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REVIEW ARTICLE

The health consequences of loneliness

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ABSTRACT

In this paper, through a thematic literature review of recent studies, our objective was to explore the impact of loneliness and its effects on health. We emphasize the human need for a sense of belonging and societal inclusion. We further discuss the link of loneliness to physiological alterations, to the development and exacerbation of mental health conditions, the influence it has on cognitive processes, and the role it plays in contributing to maladaptive coping strategies. Contrary to the feelings of loneliness, solitude and its benefits for self-reflection and personal growth are explored. The prevalence of loneliness and its cultural similarities and differences are discussed at a global level. Moreover, this review explores the intricate relationship between loneliness and various health outcomes, including chronic illness and mortality risks. It further emphasizes the importance of acknowledging loneliness as a public health concern and the need for interventions at the individual and societal level to mitigate its adverse effects.

Keywords: loneliness; isolation; health; illness; negative effects; mental health

1. Navigating loneliness: Understanding its impact on physical and emotional well-being

As echoed already by Aristotle, the ancient Greek philosopher, humans are social beings[1]. We naturally seek out social connections to develop meaningful and long-lasting interpersonal relationships which provide us with a sense of belonginess. On the contrary, when our social needs are not being met, we may experience loneliness. Broadly, loneliness is a subjective experience where there is perceived dissatisfaction between the social interactions one desires in terms of quantity and quality and the actual level of relationships they have[2,3].

Loneliness is found to be more prevalent among older adults. A 2018 survey study by the AARP Foundation found one in three older adults aged 45 and older reported feeling lonely[4]. As indicated by the findings of the survey completed by the AARP Foundation, loneliness is a societal concern with its prevalence reaching alarming levels. Although individuals are becoming more globally connected through technology use, paradoxically, many find themselves contending with a growing sense of disconnection[5,6] and social fragmentation.

This review embarks on a comprehensive exploration of the profound impact of loneliness on well-being and its physiological, affective, cognitive, and behavioral effects. Understanding the complexity of loneliness

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and its associated health consequences is not only an academic pursuit but rather a significant public health imperative. As the world navigates through social transformations and unexpected pandemics, it is essential to understand how loneliness shapes our physical, emotional, and behavioral health.

2. Methodology

In conducting a comprehensive review of the available literature on the consequences of loneliness for both physical and emotional health, an extensive search was conducted using Google Scholar. The search was conducted using a combination of keywords and MeSH terms to capture relevant literature. The primary terms used included "loneliness," "physical health," "mental health," "emotional health," "health consequences," and any associated synonyms. To ensure a focused search, we restricted the use of keywords and MeSH terms to the article titles. This restriction aimed to identify relevant articles that emphasized their focus on loneliness and its physical, emotional, and health consequences. Further, Boolean operators "AND" and "OR" were used to appropriately combine terms. The search was limited to articles that were published within the last 10 years, ending in 2023, to ensure the inclusion of recent literature. In Google Scholar, the keywords generated 703 articles. From this amount, a total of 100 studies were considered relevant to the topic and included in this paper. The articles were drawn from recent peer reviewed journals published worldwide, which dealt with, both, loneliness, and its affect on health: mental, physical, emotional. Articles in English, those that were originally published in English, or translations that were provided by foreign journals, and that were based on quantitative methods, were included. Articles whose full text is not in English were excluded. Each study had more than 100 participants that formed a representative sample of the targeted population, in order to increase the of generalization of results. Only scientific articles describing experimental studies and descriptive or review articles and which were published in peer-reviewed journals were included. Documents such as book chapters, doctoral theses and conference or congress papers were excluded.

2.1. About belonging

We all yearn to belong. Looking at the animal kingdom, it becomes clear that we cannot survive, individually, as a community and even as a species without being part of a larger group[7]. Being part of a community, for animals and humans alike, ensures survival, assistance when needed, and provides a direction for the individual as to how to operate within a larger body of individuals. Most animals, just like humans cannot survive not being part of a group, and for humans it is even more crucial, as until they reach the age of about six years old, they are almost totally dependent on their significant others[3]. Not belonging, either being separated geographically or just perceiving it, brings about loneliness. Today's Western culture created a paradox, in that on the one hand we yearn and search for closeness and intimate relationships, and on the other hand our social conditions do not encourage developing the very human relations which we long for. That is so, particularly in the U.S. and the other English-speaking countries. In those cultures, the 'Me' is hailed as more important than the "We', and people are encouraged to appear strong and able to handle their lives on their own. Additionally, there is a stigma associated with loneliness, which people are desperately trying to avoid being labeled so[3].

