

LONELINESS AND ITS RELATIONSHIP WITH CANCER

Dr. Shashi K. Agarwal
Center for Contemporary and Complementary Cardiology
2227 US Highway 1, Suite 309, North Brunswick, NJ 08902, USA
E-mail: usacardiologist@gmail.com

ABSTRACT

Cancer is one of the leading and most feared non-communicable diseases diagnosed in humans. Despite significant improvement in cancer screening, diagnostics, and therapeutics, it is far from being controlled and its incidence is expected to continue to rise worldwide. Cancer is expected to become the leading cause of global deaths in the coming decades. As a result, cancer preventive therapy is experiencing a noticeable upsurge in interest. Loneliness, a pernicious emotional and social phenomenon, is not only a risk factor for cancer and but is also closely associated with lifestyles. Healthy lifestyles play an important role in cancer prevention, and positively modulate every aspect of cancer throughout its course. Unfortunately, loneliness is ubiquitous in our society, and its prevalence appears to be rising. Further, cancer itself promotes the development of loneliness. The relationship between loneliness and cancer is intricate and bidirectional and is associated with ominous outcomes. This manuscript briefly reviews this deleterious relationship.

Keywords: Loneliness, Social Isolation, Cancer, Depression, Unhealthy Lifestyles.

INTRODUCTION

Cancer is a major public health problem worldwide (<https://www.who.int/news-room/fact-sheets/detail/cancer>). The International Agency for research on cancer and the World Health Association (WHO), indicates that in 2018, there were 18.1 million new cases globally (<https://gco.iarc.fr/>). The most common cancers were those affecting the lung, breast, and prostate (<https://gco.iarc.fr/>). Cancer-related deaths reached 9.6 million in 2018 (<https://www.iarc.fr/featured-news/latest-global-cancer-data-cancer-burden-rises-to-18-1million-new-cases-and-9-6-million-cancer-deaths-in-2018/>), and cancer is now the second leading cause of death in the world (Bray et al., 2019). In the high-income countries, cancer has already overtaken cardiovascular diseases as the leading cause of death (Mahase, 2019). It may become the leading cause of global deaths in the coming decades (Dagenais et al., 2020). Cancer is also pervasive in the United States (US) (Siegel et al., 2018). An American male has a 40% lifetime risk while an American female has a 38% lifetime risk of developing cancer (Noone et al., 2018). Cancer survival, although improving, remains dismal and about 40% of cancer sufferers will not survive 5 years (de Moor et al., 2013). Second primary cancers are also on the rise and now account for 15 to 20% of all cancer diagnoses (Demoor-Goldschmidt & de Vathaire, 2019). It was estimated that the US spent \$173 billion on cancer care in 2020 (Mariotto et al., 2011). According to WHO, Europe has one-quarter of the global cases of worldwide cancers, although comprising only one-eighth of the total world population (<https://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/data-and-statistics>). Cancer is also common in China

(Yu et al., 2015), the world's most populous country, and has become its leading cause of death (Feng et al., 2019).

Loneliness is a common disorder in our society (<https://www.cigna.com/about-us/newsroom/studies-and-reports/combatting-loneliness/>) and is a major risk factor for several non-communicable diseases, including cancer (Williams et al., 2009). Lonely people also tend to lead unhealthy lifestyles and are more depressed and these contribute to the increased risk (Richard et al., 2017; Cacioppo et al., 2018). It is estimated that unhealthy lifestyles are responsible for almost 40% of all cancers (Song & Giovannucci, 2016). Studies from China indicate that the major unhealthy lifestyles responsible for cancer deaths in 2013 were smoking (Islami et al., 2017). Hepatitis B virus (HBV) infection, and low fruit/vegetable intake in men and HBV infection, low fruit/vegetable intake, and second-hand smoke exposure in women (Islami et al., 2017). Loneliness in cancer also leads to increased fatigue, more pain, frequent sleep disturbance (Jaremka et al., 2014), a poor quality of life, and higher mortality (Drageset et al., 2013; Adams et al., 2017). On the other hand, cancer patients often experience disproportional loneliness, precipitated by several related factors, such as stigma, undesirable effects of cancer and its treatment, and the fear of recurrence (Kim et al., 2009; Kroenke et al., 2013; Knapp et al., 2014; Mahendran et al., 2020). Caregivers of cancer patients also suffer from a higher level of loneliness when compared to non-caregivers (Ekwall et al., 2005).

DISCUSSION

Human beings did not evolve to be alone (Cacioppo et al., 2014), and exhibit a strong need to belong (Baumeister & Leary, 1995). However, many individuals experience the subjective perception of either quantitative or qualitative deficiencies in personal and social relationships in their lives and feel lonely (Perlman & Peplau, 1981). This feeling of loneliness has been noted in individuals all over the world (Richard et al., 2017; Rico-Uribe et al., 2016; Zhong et al., 2018; van Tilburg & Fokkema, 2018; Cohen-Mansfield et al., 2009; Victor & Bowling, 2012; Yang & Victor, 2011; Stickley et al., 2014; Griffin, 2010; Steed et al., 2007; Tiwari, 2013; Wilson & Moulton, 2010). Studies have reported loneliness in Europe (Yang & Victor, 2011; Rico-Uribe et al., 2016), Asia (Yang et al., 2018; Chokkanathan, 2020) and Africa (Ojembe & Ebe Kalu, 2018). In the US, loneliness has been reported in all age groups (Asher et al., 1984; Cassidy & Asher, 1992; De Jong and van Tilburg, 1999; Victor et al., 2005). One study involving kindergarteners and first graders reported that 12% felt lonely at school (Cassidy & Asher, 1992) while 8.4% of third through sixth graders reported being lonely (Asher et al., 1984). De Jong Gierveld and van Tilburg found that up to 32% of adults over the age of 55 report experiencing loneliness at any given time (De Jong & van Tilburg, 1999). It is also common in the 65+ age group (Victor et al., 2005). A recent study in the US of adults aged 18 and older found that 46 percent reported "sometimes or always feeling alone" (<https://www.cigna.com/about-us/newsroom/studies-and-reports/combatting-loneliness/>).

