovascular disease exist in the middle-aged and elderly population, social isolation is one common predictor of the morbidity and mortality of the disease. Various studies have found that those with limited social interaction and social support have a much higher risk of developing rapidly progressing atherosclerosis with an even greater risk of a stroke or heart attack (Bhatti & Haq, 2017). Not only can loneliness and social isolation contribute to the occurrence of a myocardial infarction, but it has also been found that these factors increase the mortality of post-myocardial infarction patients (Leigh-Hunt et al., 2017). Bu et al. (2020) found that this risk factor for loneliness, but not social isolation is a factor in cardiovascular disease. This resulted in the idea that the risk is primarily subjective in the perceived quality of social connections, as opposed to the objective nature of social isolation (Bu et al., 2020). Along with these observational studies of humans, experimental animal studies have shown that increasing an animal's social isolation increases their risk for obesity and type 2 diabetes mellitus. This is in addition to the development of cardiovascular disease, increased overall inflammation, and an increased stress response. This can lead to an endless cycle of the stress response causing increased workload on the heart and vascular system, which can later contribute to organ damage. These animal findings can be paralleled to the findings of human participants having exaggerated fight-or-flight response in stressful situations with a significantly slower recovery time (Bhatti & Haq, 2017). This correlation is supported by studies showing the impact of prolonged psychological stress on the cardiovascular system (Bu et al., 2020).

An additional unique finding in human participants is hypertrophy of the left ventricle (Bhatti & Haq, 2017). Left ventricular hypertrophy (LVH) points back to the significantly increased workload of the heart due to the hypertension found in socially isolated individuals. Coronary artery disease and atherosclerosis can also play a part in the development of LVH. This is specifically caused by the attempts of the myocardium to compensate for ischemic heart tissue. LVH can lead to the development of myocardial fibrosis, which presents itself with both diastolic and eventual systolic dysfunction (Bornstein et al., 2021). Because LVH has been found to be a component of hypertension, it is likely that this finding is linked to the hypertension caused by social isolation or loneliness.

Sympathetic Nervous System

Several mechanisms indicate the association between loneliness and hypertension. One of these is the sympathetic nervous system (SNS) and its response to loneliness, which can be categorized as a social stressor. The presence of SNS response to this social stress is indicated in an increase in catecholamines such as epinephrine and norepinephrine, which are released in response to acute stress. While there is not strong evidence that shows a direct association between loneliness and a systemic effect, it has been found that loneliness increases norepinephrine levels in the thymus, spleen, lymph nodes, and certain tumors. The SNS and these catecholamines produce immature and proinflammatory monocytes in the presence of social stress, which is mediated by β -adrenergic receptors. This leads to a proinflammatory state, which can promote damage to the blood vessels and the development of hypertension (Xia & Li, 2018). Although the exact pathophysiology is not fully understood, various studies have shown that this inflammatory state is associated with arterial stiffness, renin-angiotensin-aldosterone system (RAAS) activation, oxidative stress, and endothelial dysfunction, all of which are

exacerbated by inflammation and contribute to an increase in blood pressure (Angeli et al., 2021).

Neuroendocrine System

A common finding when studying lonely individuals is the activation of the hypothalamic-pituitary-adrenal (HPA) axis, which produces the glucocorticoid cortisol in the important process of regulating the body's stress response. Studies have found a connection between loneliness and increased levels of cortisol in the morning, as well as decreased glucocorticoid receptor sensitivity (Xia & Li, 2018). The increased levels of cortisol affect not only inflammatory health, but also sleep health. Cortisol disrupts the Circadian rhythms, thus disrupting the sleep-wake cycle in a person with the chronic stress of social isolation or loneliness (Rateau, 2019). Without the social stress of loneliness, stimulation of glucocorticoid receptors suppresses proinflammatory gene networks. Because of the increased stress of chronic social isolation and loneliness, there is an increase in glucocorticoid resistance, which leads to excessive inflammation, hyperactivity of corticotropin-releasing hormone, and the SNS pathway activation. As previously mentioned, this inflammation can play a part in the development of atherosclerosis, diabetes, and tumor metastasis. Studies of socially isolated animals have also shown a β -adrenoceptor blockade, which further contributes to glucocorticoid resistance (Xia & Li, 2018).