In the 21st century, we live in a manner that enhances isolation, while people, by nature, continue to look for others with whom to connect[8]. During the second half of the 20th century and from then on, more and more people have "no one to talk to", despite all the technological advances that we hoped would enhance our social connection[9]. At the dawn of the 21st century, our Western culture magnifies the alienation and separateness that we experience, while we actually yearn to belong.

Holt-Lunstad, Robles, and Sbarra[10] reviewing various epidemiological studies, observed that there is clear evidence that social relationship can predict and affect important health outcomes and risk for early death.

Epidemiologists, psychologists and sociologists have been aware of that fact for now there is increased experimental activity in this field. The World Health Organization now lists "social support networks" as an important factor in health[11]. Although there is increased awareness of the importance of social relations, and the important effect of loneliness on societal health and illness[12], As Hold-Lunstad, Robles, and Sbarra[10] observed that a 'significant portion' (no percentages were provided) of the U.S. population lack social connections, suggested, and that is associated with increased possibility that they will face morbidity and untimely mortality.

2.2. Loneliness

Lippke and Warner[13] explored when is the greatest need for humans to connect, and found that Internet searches around, say, Christmas time, or in relation to "Covid-19", "climate", or "war", are triggered by these events[14,15]. In a well-known meta-analysis, Pinquart and Sorensen[16] found that adolescents appear particularly prone to loneliness due to the process of human development which involves separation from parents, identity diffusion, and excessive rejection experiences. As people get older, they have fewer social contacts and experience a slight increase in loneliness. In all age groups, limited health and functionality increase the likelihood of loneliness[17].

Various theories exist regarding the definition of loneliness. The following characteristics of the experience of loneliness are shared by various approaches to the topic[18]:

- Loneliness, so familiar to most of us, is an experience of separation.
- Loneliness appears to be closely related to the person's attachment style, which was established in the early years, but also to the individual's experience in life.
- While solitude is pleasant and may be sought after, loneliness is painful, unwanted, and causes suffering.
- Loneliness, being so aversive, causes those who experience it to seek meaning and connection. Looking at it evolutionarily, it is suggested that loneliness is meant to encourage connectedness in order to increase our chances of survival, finding a role and meaning within the group.
- On the positive side, loneliness has the potential to motivate us, to grow, and connect with those who may become our supporters.

Loneliness is shared by all of us, and is a subjective experience which, consequently, is affected by one's personality, environmental and social changes, and history[3].

Mann et al.[19] defined loneliness as a distressing mismatch between the quantity and/or quality of social relationships a person has, vs. what they actually want. That may or may not commensurate with the objective reality they are in. Research points out that loneliness is mostly experienced by the oldest old and by emerging adults (those under 25), giving a roughly 'U-shaped' distribution. Mann et al.[19] asserted that the lonely are twice as likely to become depressed, compared to the non-lonely.

Recent research indicates that many do not have a close person in whom they can confide in, resulting in a fundamental loss of human contact that was so essential to previous generations and were thus preserved[20,21].

2.3. Physiological effects of loneliness

Loneliness has been associated with increased mortality, depressive symptoms, neurological irregularities and a compromised immune system, heightened blood pressure[22]; premature aging[23], heightened hypothalamic pituitary adrenocortical activity[24], inflammation and even the development of Alzheimer's disease[25].

Loneliness has been theorized as a form of an alarm system, similar to the physiological alarms we receive from our body when feeling thirsty or hungry[26–28]. People who are reporting chronic loneliness show long-

term consequences which are associated with the body's metabolic, neuroendocrine, and immune systems possibly leading to chronic mental and physical conditions[29]. Research further suggests loneliness plays a role in dysregulating immune responses. Specifically, lonely individuals present with weaker immune systems when attempting to adjust to stressful situations such as pathogens[30].