Loneliness has severe detrimental physical and mental effects on the human body (Richard et al., 2017). Physical ailments linked with loneliness include obesity (Lauder et al., 2006), diabetes (Lauder et al., 2020), elevated blood pressure (Hawley et al., 2006), coronary artery disease (Valtorta, et al., 2018), cognitive decline (Wilson et al., 2007), recurrent stroke (Cacioppo et al., 2014), and insomnia (Cacioppo et al., 2002). It is also associated with premature mortality (Luo et al., 2012). Psychiatric dysfunctions associated with loneliness include depression (Cacioppo et al., 2010), alcoholism (Akerlind & Hörnquist, 1992), suicidal ideation

(Rudatsikira et al., 2007), aggressive behaviors, and impulsivity (Ernst & Cacioppo, 1999; Cacioppo et al, 2014).

Impact of loneliness on cancer

Loneliness exerts several negative effects on cancer (Williams et al., 2009; Jaremka et al., 2014; Nausheen et al., 2010; Adams et al. 2017; Drageset et al. 2013) including increasing its risk (Williams et al., 2009), magnifying the symptoms (Jaremka et al., 2014), accelerating the disease progression (Nausheen et al., 2010), worsening the health-related quality of life (Adams et al. 2017), and decreasing survival (Drageset et al., 2013). The deleterious effects of loneliness on cancer are also influenced by unhealthy lifestyles (Behrens et al., 2018). Lonely people have reduced self-regulation (Hawkley & Cacioppo et al., 2010) and this contributes to the increased prevalence of unhealthy lifestyles noted in these individuals (Stickley et al., 2013; Richard et al., 2017; Algren et al., 2020). Unhealthy lifestyles include physical inactivity (Shiovitz-Ezra & Litwin, 2012), smoking (Christakis & Fowler, 2008), high alcohol intake (Shiovitz-Ezra & Litwin, 2012), having an improper diet (Locher et al., 2005), being overweight/obese (Whisman, 2010), and engaging in risky sex (Torress & Gore-Felton, 2007). Unhealthy lifestyles have a major negative impact on cancer incidence and progression (Khan et al., 2009). Individuals with stronger social connections are less likely to practice poor lifestyles (Samuel et al., 2015). Lonely people are more physically inactive and less likely to exercise (Hawkley et al., 2009; Page & Hammermeister, 1995; Vancampfort et al., 2019; Netz et al., 2013) Physical activity, including exercise, helps prevent several cancers (Physical Activity Guidelines Advisory Committee, 2018), decreases cancer-related symptoms such as fatigue, anxiety, and depression (Schmitz et al., 2019), improves the quality of life (Bourke et al., 2014), and increases survival (Patel et al., 2019). Lonely people tend to smoke more than non-lonely people (Dyal & Valente, 2015; Kobayashi & Steptoe, 2018; Shankar et al., 2011). Cigarette smoke is rich in carcinogens (Secretan et al., 2009), and can cause cancers almost in any bodily part, especially in the lungs (Lee et al., 2012), colon (Botteri et al., 2008), breast (Gaudet et al., 2013), stomach (Ladeiras-Lopes et al., 2008), and uterus/cervix (ICESCC, 2007). Continued smoking in cancer patients leads to poor treatment response, increased treatment-related side effects (NCCDPHP, 2014; Daniel et al., 2009), diminished quality of life (Danson et al., 2016), a higher risk of cancer recurrence (Warren et al, 2019), and an increase in the risk of developing a second primary cancer (Do et al., 2004). Lonely people are more likely to abuse alcohol (Canham et al., 2016). Cancers related to alcohol intake are numerous (Islami et al., 2018), and include those of the esophagus and stomach (Choi et al., 2018; Day et al., 1994), breast (IARC, 2010), colon/rectum (Fedirko et al., 2011), liver (Bagnardi et al., 2015), prostate (Watters et al., 2010), lung (Bagnardi et al., 2015), and skin (Rota et al., 2017). Diet also plays an important role in cancer (Potter et al., 2016). Lonely people are less likely to consume fruits and vegetables and more likely to consume excessive amounts of red meat, processed meat, and junk food (Locher et al., 2005). Greater vegetable and fruit consumption helps prevent cancers of the stomach, esophagus, lung, breast, oral cavity and pharynx, endometrium, pancreas, and colon (Steinmetz & Potter, 1996), while a diet rich in meat and animal products, especially processed meat (hot dogs, bacon, sausages, deli meat) increases the risk of getting cancers of the breast, colon, stomach, and prostate (Chan et al., 2011; Bouvard et al., 2015). A prudent diet also helps reduce many cancer-associated symptoms such as pain and fatigue (Arthur et al., 2014), improves the quality of life in these individuals (Kassianos et al, 2015), and increases survival (Kushi et al., 2012). It also retards the development of second primary cancers in cancer survivors (Murphy et al., 2017).