Mental Health

Another aspect that goes hand-in-hand with the effect on the HPA axis is the condition of 5-HT neurons, which is the serotonin-producing neuron. These neurons are highly sensitive to stress in the body, which results in decreased activity level of these neurons. Studies have found that chronic social isolation leads to decreased excitability, thus providing less response to

stimulation. As a result, 5-HT neurons are unable to produce adequate serotonin, which is characteristic of major depression and anxiety (Sargin et al., 2016). Studies have also shown that individuals diagnosed with depression tend to have higher cortisol responses to stress than those without depression (Krishnan, 2018). This correlates to the aforementioned studies that show a relationship between social isolation and increased cortisol and decreased glucocorticoid resistance (Xia & Li, 2018). It has also been noted that there is an increased level of inflammatory markers, specifically C-reactive protein, in patients with depression (Long, 2018). This further supports the idea that, through a chain of events prolonged loneliness and/or social isolation can attribute to cardiovascular disease, higher levels of inflammation, and other health concerns (Håmmig, 2019).

Further, research has shown an imbalance of serotonin in depression and other similar psychiatric disorders. Researchers have primarily attributed depression to decreased levels of serotonin, epinephrine, and dopamine in the synaptic cleft. This can be due to either decreased presynaptic release or postsynaptic activity (Long, 2018), which can be further supported by the effectiveness of selective serotonin reuptake inhibitors (SSRI's) used in the treatment of depressive disorders (Halverson et al., 2020). This goes on to affirm the previously discussed response of 5-HT neurons to chronic social isolation. When examining brain structures in patients with depression, it was found that the hippocampal volume was significantly smaller than that of patients in remission, along with decreased activity in the prefrontal cortex. These structures play a part in emotional response and are connected to the raphe nuclei, or area responsible for the regulation of 5-HT neurons and therefore serotonin production (Halverson et al., 2020). When an individual becomes chronically socially isolated, each of these areas are widely impacted, thus contributing to depression (Sargin et al., 2016).

One of the contributing factors to the development of depression, along with neurophysiological factors, is the presence of early life stressors including neglect or trauma (Long, 2018). This can be partially attributed to the effect of stress on telomere length. Telomeres are the protective caps that are found on the end of chromosomes. In general, the diminishing size of telomeres points to normal aging, however telomeres are also found to be shortened in stressed people, which can influence the development of depression and the genetic rate at which our cells age (Rateau, 2020). Childhood trauma can also often contribute to attachment issues, specifically with the tendency to withdraw and self-isolate from relationships. This can in turn exacerbate the development of depression, whether it be earlier or later into adulthood (Lahousen et al., 2019). This will be further elaborated upon in the section entitled “Pediatrics.”

While depression and anxiety are often associated with loneliness, they can also propel individuals to further health complications. One of the key characteristics of depression, especially in those with a low support system due to social isolation, is poor self-care. This may present itself as inability to brush their teeth or low motivation to eat or partake in regular physical activity. Each of these complications can lead to further issues, such as worsening cardiovascular disease and nutrient deficiencies (Halter, 2018). Other complications from depression include chronic pain, social phobia, relationship difficulties, and self-harm or suicide. These cannot only be caused by social isolation, but further exacerbate the issue of chronic isolation, indicating the possibility of an endless cycle if proper treatment is not obtained (MayoClinic, 2021).

Spiritual Health

Another important part of overall health and wellbeing is spiritual health, also known as religiosity or spirituality. Regardless of the religion, spiritual health needs can be met through prayer, emotional support, and religious activities. Each of these, however, is often connected to social interactions. Research and other sources have shown that when an individual withdraws from spiritual connectedness, he or she can quickly slide into depression or further withdrawal. (Long, 2021). Spirituality or the pursuit of any religion also encourages an individual towards self-betterment. When one is focusing on improving him or herself, there is less feeling of loneliness or isolation, thus improving outcomes among spiritual people. Spirituality in any form is found to increase well-being, improve response to illness, and enhance coping ability. Because these implications of spirituality are so high, it is important to be able to educate the population on the importance of social connectedness through spirituality (Janzen et al., 2019).

Pediatrics

Pediatric Isolation and Mental Health

The importance of socialization among children throughout their development is widely known. More studies are emerging, however, discussing the science and physiology behind the role of socialization in pediatrics as isolation and loneliness increase in prevalence among this population. As quarantining and lockdowns have become far more common in children and adolescents, the historically suspected results of prolonged social isolation have become the reality in many children's lives (Loades et al., 2020). Another historical factor to mental health in the pediatric population is chronic physical health conditions often requiring hospitalization. One of the primary explanations for this is the toll this takes on social connections in a pivotal period of childhood. When children with chronic conditions are hospitalized significantly more than

their peers, they miss out on valuable opportunities to socialize and build connections whether at school or other activities. One study found that implementing psychological and social support during and shortly after a pediatric hospitalization greatly increases the mental health outcomes of that patient. This also supports the hypothesis that the stress of isolation in pediatric hospitalization influences the mental and overall health of an individual (Doupnik et al., 2016).