2.4. Affective features

Loneliness, commonly includes a large group of negative and upsetting emotions, such as feeling undesirable, dismissed or ignored, feeling miserable and unattractive. Additionally, people reported feeling anxiety, rejection, feelings of being irrational, rejected, and inferior[31–33]. Meta-analyses studies have found significant associations between loneliness and mental health concerns such as depression[19], suicidal ideation[34], altered responsiveness to stress, withdrawal from social activities[35,36], poor self-related health[37,38], lower self-esteem[39], increased emotional distress[39], decreased life satisfaction[38], and decreased quality of life[40–42]. Of particular interest is the 2020 study by Buecker and colleagues[43] where they examined the association between loneliness and the five dimensions of personality which is the cognitive, emotional, and behavioral qualities that form the unique characteristics of an individual[44]. The five-factor model includes the following traits: openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism[45]. In the 2020 meta-analysis, Buecker et al.[43] found that loneliness was positively related to neuroticism and negatively related to extraversion.

2.5. Cognitive features

Lonely individuals seem to possess low self-esteem, which plays a role in the growth and upkeep of each other[18,46]. Lonely individuals often report that they perceive themselves to be useless, ugly, unlovable, and socially clumsy, and are hyper-sensitive to being rejected[47]. It is obvious that this may create a negative feedback loop leading to worthlessness, hopelessness and of course, further loneliness.

In a sample of 1972 individuals in Hong Kong, a cross-sectional study found that feelings of rumination, which is defined as uncontrollable dwelling and repetitive focus on negative thoughts[48,49], were more intense in lonely individuals[50]. Both loneliness and rumination were found to be positively related to symptoms of depression[50].

Individuals who are lonely have been found to pay increased attention to negative interactions and demonstrate poor self-regulation skills[51]. Compared to individuals who are not lonely, lonely individuals present with poor cognitive functioning[38], decreased executive functioning, and they are more likely to engage in unhealthy lifestyle behaviors[20,27,35,52] such as substance abuse.

2.6. Loneliness behaviorally

People who experience loneliness are known to be inhibited and possess ineffective social skills, less inclined to face social challenges, lack assertiveness, and have lacking social skills, where they may exaggerate their self-disclosure in a way of letting the world know of their misery[20,53]. They appear to be helpless and act in a passive and inefficient manner, continuously needing and even demanding attention[21]. This may lead to increased difficulties with forming new relationships and maintaining existing relations as well as negatively impacting effective communication in one's personal and professional life.

Another behavioral consequence of those who report chronic loneliness is withdrawal from social activities. Individuals who are lonely may deliberately avoid gatherings or decrease interactions with others[54]. Social withdrawal can worsen feelings of loneliness and create a cycle where lonely individuals may experience a preference for being alone[55] and thereby are further isolated from potential sources of support and companionship. Further, loneliness may drive individuals to embrace unhealthy coping behaviors. For

example, in an attempt to cope with the feelings of loneliness, lonely individuals may turn to substance abuse in efforts to numb their emotional pain[56,57].

2.7. Solitude

Being alone, meaning separated from others, does not necessarily mean that one is lonely. Essentially, one can be alone and not lonely. Being alone is neither good nor bad, it is just a description of one's objective reality. Cacioppo et al.[22], likened solitude to the glory of aloneness, while loneliness is the pain of aloneness. Long[58,59] observed that there may be nine different kinds of solitude, which he then classified into three categories: the solitude of self-expansion which is expressed through creativity and self-knowledge, negative solitude which basically translates to feeling lonely, and solitude associated with a sense of intimacy and a spiritual connection with others. Solitude, enhances people's ability to engage in self-exploration and creativity[59]. Solitude, which is not imposed or painful -like loneliness often is- is commonly seen as one's desire to be alone to do what one can do only when left alone. Immense joy and fulfilment can be found in solitude, which allows us to get away from the daily barrage of tasks, expectations, stimulations, and often time inconveniences. Solitude allows us to be at peace, ponder, meditate write, create, and thus getting a chance to revitalize, reenergize, and reinvigorate[26,59]. It is, therefore, not surprising that various spiritual traditions, Buddhism for instance, direct followers to practice solitude as a way to become more grounded[60]. Various religious and mythological figures, such as Moses, Jesus, Mohammed, Buddha, and Guru Nanak to name a few, have been known to spend significant periods of time on their own. For example, Jesus' journey into the wilderness, Buddha's meditation under the Bo Tree, and Odysseus's 10-year voyage into his homeland were all moments where solitude led to enlightenment[3]. Various revered writers (e.g., Kafka, Rilke) and philosophers (e.g., Kant, Hume, Wittgenstein) were able to create their deepest and most profound work when they retreated into solitude. Henry David Thoreau provided a well-known example when he retreated to the Walden Pond for a period of about two years in order to seek solitude, following which he produced very insightful writings[61]. It was observed that several of the most creative minds on our planet require solitude in order to create and become[62]. Moustakas[63], who was one of the first writers to examine loneliness, spoke openly about the healing and growth-promoting process of solitude which may result in unique revelations, and enhance our ability to connect to others. Those who can practice and find joy in solitude, are not desperately attached to others and are then free to engage in social intercourse when the time is right[64]. Although both loneliness and solitude refer to being alone, how we experience it is what determines the two constructs. Feeling forgotten, irrelevant, and abandoned by those around us, often results in loneliness. However, we may seek solitude for the opposite needs we have at the time: needing to be alone in order to participate in pursuits that are important to us such as introspection, or relaxing from the daily onslaught of stimuli and demands[21].