Loneliness leads to higher (Rotenberg & Flood; 1999) and unhealthy food consumption (Baumeister et al., 2005) and reduced exercise (Hawley et al., 2009), contributing to the increased obesity seen in these individuals (Lauder et al., 2006). Excess body fat is responsible for many cancers (Islami et al., 2018), including cancers of the esophagus (Kubo & Corley, 2006), liver (Larsson & Wolk, 2007), gallbladder (Larsson & Wolk, 2007a), pancreas (Larsson et al., 2007) breast (Feola et al., 2006), stomach (Kubo & Corley, 2006), uterus (Brinton et al., 2007), ovary (Bandera et al., 2016), kidney (Golabek et al., 2016), colon/rectum (Dong et al., 2017), and the meninges (Wiedmann et al., 2013). Obesity also plays a detrimental role in cancer recurrence and the development of second primary cancers (Sang et al., 2016). It is associated with an increase in mortality in cancer patients (Calle et al., 2003). Obesity-related stigma results in lower rate of work hire, lesser promotions, and higher wrongful dismissal - factors that further fuel social isolation (Chen et al., 2012). Lonely people are also more likely to engage in risky sex (Torress & Gore-Felton, 2007). Risky sex promotes sexually transmitted infections (Holmes & Levine, 2004) and some of these can lead to cancer (IARC, 2012). Hepatitis B (Mahale et al., 2019) and hepatitis C (Mahale et al., 2017) infections are associated with liver cancer. Human papillomavirus infection can lead to cervical, anal, vaginal, and penile cancer (Barchitta et al., 2018). Epstein-Barr virus infection is associated with Burkitt lymphoma and Hodgkin lymphoma (Thun et al., 2017). HIV has profound immunosuppressive effects, and this makes it a co-carcinogen for oncogenic viruses, especially the Kaposi Sarcoma virus (Tso et al., 2017). It is estimated that healthy lifestyle habits and preventable screening can prevent a significant number of cancers, including 33% of lung cancers, 42% of breast cancers, 43% of colon cancers, and 20% of prostate cancers (<https://www.nhs.uk/news/cancer/lifestyle-and-cancer-rates/>).

Lonely people are also more depressed than non-lonely people (Cacioppo et al., 2006). Depressive symptoms include low mood, lack of energy, sadness, and insomnia (DSM-V, 2013) which tend to worsen cancer and its treatment-associated symptoms. Co-morbid depression also leads to an increased treatment noncompliance (DiMatteo et al., 2003), a more rapid disease progression (Satin et al., 2009), a further decrease in the quality of life in these patients (Brown et al., 2014), and decreased cancer survivorship (Pinquart & Duberstein, 2010).

Lonely cancer patients are prone to experience more pain, depression, and fatigue than non-lonely individuals with cancer (Jaremka et al., 2013). They are less likely to be compliant with preventive cancer screening (Lagerlund et al., 2014), and preventive vaccinations (Hajek et al., 2014). They may be more likely to be non-compliant with treatment and other beneficial interventions (Swiatoniowska et al., 2019).

Impact of cancer on loneliness

Cancer itself is conducive to the development of loneliness (Wells & Kelly, 2008; Deckx et al., 2014). Cancer-induced loneliness is commonly seen in younger patients, those who are living under deprived circumstances, those treated with chemotherapy or radiotherapy, and those with advanced disease (Dahill et al., 2020). The severity of loneliness rises with increasing time after cancer diagnosis (Deckx et al., 2014). Cancer patients often suffer from a plethora of unpleasant and often disabling symptoms such as anorexia, fatigue, nausea and vomiting, severe pain, and cognitive dysfunction (Kim et al., 2009; Duncan et al., 2009) and these affect social relationships and precipitate or aggravate loneliness (Foster et al., 2009). Cancer patients may also experience loneliness due to personal issues, such as fear of cancer recurrence and premature death, hopelessness, being a burden to others, and a sense of profound loneliness, grief, regret, or embitterment about what has been missed in life (Campbell-Enns & Woodgate, 2015; Vehling &

Kissane, 2018). They also experience several social issues such as feeling that family members and other social acquaintances are not concerned or receptive to discuss their cancer-related concerns (Adams et al., 2015; Adams et al., 2016). Cancer-related stigma is also common, especially in patients whose cancer is attributed to their behavior, for example, smoking in lung cancer (Lebel & Devins, 2008; Knapp et al., 2014). Cancer patients may also harbor a belief that their disease is a deserved punishment (Peters-Golden, 1982). This can further hinder social participation (Adams et al., 2016). Cancer induced negative social expectations, often help sustain the loneliness (Adams et al., 2017). Cancer treatment itself may cause bleeding, bruising, constipation, delirium, diarrhea, edema, fertility problems, alopecia, memory or concentration problems, mouth and throat issues, peripheral neuropathy, sexual concerns, skin and nail changes, and urinary/bladder problems (Kim et al., 2009), and further increase social isolation. The resultant loneliness may aggravate the fatigue, pain, and cognitive dysfunction often experienced by these patients (Jaremka et al., 2014), result in increased treatment noncompliance (DiMatteo et al., 2003), and decrease the quality of life (Adams et al., 2017).

Mechanisms

Loneliness is associated with dysregulation of the hypothalamo–pituitary–adrenal (HPA) axis and altered cortisol activity (Doane et al., 2010) characterized by blunted morning cortisol rise and a flattened diurnal cortisol rhythm (Zilioli et al., 2017). An overactive HPA axis can lead to increased cancer risk and increased cancer progression (Spiegel, 2012). Loneliness also increases the levels of three systemic inflammation biomarkers: interleukin-6 fibrinogen and C-reactive protein (Smith et al., 2020; Nersesian et al., 2018). Inflammation is associated with the development and progression of cancer (Singh et al., 2019). Loneliness also decreases immunity (Walker et al., 2019). An impaired immune system can play a significant role in cancer emergence and progression (Palmer et al., 2018). Though a disturbed autonomic system may also play a role (Gouin et al., 2015), the above three appear to be the main mechanisms as to how loneliness contributes to the development and a detrimental prognosis in cancer (Reiche et al., 2004). A decrease in healthy behaviors adds a plethora of other mechanisms that are associated with cancer initiation or progression (Sinha et al., 1998; Seitz & Stickel, 2007; Patrelli et al., 2009; Seitz & Stickel, 2010; Rock et al., 2012; Berg et al., 2014; Leitzmann et al., 2015; Bortolato et al., 2017).