NICU Background

One source of isolation that is not frequently considered is the neonatal intensive care unit (NICU), specifically for premature babies with extended stays in this unit. Parental effects of having a child isolated in the NICU include loss of parental role, trauma or psychological distress, and disrupted bonding with the infant (Lean et al., 2018). NICU hospitalization can often be seen with impaired attachment abilities later in life due to separation from the family (Kim et al., 2020). A study performed by Kim et al. (2020) has shown that a disorganized attachment style is over six times more prevalent in NICU infants than those who remain with their mother immediately after birth. Long-term, adults with a disorganized attachment style lack a consistent approach towards relationships of any kind. Although those with disorganized attachment desire relationships, they fear the intimacy of one (The Attachment Project, 2020). This can be partially attributed to the alteration in parental role due to separation in the NICU (Kim et al., 2020), as the lack of consistency in caregivers can often increase the development of this attachment style (Granqvist et al., 2017).

In an infant, healthy attachment has been influenced by nurturing touch, closeness to the mother, understanding the infant's cues, and responding appropriately according to those needs. Along with the trauma of NICU hospitalizations, such early separation between a preterm infant and his or her mother can greatly disrupt the process of attachment-building (Kim et al., 2020).

Another factor which further impairs the attachment-building relationship is maternal and paternal mental health. Studies have found that 35% of mothers and 24% of fathers experience stress disorders such as post-traumatic stress disorder (PTSD) following NICU hospitalization. This poor parental mental health often disrupts parent-infant bonding and promotes more withdrawn tendencies in both the newborn and parents (Lean et al., 2018). Because of the disruption in the process of bonding and attachment-formation, there often arises a series of complications seen throughout the lifespan. As previously mentioned, one of these effects can be seen in the development of depression (Long, 2018).

Additionally, NICU hospitalization often increases the risk for short and long-term neurodevelopmental implications due to isolation and impaired attachment or bonding experiences following birth. A preterm infant born anytime between 24 and 40-weeks' gestation go through a critical period in the NICU during which a series of complex neurological events occur. During this time frame, many synaptic and neuronal connections are made, and brain structures such as the thalamus, cortex, and cerebellum are matured. These are all extremely vulnerable to the infant's experiences of isolation and trauma while in the NICU (Aita et al., 2017).

Previous Studies Completed

Multiple studies have been completed on the longer-term effects of NICU hospitalization of infants. Pennestri et al. (2015) noted that a majority of research addressed the promotion of attachment and bonding during the NICU stay as a preterm infant. This prompted a study of longer-term attachment styles of NICU babies without the confounding variable of prematurity. Through this study, researchers recruited mothers during pregnancy between the weeks of 13 and 20. Mothers had to be 18 years of age and older and were unable to participate with serious

obstetric complications or chronic illnesses. In order to prevent the confounding variable of prematurity, participating infants had to be born at full-term, or greater than 37 weeks' gestation (Pennestri et al., 2015).

Data was collected observationally when the children were born, being separated into categories of NICU hospitalization and non-NICU babies. By 36 months of age, 55.4% of the non-NICU group were securely attached, 24.5% were insecure, and 20.1% had the attachment style of disorganized. In the NICU group, only 43.5% were securely attached, 8.7% were insecure, and 47.8% were disorganized. While lifestyle, socioeconomic, and parenting factors each play a part in the formation of attachment styles, statistical analyses were performed to rule out these confounding variables. Other confounding variables that were ruled out were maternal mood and anxiety, sensitivity to infants' needs, developmental indexes, birth weight, delivery complications, infections, and general health. While this study provides valuable insight in just one effect of separation in NICU infants, it does not include premature babies, which represent a majority of the population in the NICU (Pennestri et al., 2015).

Elderly

Cognitive Function

Loneliness can severely impair an individual's cognitive functioning as he or she ages. These effects can often lead to decreased quality of life and motivation, thus damaging the individual's desire to participate in life's activities, and further contributing to the exacerbating cycle of loneliness (Bhatti & Haq, 2017). As previously mentioned, prolonged social isolation has been connected to the increase in glucocorticoids and glucocorticoid resistance within the body. This chronic excessive secretion of cortisol can lead to hippocampal atrophy and the suppression of neurogenesis (Krishnan, 2018). This neurogenesis inhibition can be a risk factor

for cognitive decline leading to the development of dementia (Bhatti & Haq, 2017). In fact, many studies point to a connection between limited social connections and the development of dementia. In comparison, those with larger social networks have a decreased risk of developing dementia. Socialization, whether found in church attendance, volunteering, recreational activities, or work, is found to protect against the mechanisms of cognitive decline (Poey et al., 2016).