2.8. Social relations and health

Individualism and autonomy have long been celebrated in western cultures. While, in the past, we used to think that infants need mainly to have their materialistic needs fulfilled, our view of human needs is beginning to change. The biological fact is that we are first and foremost a social species, and our nature is to recognize, interact, and form relationships with conspecifics[27]. Research has indicated that social relations are important for mental as well as physical wellbeing throughout our life span[65]. Cacioppo and Cacioppo[27] noted the various demands of social living to be "(a) learning by social observation; (b) recognizing the shifting status of friends and foes; (c) anticipating and coordinating efforts between two or more individuals; (d) using language to communicate, reason, teach, and deceive others; (e) orchestrating relationships, ranging from pair bonds and families to friends, bands, and coalitions; (f) navigating complex social hierarchies, social norms, and cultural developments; (g) subjugating self-interests to the interests of the pair bond or social group in

exchange for the possibility of long-term benefits; (h) recruiting support to sanction individuals who violate group norms; and (i) doing all this across time frames that stretch from a person's distant past to multiple possible futures". They also noted that the social structures that are so central to humans resulted in the development of neural, hormonal, genetic, and molecular mechanisms as a way of supporting them since they help people survive and reproduce. For a long time, researchers focused on the physical environment when they aimed to find out what influences physical health. In the past few decades that exploration broadened to include the person's social relations that may have a significant impact on one's health behavior and on one's brain, biology, and health[66,67].

2.9. Loneliness = lack of social connections

We now know that social connections are very important for our health and wellbeing. Lack of such connections usually negatively affects our health, life, and genetic legacy. Among the negative effects of social isolation in nature, Cacioppo and Cacioppo[66] outlines "social isolation has been shown to decrease the lifespan of the fruit fly, Drosophilia melanogaster … promote the development of obesity and type 2 diabetes in mice … exacerbate the infarct size and edema and decrease post-stroke survival rate following experimentally induced stroke in mice… delay the positive effects of running on adult neurogenesis in rats… increase the activation of the sympathetic adrenomedullary response to acute stressors in rats … decrease the expression of genes regulating glucocorticoid response in the frontal cortex of piglets … decrease open field activity, increase basal cortisol concentrations, and decrease lymphocyte proliferation to mitogens in pigs". Humans when born, are totally dependent and do not usually thrive if they are in isolation. In a large-scale study which was carried out in the US, feelings of loneliness were found to be associated with increased mortality risk[68]. Research found higher rates of morbidity and mortality in lonely people compared to non-lonely adults[14,69]. Loneliness was found to be a risk factor for increased blood pressure, sleep disturbance, increased hypothalamic pituitary adrenocortical activity, it negatively affected the immune system, and reduced impulse control[70–72].