Therapeutic Interventions

Several therapeutic interventions have been developed to treat loneliness and include antidepressants, neuro-steroids, and oxytocin (Masi et al., 2010). The use of antidepressants in cancer patients is not uncommon and helps other cancer-related symptoms such as pain, fatigue, anorexia, nausea, vomiting and hot flashes (Grassi et al., 2018). Cognitive behavioral therapy has been shown to be beneficial in lonely individuals and helps cancer patients to improve their quality of life (Daniels, 2015). Social support is important for physical and psychological adjustment to cancer and helps reduce chronic loneliness often experienced by these patients and may help improve cancer prognosis (Usta, 2012; Nausheen et al., 2009). Loneliness plays an important role in the practice of healthy lifestyles and the latter is causally associated with cancer prevention and better outcomes (Khan et al., 2010). Practicing healthy lifestyles should also help prevent non-cancerous chronic diseases such as cardiovascular, diabetes, COPD, arthritis, etc. in the pre- and post-cancer diagnosed patients (Elmwood et al., 2013). Besides targeting loneliness,

lifestyle counseling, and modification should also be a major therapeutic target in cancer patients (Hawley & Cacioppo, 2003; Masi et al., 2010; Cleary & Stanton, 2015).

CONCLUSION

Loneliness is pervasive in our society. Cancer is soon expected to topple cardiovascular diseases to become the number one killer in the world. Loneliness plays an important role in increasing the risk of cancer, amplifying the adverse effects, generating a poor response to treatment, increasing the risk of recurrence, increasing mortality, and increasing the development of second primary cancers in cancer survivors. Cancer itself, due to social stigma and other co-morbid factors, can initiate loneliness or exacerbate it. Lonely individuals are less likely to adopt and adhere to healthy behaviors, further increasing the risk of developing cancer, exaggerating cancer-related symptoms, increasing resistance to therapy, promoting recurrences and the development of secondary cancers, and decreasing survival. Due to the increased survival of cancer patients, loneliness related unhealthy lifestyles make them more susceptible to increased morbidity and mortality from other non-cancerous chronic diseases. Both loneliness and cancer cause depression, another deleterious co-morbidity perniciously impacting all phases of cancer. To summarize, loneliness and cancer are bidirectionally and intricately interlinked, with deleterious outcomes.

Acknowledgement: None

Funding: None

Conflict of interest: None

REFERENCES

Adams RN, Mosher CE, Abonour R, Robertson MJ, Champion VL, Kroenke K. (2016). Cognitive and situational precipitants of loneliness among patients with cancer: A qualitative analysis. *Oncology Nursing Forum*. 43(2):156–163. doi: 10.1188/16.ONF.156-163.

Adams RN, Mosher CE, Rand KL, Hirsh AT, Monahan PO, Abonour R, Kroenke K. (2017). The Cancer Loneliness Scale and Cancer-related Negative Social Expectations Scale: Development and validation. *Quality of Life Research*. 1–13. doi: 10.1007/s11136-017-1518-4.

Adams RN, Winger JG, Mosher CE. (2015). A meta-analysis of the relationship between social constraints and distress in cancer patients. *Journal of Behavioral Medicine*. 38(2):294–305. doi: 10.1007/s10865-014-9601-6.

Akerlind I, Hörnquist JO. (1992). Loneliness and alcohol abuse: a review of evidences of an interplay. *Social Science & Medicine*. 34:405–414. doi: 10.1016/0277-9536(92)90300-F.

Algren MH, Ekholm O, Nielsen L, Ersbøll AK, Bak CK, Andersen PT. (2020). Social isolation, loneliness, socioeconomic status, and health-risk behaviour in deprived neighbourhoods in Denmark: A cross-sectional study. *SSM Popul Health*. 10:100546. doi:10.1016/j.ssmph.2020.100546.

Arthur AE, Peterson KE, Shen J, Djuric Z, Taylor JMG, Herbert JR, Duffy SA, Peterson LS, Bellile EL, Douglas BW, CHepeha DB, Schipper MJ, Wolf GT, Rozek LS. (2014). Diet

and proinflammatory cytokine levels in head and neck squamous cell carcinoma. *Cancer*. 120:2704-2712.

Asher S, Hymel S, Renshaw PD. (1984). Loneliness in children. *Child Development*. 55:1456–1464.

Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E, Pelucchi C, Galeone C, Bellocchio R, Negri E, Corrao G, Boffetta P, La Vecchia C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer*. 2015 Feb 3;112(3):580-93. doi: 10.1038/bjc.2014.579.

Bandera EV, Qin B, Moorman PG, Alberg AJ, Barnholtz-Sloan JS, Bondy M, Cote ML, Funkhouser E, Peters ES, Schwartz AG, Terry P, Schildkraut JM. (2016). Obesity, weight gain, and ovarian cancer risk in African American women. *Int J Cancer* 139:593–600.

Barchitta M., Maugeri A., Quattrocchi A., Agrifoglio O., Scalisi A., Agodi A. (2018). The Association of Dietary Patterns with High-Risk Human Papillomavirus Infection and Cervical Cancer: A Cross-Sectional Study in Italy. *Nutrients*. 10:469. doi: 10.3390/nu10040469.