Along with glucocorticoid resistance and excessive cortisol secretion, oxidative stress has been found to play a part in the progression of cognitive decline (Long, 2018). The discovery of oxidative stress in socially isolated individuals helped to make the connection between chronic psychosocial stress and vascular disease. Oxidative stress is also linked to isolation-induced changes in the HPA, SNS, and immune system. In a study involving socially isolated rats, there was an increase in oxidative stress markers in the hypothalamus which likely triggered a systemic stress response along with the activation of the HPA axis. From the standpoint of the vascular system, social isolation-induced oxidative stress has also been found to promote the development of atherosclerosis and further contribute to inflammation of the vasculature (Xia & Li, 2018). The vascular damage caused by the oxidative stress may play a significant role in the development of Alzheimer's disease, dementia, and cognitive decline (Long, 2018).

One study establishes the connection between genetic susceptibility, social environment, and the development of Alzheimer's disease and dementia. Specifically, the APOE e4 allele is associated with control of lipids, cholesterol, neuroplasticity, neurogenesis, and inflammatory response of the brain. Each of these in turn can contribute to the development of Alzheimer's disease, making the allele the strongest genetic risk factor for the progression of the disease. Although this is a strong risk factor for Alzheimer's disease, it also interacts with an individual's

social environment to impact cognitive functioning. Many studies show a connection between social contexts and parts of the brain associated with memory (Poey et al., 2016).

Poey et al. (2016) completed a study to determine if this connection in individuals with the APOE e4 allele was strong enough to reduce the risk of cognitive impairment. During this study, researchers analyzed data from a retirement study sponsored by the National Institute of Aging. Social variables were assessed based on family size, social engagement in volunteer activities, current work status, marital status, and living arrangements. Subjects were also asked about their perception of social support in order to evaluate loneliness and perceived isolation. Each of these results were then evaluated based off of the presence of the APOE e4 allele. This study produced several valuable findings. Marriage and social engagement were found to be associated with a decreased risk of dementia or any kind of cognitive impairment. The study also found that subjects with the APOE e4 allele and decreased social functioning had a nine times greater risk for development of Alzheimer's disease when compared to the socially connected individuals possessing the allele. The same was true with perceived social support, indicating that those who did not perceive the presence of social support had an increased risk for the development of Alzheimer's disease and cognitive impairment. It also concluded, however, that the presence of social ties or marriage was not significant enough to eliminate the risk of Alzheimer's in those with the allele. Although the risk is not entirely eliminated, this provides substantial evidence that strong social connections and support can provide protection from some level of cognitive decline (Poey et al., 2018).

Another study performed by Elovainio et al. (2018) determined the limitation of cognitive performance on many different studies that looked at isolation and health outcomes. This study looked at participants from the Whitehall II Study, which examined the mortality of

civil servant employees in London. The participants used for this study were between the ages of 35 and 55 years and included both men and women. In order to measure social relations and incidence of isolation, Elovainio et al. (2018) provided a self-reporting survey on social contacts and marital status. Cognitive functioning was then studied through verbal, mathematical, fluency, and memory-associated tests. These variables of socialization and cognitive function were then analyzed using statistical analyses. The results were compared by categorizing into levels of social connection and cognitive abilities. Confounding variables such as age, sex, ethnicity, and socioeconomic group were then listed and studied to rule out any effect that they may have had on results of the study. Through this research, clear differences were found between social connectedness and rate of cognitive decline. The baseline level of cognitive functioning did not play a significant role in the average rate of decline through this study. This research contributes to the widely accepted evidence that connectedness is vital for successful aging because of the focus on changing cognitive abilities, which has typically been used as a limitation to former research (Elovainio et al., 2018).

The Immune System

While the immune system is affected by social isolation and loneliness across all ages, it is most commonly seen in the elderly due to the natural aging process which often causes a weakened immune response (Ali & Chawla, 2020). Because loneliness is seen as a chronic stressor in the life of an affected individual, it can be assumed that the effects of stress on the immune system are in play in this individual. Stress has been linked to the development of immunosuppression by decreasing the number and functional capabilities of natural killer cells, which are vitally important in fighting pathogens. Stress also decreases lymphocyte proliferation, alters the production of cytokines, and decreases phagocytosis performed by neutrophils and

monocytes. Each of these immune system effects can increase the risk or worsen the preexisting conditions of multiple sclerosis, asthma, rheumatoid arthritis, and cancer, along with other immune-related diseases (Rateau, 2020). Another concept, discussed later, is failure to thrive and malnutrition, which greatly decrease an elderly individual's immune response (Ali & Chawla, 2020). The effects of loneliness on the immune system have been molecularly traced back to chemicals within the brain and gene expression. Namely, the SNS activation occurring in lonely individuals results in instability between pro- and anti-inflammatory signaling which leads to an unpredictable immune response (Xia & Li, 2018).