2.10. Looking at loneliness evolutionarily

Given the negative consequences of humans being on the social perimeter, the brain adapted to that danger by learning to monitor the status of one's social body similarly to having learned to monitor the status of one's physical body. Just like physical pain serves as a signal to draw attention and respond to threats or damage to one's physical body, loneliness serves as a signal to draw attention to and motivate the individual to possible damage to one's social body[28]. People survived, since the beginning of history, by banding together, in couples, in families, in tribes to provide support and protection to the group's members. Loneliness is aversive, and it is possible that it is so in order to motivate us, humans, to renew the social connections we need in order to create social trust, and cohesiveness. Just like when ignoring physical needs like thirst of hunger, ignoring loneliness may contribute to deleterious mental and physical health. Just like foods that may be healthy or unhealthy for us, interactions with people can also be figuratively poisonous or nutritious in their effect on us[28].

2.11. Loneliness, globally

Aside from the various health consequences that were pointed out, it may also negatively affect our behavioural, mental, and social health. Moreover, those who are chronically lonely, have a 26% increased risk of mortality[73]. Culture is known to affect how loneliness is experienced Cacioppo and Cacioppo[74] postulated that age, interacts with retirement for instance, resulting in loneliness. They also observed that one third of the population in industrialised countries experience loneliness, with 8% of them experiencing severe loneliness.

In a survey of 113 countries, done by Surkalim et al.[73] during the period 2000–2019, They found that loneliness is a common experience worldwide. And while their data pointed out that young and middle-aged

adults have experienced lower rates of loneliness, though those findings are different from what other studies found[75]. Surkalim et al.[73] concluded in light of their data, the prevalence of loneliness is highly heterogenous across countries. They noted, for instance, that northern European countries reported the lowest prevalence of loneliness, while eastern European countries reported the highest. One study saw those differences as a result of demographic characteristics such as health status, social participation, and social support[76], other studies attributed it to welfare systems and social security schemes in those countries[77]. It appears that a combination of high socioeconomic status, which is negatively associated with loneliness, overall health, a well functioning welfare system, and an active social participation may shed light on the low prevalence of loneliness in northern European countries[73]. In contrast, in eastern European countries who have lacking healthcare services, loneliness is more prevalent. It was suggested that in those eastern European countries which may be transitioning form socialism, care arrangements are being changed in addition to reduced social trust may shed light on the causes of the high levels of loneliness found there[76].

2.12. Lonely people

The lonely behave somewhat differently than non-lonely people. They perceive interpersonal relationships as menacing, and are careful of negative social contacts. Consequently, they may avoid meeting social partners. As a result, they may experience hostility, stress, anxiety, and low self-esteem, which in turn may activate neurobiological and behavioural mechanisms that affect health negatively[78]. Interestingly, loneliness was found to more significantly affect health status than any other element of the social network, like number of individuals one is connected with, and negatively impacts mortality[79]. The United States, Germany, Australia and the United Kingdom, suggested that the world is dealing with a loneliness epidemic[10], raising up the possibility of a public health crisis.

Loneliness has recently been reported to affect as much as one third of individuals in industrialized countries, across all age groups[74]. Loneliness has been negatively associated with various health factors such as mental and physical health[80], sleep[81], cognition[82], and cardiovascular health[83], as well as loneliness being positively correlated with morbidity and mortality[79]. Park et al.[24] found a significant correlation between loneliness and depression. Similarly, they found an association between loneliness and anxiety symptoms[84]. Several meta-analyses have demonstrated a strong association between loneliness and risk of cardiometabolic disease and overall mortality[79,83,84]. Loneliness is associated with an increased risk of dementia[85,86].

Loneliness is a potent stressor, which has been associated with poor health and many adverse health outcomes, including cardiovascular disease, lung disease, diabetes, and functional limitations[87,88]. The association between loneliness and health appears to be bidirectional, in that loneliness may adversely effect health while poor or worsening health may create difficulties for people to remain socially connected, and thus intensify their loneliness[27,89,90]. Many physiological changes are correlated with loneliness which result in poor health as well as in reduced health related behavior, like diet and exercise, as well as reduced sleep quality[91,92].

The impact of loneliness on health is now gaining increased attention from policy makers, governments, and voluntary sector organisations throughout the world[93,94]. Various European countries are developing plans to address loneliness across the life course[95,96]. Loneliness is implicated in mental ill-health[97]. Loneliness and depression are closely intertwined, with longitudinal evidence that loneliness predicts future depression over many years[98].