Baumeister RF, DeWall CN, Ciarocco NJ, Twenge JM. (2005). Social exclusion impairs self-regulation. *Journal of Personality and Social Psychology*. 88(4):589–604.

Baumeister RF, Leary MR. (1995). The Need to Belong: Desire for Interpersonal Attachment as a Fundamental Human Motivation. *Psychological Bulletin*. 117:497–529.

Behrens G, Gredner T, Stock C, Leitzmann MF, Brenner H, Mons U. (2018). Cancers Due to Excess Weight, Low Physical Activity, and Unhealthy Diet. *Dtsch Arztebl Int*. 115(35-36):578-585. doi:10.3238/ärztebl.2018.0578.

Berg G, Erlacher A, Smalla K, Krause R. (2014). Vegetable microbiomes: is there a connection among opportunistic infections, human health and our 'gut feeling'??. *Microb Biotechnol*. 7(6):487-495. doi:10.1111/1751-7915.12159.

Bortolato B, Hyphantis TN, Valpione S, Perini G, Maes M, Morris G, Kubera M, Köhler CA, Fernandes BS, Stubbs B, Pavlidis N, Carvalho AF. (2017). Depression in cancer: The many biobehavioral pathways driving tumor progression. *Cancer Treat Rev*. Jan;52:58-70. doi: 10.1016/j.ctrv.2016.11.004.

Botteri E, Iodice S, Bagnardi V, Raimondi S, Lowenfels AB, Maisonneuve P. (2008). Smoking and colorectal cancer: a meta-analysis. *JAMA*. 300(23):2765–78. doi: 10.1001/jama.2008.839.

Bourke L, Gilbert S, Hooper R, Steed LA, Joshi M, Catto JW, Sexton JM, Rosario DJ. (2014). Lifestyle changes for improving disease-specific quality of life in sedentary men on long-term androgen-deprivation therapy for advanced prostate cancer: a randomised controlled trial. *European Urology*. 65:865-72.

Bouvard V; Loomis D; Guyton KZ; Grosse Y; Ghissassi FE; Benbrahim-Tallaa L; Guha N; Mattock H; Straif K. (2015). Carcinogenicity of consumption of red and processed meat. *Lancet Oncol*. 15: 1599- 1560.

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 68(6):394–424.

Brinton LA, Sakoda LC, Frederiksen K, Sherman ME, Kjaer SK, Graubard BI, Olsen JH, Mellemkjaer L. (2007). Relationships of uterine and ovarian tumors to pre-existing chronic conditions. *Gynecol Oncol* 107:487–94.

Brown Johnson CG, Brodsky JL, Cataldo JK. (2014). Lung cancer stigma, anxiety, depression, and quality of life. *J Psychosoc Oncol.* 32(1):59-73. doi: 10.1080/07347332.2013.855963.

Cacioppo J.T., Hughes M.E., Waite L.J., Hawkley L.C., Thisted R.A. (2006). Loneliness as a specific risk factor for depressive symptoms: cross-sectional and longitudinal analyses. *Psychology and Aging.* 21: 140-151. <https://doi.org/10.1037/0882-7974.21.1.140>.

Cacioppo J.T., Hughes M.E., Waite L.J., Hawkley L.C., Thisted R.A. (2006). Loneliness as a specific risk factor for depressive symptoms: cross-sectional and longitudinal analyses. *Psychology and Aging.* 21: 140-151.

Cacioppo JT, Hawkley LC, Berntson GG, Ernst JM, Gibbs AC, Stickgold R, Hobson JA. (2002). Do lonely days invade the nights? Potential social modulation of sleep efficiency. *Psychological Science.* 13:384–387. doi: 10.1111/1467-9280.00469.

Cacioppo JT, Hawkley LC, Thisted RA. (2010). Perceived social isolation makes me sad: Five year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychology and Aging.* 25:453–463.

Cacioppo S, Capitanio JP, Cacioppo JT. (2014). Toward a neurology of loneliness. *Psychol. Bull.* 140:1464. doi: 10.1037/a0037618.

Calle E.E., C. Rodriguez, K. Walker-Thurmond, M.J. Thun. (2003). Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med,* 348, pp. 1625-1638.

Campbell-Enns H, Woodgate R. (2015). The psychosocial experiences of women with breast cancer across the lifespan: a systematic review protocol. *JBIR Database System Rev Implement Rep.* 13(1):112-121. doi:10.11124/jbir-2015-1795.

Canham SL, Mauro PM, Kaufmann CN, Sixsmith A. (2016). Association of Alcohol Use and Loneliness Frequency Among Middle-Aged and Older Adult Drinkers. *Journal of Aging and Health.* 28(2):267-284. doi:10.1177/0898264315589579.

Cassidy J, Asher SR. (1992). Loneliness and peer relations in young children. *Child Development.* 63(2):350–365.

Chan DS; Lau R; Aune D; Vieira R; Greenwood DC; Kampman E; Norat T. (2011). Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies [serial online]. *PLoS One.* 6: e20456.

Chen E, Fettich K, McCloskey M. (2012). Correlates of suicidal ideation and/or behavior in bariatric-surgery-seeking individuals with severe obesity. *Crisis.* 33:137.

Choi YJ, Lee DH, Han KD, Kim HS, Yoon H, Shin CM, Park YS, Kim N. (2018). The relationship between drinking alcohol and esophageal, gastric or colorectal cancer: A nationwide population-based cohort study of South Korea [published correction], *PLoS One.* May 21;13(5):e0197765.

Chokkanathan S. (2020). Prevalence of and risk factors for loneliness in rural older adults. *Australas J Ageing.* Oct 23. doi: 10.1111/ajag.12835.