Along with SNS activation, there is also a relationship between isolation and conserved transcriptional response to adversity (CTRA) gene expression. This often decreases the antibody- and antiviral immunity-related genes in an individual, thus leading to decreased immune response to pathogens. CTRA simultaneously causes the upregulation of proinflammatory cells which cause further glucocorticoid resistance. The inhibition of the anti-inflammatory effects of glucocorticoids on the body can then contribute to the development of chronic disease known to be associated with loneliness. CTRA gene expression can also cause a positive feedback loop which exacerbates the presence of loneliness. Studies have found that the release of proinflammatory cytokines, caused by CTRA gene expression, may push the development of behaviors which increase loneliness. These behaviors can be seen in damaged affective, perceptual, and motivational processes that may decrease one's perceived need for social interaction (Xia & Li, 2018). Multiple studies have confirmed this association between an impaired immune response and social isolation as evidenced by a high level of Epstein-Barr virus (EBV) antibody titers in individuals experiencing higher levels of social isolation (Bhatti & Haq, 2017).

Failure to Thrive

Failure to thrive is a term commonly used when describing a child's growth and development being slowed by weight loss, decreased appetite, and poor nutrition (Ali & Chawla, 2020). The National Institute of Aging defines failure to thrive as a "syndrome of weight loss, decreased appetite and poor nutrition, and inactivity, often accompanied by dehydration, depressive symptoms, impaired immune function, and low cholesterol" (Agarwal, 2020, para. 1). Rather than being a single medical condition, it is a collection of symptoms related to an underlying physical, mental, or psychosocial condition. Because this is not a specific disease process, the pathophysiology widely varies on the cause of failure to thrive. The most common causes of the symptoms are individual disease processes such as cancer, as well as medication side effects (Ali & Chawla, 2020). According to Ali and Chawla (2020), the depression and despair caused by social isolation of the elderly can also play a part in the development of failure to thrive. This can be a result of the hopelessness that leads to poor intake of food. Many elderly persons report feelings that their life is not worth living anymore due to both physical limitations and social circumstances. This will often lead to poor appetite or refusal to eat as a manifestation of this emotion (Ali & Chawla, 2020).

When an elderly adult becomes significantly isolated and depressed, a multitude of physiological processes can occur. The malnutrition that is often seen in failure to thrive can lead to clinically significant weight loss, which is defined as a loss of greater than 5% over six to twelve months (Agarwal, 2020). Researchers have examined various complications resulting from weight loss in the elderly and have inconclusive results on the relation between body mass index (BMI) and rate of functional decline. One study examining 983 community-dwelling older adults did, however, show an association between unintentional rapid weight loss and functional

abilities throughout aging (Ritchie et al., 2008). This study specifically examined the changes in activities of daily living (ADLs) and mobility over a 4-year time period. One potential contributing factor to the loss of function due to unintentional weight loss seen in failure to thrive is the lack of protein and therefore loss of lean body mass that allows for more functional abilities. Another factor is the risk for injury with decreased body fat that comes with malnutrition. Because of a patient's risks with mobility, the elderly adult may choose to remain even more sedentary, contributing to further loss of range of motion and function (Ritchie et al., 2008). Additional studies have also found that unintentional weight loss associated with failure to thrive in older adults can contribute to increased hospital complications, admissions to nursing homes, and poor quality of life (Agarwal, 2020).

Quality of Life and Resilience

Before considering how loneliness affects quality of life and mental health in the elderly, it is important to understand the meaning of the phrase "quality of life." Quality of life can be defined as the perception of an individual's positioning in life based on psychological factors as well as culture, values, expectations, aims, independence, and personal beliefs, and how each one influences the capacity to do life in relationships. This view often combines subjective and objective factors related to satisfaction with life. As already mentioned, many studies have found a relationship between depressive symptoms and loneliness in the elderly. Often times, research can go even further to name loneliness as a significant predictor of depressive symptoms within one year of onset of loneliness. Along with the increased prevalence of depression, many aging individuals experience severe anxiety related to the increased feelings of loneliness due to expectations they possess about themselves. This can all therefore contribute to the decreased satisfaction in life, which leads to overall decreased well-being (Gerino et al., 2017).

This loneliness-induced dissatisfaction with life has been associated with many physical and mental health issues. One issue is specifically centered around how capable lonely individuals view themselves when it comes to dealing with different demands and situations. This ability to cope and adapt to stressful or traumatic experiences is known as resilience. The concept of resilience is essential to successful aging, often promoting longevity due to its protective factors. The primary function of resilience protects the body from the long-term complications that arise from chronic stress. In a lonely or isolated individual, they are under the stress of that loneliness, and the resulting depression often leads to further decreased resilience to cope with that stress. This increases overall susceptibility to complications from the stress of social isolation and loneliness in older adults (Gerino et al., 2017).