Martín-María et al.[78] examined the health status of people who complained of transient vs. chronic loneliness. They found a significant relationship of loneliness to deteriorating health status in both groups, validating the repeated findings that loneliness impairs health status. It is unclear, yet, what are the possible

mechanisms that underlie this association remain, but it is clear that the onset of loneliness contributes to the detriment of the physiological and the immune stress response in lonely population[35]. Research found that chronic loneliness was associated with inflammatory disorder involving a hampered transcription of glucocorticoid regulation, and with impairment of the executive functioning which may lead to the person engaging in unhealthy behaviors contributing to higher rates of morbidity and mortality[79,99].

2.13. Illness and loneliness

Modern medical science has been focused, even obsessed, with death, which provided medicine with a clear "enemy", and consequently, medical research has focused on conquering the diseases that cause death[100]. Physicians stand at the frontline of fighting diseases and mortality. The medical profession attending to patients has changed its approach from initially conquering the illness, to later caring for the person who has that illness[101]. Research demonstrated that social support was positively correlated to stronger immune systems, while those who lack social support are more amenable to illness. Loneliness and social isolation have negative consequences on our health as much as obesity, high blood pressure or cigarette smoking[22,102]. Segrin et al.[103] examined the connection of loneliness and ill health and confirmed that the lonely seem to neglect their health and do not practice healthy eating and living since there is no one there to encourage the person to engage in health promoting behaviors[104,105]. Moreover, acute cardiovascular stress responses happens more frequently amongst the lonely than the non-lonely and lowers their ability to withstand stress[106]. Not only that loneliness may bring about illness, but may also corrupt the recuperative process[103].

2.14. Loneliness and chronic pain

Chronic pain was described as "an unpleasant sensory and emotional experience associated with actual tissue damage or described in terms of such damage. While it is unquestionably a sensation in part or parts of the body, it is always unpleasant and therefore an emotional experience"[107]. Piotrowski[108] asserted that chronic pain is quite prevalent, affecting about half of the population of the U.S. The person suffering from pain directs most of his or her attention to relieving it, and thus seems to lose his independence and his motivation for social intercourse[107,109,110]. Expectations, mood, and behavioral factors affect our perception of pain and significantly impact the sufferer's close relationships and social[111]. Apparently, social isolation is a frequent and central issue confronting chronic pain patients[112]. There is a strong positive correlation between chronic pain and loneliness, and that naturally lowers life satisfaction[113]. Comparing patients with Fibromyalgia and Rheumatic diseases, it was found that those with fibromyalgia experienced significantly more loneliness than those with rheumatoid arthritis[114]. Continuing to explore the effect of loneliness on ill health, another study found higher rates for both loneliness and depression in sickle cell disease patients[115]. Loneliness was a major risk factor for the development of pain, fatigue, and depression in cancer patients[116]. Social support and involvement, as well as familial cohesion can positively affect coping with pain[117,118]. Familial relationships can help the chronic pain sufferer tremendously.

2.15. Chronic illness and loneliness

Research demonstrates a robust directional effect of loneliness on physical health problems across the life span[72]. An association which is particularly evident in old age when loneliness is associated with morbidity and mortality[35]. With its association with depression, high blood pressure, disrupted sleep, and dysregulation of neuroendocrine and immune responses, loneliness may speed up physical health decline[3]. Illnesses which affect functional ability, such as cardiovascular disease, cancer or osteoarthritis, may prevent the patient from participating in social activities, and alternatively that very functional disability may enhance their loneliness. Depression and anxiety are very common mood disorders associated with cancer, as the patients are basically forced to address their illness while the rest of the world goes on in its regular daily living[119].

2.16. Loneliness and dementia

There is a quickly rising incidence of people afflicted with dementia, so much so that it became a significant health policy concern in many countries[120]. Although it has been established that the greatest risk of dementia is due to genetic factors, research indicated that social support can serve to protect the individual from dementia, or at least delay its onset, while loneliness is positively correlated with the onset of dementia[121]. "The International Classification of Diseases Version Ten (ICD-10) defines dementia as a decline of memory, cognitive skills, planning and managing daily activities, and a loss of control of emotions and social skills"[122]. Developing Alzheimer's disease is positively correlated with chronic stress, anxiety, and the consequent structural damages to the prefrontal cortex of the brain and hippocampus, which then alter the person's stress reaction mechanism[123].