Christakis NA, Fowler JH. (2008). The collective dynamics of smoking in a large social network. *N Engl J Med.* 358(21): 2249–2258.

Cleary EH, Stanton AL. (2015). Mediators of an Internet-Based Psychosocial Intervention for Women With Breast Cancer. *Health Psychology.* 34:477–485. doi: 10.1037/hea0000170.

Cohen-Mansfield J, Shmotkin D, Goldberg S. (2009). Loneliness in old age: longitudinal changes and their determinants in an Israeli sample. *Int Psychogeriatr.* 21(6):1160-1170. doi:10.1017/S1041610209990974.

Dagenais GR, Leong DP, Rangarajan S, Lanas F, Lopez-Jaramillo P, Gupta R, Diaz R, Avezum A, Oliveira GBF, Wielgosz A, Parambath SR, Mony P, Alhabib KF, Temizhan A, Ismail N, Chifamba J, Yeates K, Khatib R, Rahman O, Zatonska K, Kazmi K, Wei L, Zhu J, Rosengren A, Vijayakumar K, Kaur M, Mohan V, Yusufali A, Kelishadi R, Teo KK, Joseph P, Yusuf S. (2020). Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *Lancet.* Mar 7;395(10226):785-794. doi: 10.1016/S0140-6736(19)32007-0.

Dahill, H. Al-Nakisbandi, K.B. Cunningham, G.M. Humphris, D. Lowe, S.N. Rogers. (2020). Loneliness and quality of life after head and neck cancer, *British Journal of Oral and Maxillofacial Surgery.* 11 Jul, 58(8):959-965. DOI: 10.1016/j.bjoms.2020.04.041

Daniel M, Keefe FJ, Lyra P, Peterson B, Garst J, Kelley M, Bepler G, Bastian LA. (2009). Persistent smoking after a diagnosis of lung cancer is associated with higher reported pain levels. *J Pain.* 10:323-8.

Danson SJ, Christine Rowland, Richard Rowe, Sue Ellis, Carol Crabtree, Janet M. Horsman, Jonathan Wadsley, Matthew Q. Hatton, Penella J. Woll & Christine Eiser. (2016). The relationship between smoking and quality of life in advanced lung cancer patients: a prospective longitudinal study. *Support Care Cancer.* 24(4):1507-1516. doi:10.1007/s00520-015-2928-x.

Day GL, Blot WJ, Shore RE, Schoenberg JB, Kohler BA, Greenberg RS, Liff JM, Preston-Martin S, Austin DF, McLaughlin JK, Fraumeni Jr. (1994). Second cancers following oral and pharyngeal cancers: Role of tobacco and alcohol. *Journal of the National Cancer Institute.* 86(2):131-137.

De Jong Gierveld J, van Tilburg T. (1999). Living arrangements of older adults in the Netherlands and Italy: Coresidence values and behaviour and their consequences for loneliness. *Journal of Cross-Cultural Gerontology.* 14(1):1-24.

de Moor JS, Mariotto AB, Parry C, Alfano CM, Padgett L, Kent EE, Forsythe L, Scoppa S, Hachey M, Rowland JH. (2013). Cancer survivors in the United States: prevalence across the survivorship trajectory and implications for care. *Cancer Epidemiol Biomarkers Prev.* Apr; 22(4):561-70. doi: 10.1158/1055-9965.EPI-12-1356.

Deckx L, van den Akker M, Buntinx F. (2014). Risk factors for loneliness in patients with cancer: a systematic literature review and meta-analysis. *Eur J Oncol Nurs.* Oct;18(5):466-77. doi: 10.1016/j.ejon.2014.05.002.

Demoor-Goldschmidt C, de Vathaire F. (2019). Review of risk factors of secondary cancers among cancer survivors. *Br J Radiol.* 92(1093):20180390. doi:10.1259/bjr.20180390.

DiMatteo MR, Robinson JD, Heritage J, Tabbarah M, Fox SA. (2003). Correspondence among patients' self-reports, chart records, and audio/videotapes of medical visits. *Health Commun.* 15:393-413.

Do KA, Johnson MM, Lee JJ, Wu XF, Dong Q, Hong WK, et al. (2004). Longitudinal study of smoking patterns in relation to the development of smoking-related secondary primary tumors in patients with upper aerodigestive tract malignancies. *Cancer.* 101:2837-42.

Doane LD, Adam EK. (2010). Loneliness and cortisol: momentary, day-to-day, and trait associations. *Psychoneuroendocrinology.* 35(3):430-441.

Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, Liu H, Zhang Y, Luo D, Xu S, Xu L, Liu J, Zhang J, Teng Z. (2017). Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. *Biosci Rep.* Dec 12;37(6):BSR20170945. doi: 10.1042/BSR20170945.

Drageset J, Eide GE, Kirkevold M, Ranhoff AH. (2013). Emotional loneliness is associated with mortality among mentally intact nursing home residents with and without cancer: A five-year follow-up study. *Journal of Clinical Nursing.* 22(1–2):106–114. doi: 10.1111/j.1365-2702.2012.04209.x.

DSM-V. (2013) Diagnostic and statistical manual of mental disorders, 5th ed.: DSM-V. Washington, DC: American Psychiatric Association.

Duncan JG, Bott MJ, Thompson SA, Gajewski BJ. (2009). Symptom occurrence and associated clinical factors in nursing home residents with cancer. *Res Nurs Health.* 32(4):453–464.

Dyal SR, Valente TW. (2015). A Systematic Review of Loneliness and Smoking: Small Effects, Big Implications. *Subst Use Misuse.* 50(13):1697-1716. doi:10.3109/10826084.2015.1027933.