Implications and Interventions

Identifying the physiological processes influenced by social isolation is very important for several reasons. One primary implication is the financial benefits that would be uncovered in implementing interventions aimed to decrease the incidence of loneliness and isolation. In the context of resilience in the elderly, finding new ways to promote socialization and decrease loneliness in the older population may result in fewer healthcare visits and therefore costs of the patient. The complications that arise from isolation-influenced stress can lead to many unnecessary hospitalizations, leading to a greatly increased cost for the healthcare company, the patient, and the insurance company. If the burden of isolation on disease process would be somewhat lightened, the costs for each of these parties may be reduced (Gerino et al., 2017).

Furthermore, the quality of life and overall satisfaction with one's life has the potential to be greatly increased by implementing new strategies to decrease isolation. In the elderly population specifically, these individuals have transitioned from total independence to relying on

another person to provide care and interaction for them. If provided the opportunity to at least build their own relationships and connections with those around them, these patients and individuals may be able to increase their feeling of independence and thus their satisfaction and quality of life (Gerino et al., 2017). Along with financial and mental health outcomes, it is important to recognize the obvious physical benefits of implementing new interventions to reduce the incidence of loneliness and isolation. Based on each study discussed, patients can experience decreased mortality, cardiovascular disease, increased coping abilities, improved attachment, increased immune function, and a plethora of other health benefits simply by providing logical interventions with various populations.

Many different interventions can be used in reducing the incidence and impact of loneliness. Both individual and group interventions were found to be effective in reducing social isolation and loneliness, specifically in older adults (Tong et al., 2021). One intervention that could be used across the lifespan is the implementation of a program to improve social skills. Starting at a young age, children with poorer social skills are likely to experience loneliness due to exclusion from activities. Programs which improve those social skills may be useful in allowing the child opportunities to build connections and relationships throughout his or her life in a meaningful way. Another recommended intervention is enhancing the already available social support. This can be used by strengthening friendships, encouraging communication within a supportive group, and allowing for healthy relationships. Increasing social support can improve some individuals' poor perception of the social support that is already in their lives. A third intervention to reduce loneliness is to increase opportunities for social interaction. This may be one of the most beneficial in the healthcare setting and nursing practice. Because of the isolation that occurs during a long-term hospitalization and in long-term care facilities such as

nursing homes, it is important to allow patients to interact with one another and with family. This can be implemented in a number of different ways, such as encouraging spending mealtimes in small groups or promoting the use of activity groups (Masi et al., 2013). It is important to note that these interventions only show effectiveness with willing and active participation from those involved (Tong et al., 2021). Loneliness can also be helped in both the younger and older populations by building a buddy program in which one younger individual is paired with an elderly individual. This shows potential to provide the older adult with a sense of purpose and relationship, while the younger individual receives valuable wisdom and connections (Masi et al., 2013). Despite a limited evidence base, virtual interaction has also recently been implemented for reducing social isolation in older adults (Tong et al., 2021).

Gaps in the Literature

Many different gaps are present in the literature used in this discussion. From the mental health standpoint, it is difficult to rule out reverse causality. While isolation and loneliness can clearly often influence the development of depression, the diagnosis of depression often also promotes isolation in an affected individual (Thoits, 2011). Additionally, many of the studies examine data utilizing self-reporting of symptoms. This is further exaggerated by the subjectivity of the concept of loneliness. While isolation is the objective variable based on a number and quality of social connections, the measurement of loneliness is simply based on an individual's report. Many studies utilize different self-reporting scales in their data collections as well, likely leading to some variability of results in this overview. This overview also does not examine or discuss any socioeconomic factors on loneliness, isolation, and health. Further studies will be needed in order to determine the most effective and practical interventions to reduce the incidence of loneliness-associated health complications. One final limitation on this review is the

consideration of culture on interventions and isolation. Many cultures vary with regards to the value of human interaction and connections. As a result, isolation and loneliness can clearly not be used interchangeably, and a subject may appear to be measured as very isolated but may not experience all of the negative implications that have been found with loneliness due to the cultural acceptability of that isolation (Thoits, 2011).

Conclusion

While it is a well-known idea that social isolation and loneliness can negatively impact an individual's health and well-being, few know the reasoning or severity of these implications. When studies show the increased mortality associated with loneliness, along with the heightened risk of cardiovascular disease, cognitive decline, and poor mental health outcomes, it becomes clear how vital human interaction is to health and well-being. Every aspect of health has been found to be highly impacted by social connectedness, including physical, emotional, social, spiritual, and intellectual health. Through the implementation of the proposed interventions, as well as continuing research on how to best support those in the populations at risk, health policies may be able to increase socialization for many individuals, thus improving health outcomes while decreasing costs.