Elovainio et al.[120] surveyed electronic records of 155,063 participants, collated by the UK National Health Service (NHS). These researchers discovered that loneliness was associated with increased risk of all-cause dementia. Further, loneliness was found to be positively correlated with poor cognitive functioning, including immediate and delayed recall, memory, as well as a general acceleration of cognitive decline[124,125]. Guarnera et al.[126] pointed out that loneliness stimulates a biological stress response which is expressed in cortisol dysfunction, that leads, over time, to poor health outcomes such as inflammation or metabolic disorders[124,127]. These may be expressed, over time, in poor health which is closely associated with loneliness. Additionally, as the hippocampus is particularly sensitive to stress hormones, its functioning is disrupted and there is a reduction in memory processing capacity[128]. Furthermore, heightened cortisol secretion affects the brain negatively and brings about neurodegeneration[129], which is notable given higher cortisol levels have been observed in patients with dementia[128]. These findings give more credence to the understanding that maladaptive hypothalamic-pituitary-adrenal (HPA) axis function mediates the relationship between loneliness and failing cognition leading to dementia[126]. Various brain regions seem to exhibit structural and functional differences in lonely individuals[130]. These include abnormal grey and white matter distributions within the prefrontal cortex, hippocampus and amygdala, posterior superior temporal cortex, and increased cerebral white matter volume[131]. Lazzari and Rabottini[122] conducted a meta-analysis on ten studies which involved 43,872 people aged 50 or older, and examined how social isolation, and consequent loneliness which was imposed during the COVID-19 pandemic, affected their cognitive functions, resulting for some in dementia. Older people reported, during the pandemic that face-to-face support was missing and they were cut off from those with whom they commonly interacted, which consequently resulted in experiences of depression and anxiety[132]. They noted that, both, the physical as well as the mental health of older people can be negatively impacted by loneliness. Social interaction affects brain and body functions, and can lead to psychological frailty which may be followed by reduced psychological and cognitive functioning. It is, thus, clear that social intercourse is vital for people, and especially the elderly[122]. Lazzari and Rabottini's[122] study indicated that the higher the level of loneliness and social isolation, the greater the risk of developing dementia. There is concern that the elderly, who were isolated during the pandemic may be amenable to increased risk of dementia, and disturbed mental stability in people who may otherwise be healthy[133].

Sutin et al.[134] examined the association between loneliness and dementia from a variety of causes, utilizing a longitudinal research approach. The diagnosis of dementia, which was derived from death records, included Alzheimer's disease (AD), vascular dementia (VaD), and frontotemporal dementia (FTD). Results indicated that loneliness accounted for a 60% increased risk of dementia from all three kinds. Sundstorm et al.[135] studied, longitudinally, 1905 individuals without dementia, and found that loneliness may be followed by AD but not so by VaD, though generally, loneliness is seen as one of the causes of dementia. Shen et al.[136] aimed to investigate the association of social isolation and loneliness with dementia. They included 462,619

participants data on which they pulled from the UK Biobank cohort. Their results pointed out that loneliness was related to dementia, but more than that, social isolation was a risk factor of dementia, independent of loneliness. They asserted that brain structure differences that are related to social isolation coupled with different molecular functions indicate that social isolation is, indeed, correlated with cognition and dementia. In their study, Qiao et al.[137] found a correlation between loneliness and increased risk for dementia. They examined the association of loneliness with three types of dementia: Alzheimer's disease (AD), mild cognitive impairment (MCI), and vascular dementia (VaD). While their findings demonstrated a positive correlation between AD and loneliness, no such correlation was found with the other two types of dementia. Qiao et al.[137] conducted a meta-analysis considered 4625 cases of dementia among 62,345 individuals included in 16 cohort studies. One of the causal explanations to for the association of loneliness and dementia is that loneliness may increase amyloid burden in the elderly who usually are the victims of dementia[138].