Ekwall AK, Sivberg B, Hallberg IR. (2005). Loneliness as a predictor of quality of life among older caregivers. *J Adv Nurs.* Jan;49(1):23-32. doi: 10.1111/j.1365-2648.2004.03260.x.

Elwood P, Galante J, Pickering J, Palmer S, Bayer A, Ben-Shlomo Y, Longley M, Gallacher J. (2013). Healthy lifestyles reduce the incidence of chronic diseases and dementia: evidence from the Caerphilly cohort study. *PLoS One.* 2013 Dec 9;8(12):e81877. doi: 10.1371/journal.pone.0081877.

Ernst JM, Cacioppo JT. (1999). Lonely hearts: Psychological perspectives on loneliness. *Applied and Preventive Psychology.* 8:1–22.

Fedirko V, Tramacere I, Bagnardi V, Rota M, Scotti L, Islami F, Negri E, Straif K, Romieu I, Vecchia CL, Boffetta P, Jenab M. (2011). Alcohol drinking and colorectal cancer risk: an overall and dose-response meta-analysis of published studies. *Ann Oncol.* 22:1958–1972. doi: 10.1093/annonc/mdq653.

Feng RM, Zong YN, Cao SM, Xu RH. (2019). Current cancer situation in China: good or bad news from the 2018 Global Cancer Statistics? *Cancer Commun (Lond).* Apr 29;39(1):22. doi: 10.1186/s40880-019-0368-6.

Feola A, Ricci S, Kouidhi S, Rizzo A, Penon A, Pietro F, Giordano A, Marina DD. (2016). Multifaceted Breast Cancer: The Molecular Connection With Obesity. *J Cell Physiol.* 232(1). DOI: 10.1002/jcp.25475.

Foster C, Wright D, Hill H, Hopkinson J, Roffe L. (2009). Psychosocial implications of living 5 years or more following a cancer diagnosis: a systematic review of the research evidence. *Eur J Cancer Care (Engl).* 18(3):223-247. doi:10.1111/j.1365-2354.2008.01001.x.

Gaudet MM, Gapstur SM, Sun J, Diver WR, Hannan LM, Thun MJ. (2013). Active smoking and breast cancer risk: original cohort data and meta-analysis. *J Natl Cancer Inst.* 105(8):515–25. 10.1093/jnci/djt023.

Golabek T, Bukowczan J, Szopinski T, Chłosta P, Lipczynski W, Dobruch J, Borówka A (2016). Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. *Ann Agric Environ Med.* 23:37–43.

Gouin JP, Zhou B, Fitzpatrick S. (2015). Social integration prospectively predicts changes in heart rate variability among individuals undergoing migration stress. *Ann Behav Med.* Apr;49(2):230-8. doi: 10.1007/s12160-014-9650-7.

Grassi L, Nanni MG, Rodin G, Li M, Caruso R. (2018). The use of antidepressants in oncology: a review and practical tips for oncologists. *Ann Oncol.* 29(1):101-111. doi:10.1093/annonc/mdx526.

Griffin J. (2010). The Lonely Society? The Mental Health Foundation; London. Available at: https://www.mentalhealth.org.uk/sites/default/files/the_lonely_society_report.pdf

Hackett RA, Hudson JL, Chilcot J. (2020). Loneliness and type 2 diabetes incidence: findings from the English Longitudinal Study of Ageing [published online ahead of print, 2020 Sep 15]. *Diabetologia.* 10.1007/s00125-020-05258-6. doi:10.1007/s00125-020-05258-6.

Hajek A., Bock J.O., König H.H. (2017). The role of general psychosocial factors for the use of cancer screening—findings of a population-based observational study among older adults in Germany. *Cancer Med.* 6:3025–3039. doi: 10.1002/cam4.1226.

Hawkley LC, Cacioppo JT. (2003) Loneliness and pathways to disease. *Brain, Behavior, and Immunity.* 17(1):98–105. doi: 10.1016/S0889-1591(02)00073-9.

Hawkley LC, Cacioppo JT. (2010). Loneliness matters: a theoretical and empirical review of consequences and mechanisms. *Ann Behav Med.* 40(2):218–27. doi: 10.1007/s12160-010-9210-8.

Hawkley LC, Masi CM, Berry JD, Cacioppo JT. (2006). Loneliness is a unique predictor of age-related differences in systolic blood pressure. *Psychology and Aging.* 21:152–164. doi: 10.1037/0882-7974.21.1.152.

Hawkley LC, Thisted RA, Cacioppo JT. (2009). Loneliness predicts reduced physical activity: cross-sectional & longitudinal analyses. *Health Psychol.* 28(3):354–63. doi: 10.1037/a0014400.

Holmes KK, Levine R, Weaver M. (2004). Effectiveness of condoms in preventing sexually transmitted infections. *Bull World Health Organ.* 82(6):454-461.

<https://gco.iarc.fr/> - accessed October 3, 2020.

<https://www.cancer.org/cancer/cancer-causes/tobacco-and-cancer/carcinogens-found-in-tobacco-products.html> -accessed October 1, 2020.

<https://www.cigna.com/about-us/newsroom/studies-and-reports/combatting-loneliness/>.

<https://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/data-and-statistics> - accessed December 23, 2020.

<https://www.iarc.fr/featured-news/latest-global-cancer-data-cancer-burden-rises-to-18-1-million-new-cases-and-9-6-million-cancer-deaths-in-2018/>.

<https://www.nhs.uk/news/cancer/lifestyle-and-cancer-rates/> -accessed October 12, 2020.

<https://www.who.int/news-room/fact-sheets/detail/cancer> - accessed October 2, 2020.