References

- Aita, M., Stremmler, R., Feeley, N., Lavallée, A., & De Clifford-Faugère, G. (2017). Effectiveness of interventions during NICU hospitalization on the neurodevelopment of preterm infants: A systematic review protocol. *Systematic Reviews*, *6*(225). <http://doi.org/10.1186/s13643-017-0613-5>
- Agarwal, K. (2020). Failure to thrive in older adults: Evaluation. *UpToDate*. Retrieved October 7, 2020 from <https://www.uptodate.com/contents/failure-to-thrive-in-older-adults-evaluation>
- Angeli, F., Reboldi, G., & Verdecchia, P. (2021). The link between inflammation and hypertension: Unmasking mediators. *American Journal of Hypertension*, *34*(7), 683-685. <http://doi.org/10.1093/ajh/hpab034>
- Bhatti, A. B., & Haq, A. U. (2017). The pathophysiology of perceived social isolation: Effects on health and mortality. *Cureus*, *9*(1), 994. <http://doi.org/10.7759/cureus.994>
- Bornstein, A. B., Rao, S. S., & Marwaha, K. (2021). Left ventricular hypertrophy. *StatPearls [Internet]*. <https://www.ncbi.nlm.nih.gov/books/NBK557534/>
- Bu, F., Zaninotto, P., & Fancourt, D. (2020). Longitudinal associations between loneliness, social isolation, and cardiovascular events. *Heart*, *108*(16), 1394-1399. <http://dx.doi.org/10.1136/heartjnl-2020-316614>
- Douplik, S. K., Henry, M. K., Bae, H., Litman, J., Turner, S., Scharko, A. M., & Feudtner, C. (2016). Mental health conditions and symptoms in pediatric hospitalizations: A single-center point prevalence study. *Academic Pediatrics*, *17*(2), 184-190. <https://doi.org/10.1016/j.acap.2016.08.009>

- Elovainio, M., Sommerlad, A., Hakulinen, C., Pulkki-Raback, L., Virtanen, M., Kivimaki, M., & Singh-Manoux, A. (2018). Structural social relations and cognitive ageing trajectories: Evidence from the Whitehall II cohort study. *International Journal of Epidemiology*, *47*(3), 701-708. <http://doi.org.10.1093/ije/dyx209>
- Gerino, E., Rollé, L., Sechi, C., & Brustia, P. (2017). Loneliness, resilience, mental health, and quality of life in old age: A structural equation model. *Frontiers in Psychology*, *8*, 1-12. <http://doi.org/10.3389/fpsyg.2017.02003>
- Granqvist, P., Sroufe, L. A., Dozier, M., Hesse, E., Steele, M., Van Ijzendoorn, M., Solomon, J., Schuengel, C., Fearon, P., Bakermans-Kranenburg, M., Steele, H., Cassidy, J., Carlson, E., Madigan, S., Jacobvitz, D., Foster, S., Behrens, K., Rifkin-Graboi, A., Gribneau, N., Spangler, G., Ward, M. J., ... Duschinsky, R. (2017). Disorganized attachment theory in infancy: A review of the phenomenon and its implications for clinicians and policy-makers. *Attachment and Human Development*, *16*(6), 534-558. <http://doi.org/10.1080/1416734.2017.1354040>
- Halter, M. J., & Kozy, M. (2018). Depressive disorders. In M. J. Halter (Ed.), *Varcolis' foundations of psychiatric-mental health nursing: A clinical approach* (8th ed., pp. 242-269). Elsevier.
- Halverson, J. L., Bhalla, R. N., Moraille-Bhalla, P., Andrew, L. B., & Leonard, R. C. (2020). Depression. *MedScape*. <https://emedicine.medscape.com/article/286759-overview#a3>
- Håmmig, O. (2019). Health risks associated with social isolation in general and in young, middle, and old age. *PLoS ONE*, *14*(7), 1-18. <https://doi.org/10.1371/journal.pone.0219663>

Holt-Lundstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: A meta-analytic review. *Association for Psychological Science, 10*(2), 227-237. <http://doi.org/10.1177/1745691614568352>

Janzen, K. C., Reimer-Kirkham, S., & Astle, B. (2019). Nurses' perspectives on spiritual caregiving: Tending to the sacred. *Journal of Christian Nursing, 36*(4), 251-257. <http://doi.org/10.1097/CNJ.0000000000000575>

Kim, A. R., Kim, S. Y., & Yun, J. E. (2020). Attachment and relationship-based interventions for families during neonatal intensive care hospitalization: A study protocol for a systematic review and meta-analysis. *Systematic Reviews, 9*(61). [http:// 10.1186/s13643-020-01331-8](http://10.1186/s13643-020-01331-8)

Krishnan, R. (2018). Unipolar depression: Neurobiology. *UpToDate*. Retrieved August 31, 2021, from https://www.uptodate.com/contents/unipolar-depression-neurobiology?search=depression%20pathophysiology&topicRef=118668&source=see_link