2.17. Loneliness and mortality

The sick role ends up determining how one perceives his situation. Additionally, family members and healthcare providers are clearly aware of that role[139]. The social role of the dying is similarly to the role of the sick person who may not be so critically ill. And while the sick role terminates in the restoration of health, the dying role terminates when the person does. Noyes and Clancy[139] suggested that the dying person "has an obligation to avail himself of the necessary supports to life and to cooperate in their administration. If he fails to do so, he may impose a 'burden' upon his family and overload those on whom he has grown dependent. He is not expected to remain dependent upon the physician, who has already, in the process of diagnosing a fatal illness, transferred him from the sick to the dying role…. Another of the important aspects of the dying person's cooperation is his acceptance of the curtailment of freedom and loss of privileges imposed by caregivers. If institutional care is required he is expected to abide by the rules and routines which enable the facility to deliver that care efficiently. Lastly, dependency is encouraged in the sick role, whereas independence, within the limits of an individual's declining resources, is encouraged in the dying role".

We, in the North American culture have been conditioned to fear death, but as one gets closer to death, one endures the ultimate aloneness, leaving behind all that is loved and familiar, and which no one can save his from. Loneliness has been documented to be a central feature in both the patient and his or her caregivers[140].

For the majority of people, chronic illness is closely related to dying or suffering from grave illnesses such as heart failure, frailty or dementia[141]. People may travel on one of three routes on their way out of this world: possibly the preferred one is symbolized by good health for a long period of time, and only towards the end does the person rapidly declines, may have serious health issues, and then faces death. About 25% of older Americans face the second route which includes a slow process of declining health ending with their death. The third and least preferred route which about 40% of the elderly in the U.S. experience, includes deteriorating health, loss of cognitive functions, requiring years of personal care[142].

Hawkely[17], a seasoned loneliness researcher, found that loneliness is associated with a range of adverse health outcomes, such as effects on mortality, morbidity, health behaviours and health-care utilization[143]. Additionally, it was found to be linked with increased risk of cardiovascular disease (including coronary heart disease and stroke), metabolic syndrome, functional disability, dementia and mild cognitive impairment, as well as be a precursor to depression, anxiety, and suicidal ideation[92].

Valtorta et al.[144] conducted a meta-analysis on 11 studies involving victims of cardiac events and stroke. Their results indicated that poor social relationships, and the following loneliness, were associated with 29% increase in coronary heart disease, and 32% increase in the risk of a stroke. Possible explanation for these results were that being with others who may encourage one to engage in healthy behaviors, improve access to

health-related information, consume healthier nutrition, and exercise regularly, may all contribute to lower one's proclivity to become ill[145]. Loneliness is known to be related to depression, which naturally lowers the individual's interest in his health, or alternatively in improving it[146,147]. Grant and colleagues[148] examined key metabolic risk factors for cardiovascular mortality, including blood pressure, lipids, and cortisol responses to stress. They found dysregulated blood pressure and cortisol responses to acute stress in those who had only few close friends. These physiologic changes increase risk of heart attacks and stroke.

3. Conclusion

In closing, this paper which encompasses a thematic review of the literature, aimed to paint a comprehensive picture of loneliness and its profound repercussion on our well-being, illuminating the immediate and long-term effects that loneliness has on human health. Recent literature was reviewed on the topics of loneliness and its physiological, affective, cognitive, and behavioral effects. The foundational need to belong and the characteristics of loneliness was described. As discussed, most humans feel a yearning to belong, and when the need for social connections is not met, we are at an increased risk for experiencing negative health consequences.

It is important to consider that being alone does not necessarily constitute feelings of loneliness. Distinctions between loneliness and solitude were examined and the benefits of solitude on self-exploration and its connections for spirituality was further discussed. In fact, certain religions and spiritual traditions emphasize the importance of solitude for getting in touch with one's self and for enlightenment. From a broader perspective, the importance of social relations is explored including the shift of examining loneliness from an evolutionary perspective and reviewing loneliness at a global level. It is noted from our review that while loneliness is experienced worldwide, culture, among other variables, affects how loneliness is experienced. Further, the implications of loneliness and its association with chronic illness and pain enforces the detrimental long-term consequences loneliness has on one's physical and emotional health if left untreated.

The interconnectedness of the physiological, cognitive, emotional, and behavioral aspects of loneliness demonstrates the need for interdisciplinary and comprehensive interventions to address the negative effects of loneliness. Acknowledging that loneliness is a public health risk is the first step in combating the detrimental health consequences of loneliness. It is imperative that society as a whole prioritizes initiatives aimed at raising awareness of loneliness, fostering social connections, and the implementation of therapeutic interventions which promote resilience and belonging to address loneliness.

Conflict of interest

The authors declare no conflict of interest.

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