Lahousen, T., Unterrainer, H. F., & Kapfhammer, H. P. (2019). Psychobiology of attachment and trauma: Some general remarks from a clinical perspective. *Front Psychiatry, 10*, 1-15. <http://doi.org/10.3389/fpsyt.2019.00914>

Leigh-Hunt, N., Bagguley, D., Bash, K., Turner, V., Turnbull, S., Valtorta, N., & Caan, W. (2017). An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health, 152*, 157-171. <http://dx.doi.org/10.1016/j.puhe.2017.07.035>

- Lean, R. E., Rogers, C. E., Paul, R. A., & Gerstein, E. D. (2018). NICU Hospitalization: Long-term implications on parenting and child behaviors. *Curr Treatment Options Pediatric*, 4(1), 49-69.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986282/pdf/nihms937105.pdf>
- Loades, M. E., Chatburn, E., Higson-Sweeney, N., Reynolds, S., Shafran, R., Brigden, A., Linney, C., McManus, M. N., Borwick, C., & Crawley, E. (2020). Rapid systematic review: The impact of social isolation and loneliness on the mental health of children and adolescents in the context of COVID-19. *Journal of American Child Adolescent Psychiatry*, 59(11), 1218-1239. <http://doi.org/10.1016/j.jaac.2020.05.009>
- Long, E. M. (2018). Disorders of thought, emotion, and memory. In T. Norris (Ed.), *Porth's pathophysiology: Concepts of altered health states* (10th ed., pp. 524-544). Wolters Kluwer.
- Long, E. M. (2021). Faith community nursing: Identifying and combating social isolation and loneliness in older adults. *Journal of Christian Nursing*, 38(4), 234-239. <http://doi.org/10.1097/CNJ.0000000000000883>
- Masi, C. M., Chen, H.Y., Hawkey, L. C., & Cacioppo, J. T. (2011). A meta-analysis of interventions to reduce loneliness. *Personality and Social Psychology Review*, 15(3), 219-266. <http://doi.org/10.1177/1088868310377394>
- MayoClinic. (2021). *Depression (Major depression disorder)*.
<https://www.mayoclinic.org/diseases-conditions/depression/symptoms-causes/syc-20356007>. Retrieved September 13, 2021.

- Pennestri, M. H., Gaudreau, H., Bouvette-Turcot, A. A., Moss, E., Lecompte, V., Atkinson, L., Lydon, J., Steiner, M., & Meaney, M. J. (2015). Attachment disorganization among children in neonatal intensive care unit: Preliminary results. *Early Human Development, 91*, 601-606. <http://dx.doi.org/10.1016/j.earlhumdev.2015.07.005>
- Poey, J. L., Burr, J. A., Robertys, J. S. (2016). Social connectedness, perceived isolation, and dementia: Does the social environment moderate the relationship between genetic risk and cognitive well-being? *The Gerontologist, 57*(6), 1031-1040. <http://doi.org/10.1093/geront/gnw154>
- Rateau, M. (2019). Stress management. In M. Harding (Ed.), *Lewis's Medical-Surgical Nursing: Assessment and Management of Clinical Problems* (11th ed., pp. 76-87). Elsevier.
- Ritchie, C. S., Locher, J. L., Roth, D., L., McVie, T., Sawyer, P., & Allman, R. (2008). Unintentional weight loss predicts decline in activities of daily living function and life-space mobility over 4 years among community-dwelling older adults. *Journal of Gerontology: Medical Sciences, 63*(1), 67-75. <http://doi.org/10.1093/gerona/63.1.67>
- Sargin, D., Oliver, D. K., & Lambe, E. K. (2016). Chronic social isolation reduces 5-HT neuronal activity via upregulated SK3 calcium-activated potassium channels. *eLife Sciences*, 1-14. <https://doi.org/10.7554/eLife.21416>
- The Attachment Project (2020, July 2). *Disorganized attachment: Causes and symptoms*. <https://www.attachmentproject.com/blog/disorganized-attachment/>
- Thoits, P. A. (2011). Mechanisms linking social ties and support to physical and mental health. *Journal of Health and Social Behavior, 52*(2), 145-161. <http://doi.org/10.1177/0022146510395592>

Tong, F., Yu, C., Wang, L., Chi, I., Fu, F. (2021). Systematic review of efficacy of interventions for social isolation of older adults. *Frontiers in Psychology, 12*.

<http://doi.org/10.3389/fpsyg.2021.554145>

Xia, N., & Li, H. (2018). Loneliness, social isolation, and cardiovascular health. *Antioxidants and Redox Signaling 28*(9), 837-851. <http://doi.org/10.1089/ars.2017.7312>