IARC. International Agency for Research on Cancer. Biological agents. Volume 100B: a review of human carcinogens. <https://monographs.iarc.fr/wp-content/uploads/2018/06/mono100B.pdf> Date: 2012.

IARC. IARC working group on the evaluation of carcinogenic risks to humans. Alcohol Consumption and Ethyl Carbamate. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. International Agency for Research on Cancer; Lyon, France: 2010.

ICESCC. International Collaboration of Epidemiological Studies of Cervical C. (2007). Comparison of risk factors for invasive squamous cell carcinoma and adenocarcinoma of the cervix: collaborative reanalysis of individual data on 8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies. *Int J Cancer.* 120(4):885–91. 10.1002/ijc.22357.

Islami F, Chen W, Yu XQ, Lortet-Tieulent J, Zheng R, Flanders WD, Xia C, Thun MJ, Gapstur SM, Ezzati M, Jemal A. (2017). Cancer deaths and cases attributable to lifestyle factors and infections in China, 2013. *Ann Oncol*. Oct 1;28(10):2567-2574. doi: 10.1093/annonc/mdx342.

Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, McCullough ML, Patel AV, Ma J, Soerjomataram I, Flanders WD, Brawley OW, Gapstur SM, Jemal A.. (2018). Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin*. Jan;68(1):31-54. doi: 10.3322/caac.21440

Jaremka LM, Andridge RR, Fagundes CP, Alfano CM, Povoski SP, Lipari AM, Agnese DM, Arnold MW, Farrar WB, Yee LD, Carson WE 3rd, Bekaii-Saab T, Martin EW Jr, Schmidt CR, Kiecolt-Glaser JK.. (2014). Pain, depression, and fatigue: Loneliness as a longitudinal risk factor. *Health Psychology*. 33(9):948–957. doi: 10.1037/a0034012.

Jaremka LM, Fagundes CP, Glaser R, Bennett JM, Malarkey WB, Kiecolt-Glaser JK. (2013). Loneliness predicts pain, depression, and fatigue: understanding the role of immune dysregulation. *Psychoneuroendocrinology*. Aug;38(8):1310-7. doi: 10.1016/j.psyneuen.2012.11.016.

Kassianos, A. P. , Raats, M. M. , Gage, H. , & Peacock, M. (2015). Quality of life and dietary changes among cancer patients: A systematic review. *Quality of Life Research*, 24, 705–719.

Khan N, Afaq F, Mukhtar H. (2009). Lifestyle as risk factor for cancer: Evidence from human studies. *Cancer Lett*. 293(2):133-143. doi:10.1016/j.canlet.2009.12.013.

Kim JE, Dodd MJ, Aouizerat BE, Jahan T, Miaskowski C. (2009). A review of the prevalence and impact of multiple symptoms in oncology patients. *J Pain Symptom Manage*. 37:715–36.

Knapp S, Marziliano A, Moyer A. (2014). Identity threat and stigma in cancer patients. *Health Psychol Open*. 1(1):2055102914552281. Published 2014 Sep 25. doi:10.1177/2055102914552281.

Kobayashi LC, Steptoe A. (2018). Social Isolation, Loneliness, and Health Behaviors at Older Ages: Longitudinal Cohort Study. *Ann Behav Med*. 52(7):582-593. doi:10.1093/abm/kax033.

Kroenke K, Johns SA, Theobald D, Wu J, Tu W. (2013). Somatic symptoms in cancer patients trajectory over 12 months and impact on functional status and disability. *Supportive Care in Cancer*. 21:765–773. doi: 10.1007/s00520-012-1578-5.

Kubo A, Corley DA. (2006). Body mass index and adenocarcinomas of the esophagus or gastric cardia: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 15:872–8.

Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, Gapstur S, Patel AV, Andrews K, Gansler T; (2012). American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 62:30-67.

Ladeiras-Lopes R, Pereira AK, Nogueira A, Pinheiro-Torres T, Pinto L, Santos-Periera R, Lunet N. (2008). Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. *Cancer Causes Control*. 19(7):689–701. 10.1007/s10552-008-9132-y.

Lagerlund M, Sontrop JM, Zackrisson S. (2014). Psychosocial factors and attendance at a population-based mammography screening program in a cohort of Swedish women. *BMC Womens Health.* 14(1):33. Published 2014 Feb 24. doi:10.1186/1472-6874-14-33.

Larsson SC, Orsini N, Wolk A. (2007). Body mass index and pancreatic cancer risk: A meta-analysis of prospective studies. *Int J Cancer* 120:1993–8.

Larsson SC, Wolk A. (2007). Overweight, obesity and risk of liver cancer: a meta-analysis of cohort studies. *Br J Cancer* 97:1005–8.

Larsson SC, Wolk A. (2007a). Obesity and the risk of gallbladder cancer: a meta-analysis. *Br J Cancer* 96:1457–61.

Lauder W, Mummery K, Jones M, Caperchione C. (2006). A comparison of health behaviours in lonely and non-lonely populations. *Psychol Health Med.* 11:233–245. doi: 10.1080/13548500500266607.

Lebel S, Devins GM. (2008). Stigma in cancer patients whose behavior may have contributed to their disease. *Future Oncol.* 4:717–733. doi: 10.2217/14796694.4.5.717.

Lee PN, Forey BA, Coombs KJ. (2012). Systematic review with meta-analysis of the epidemiological evidence in the 1900s relating smoking to lung cancer. *BMC Cancer.* 12:385 10.1186/1471-2407-12-385.

Leitzmann M, Powers H, Anderson AS, Scoccianti C, Berrino F, Baoutrou-Ryaykt M. (2015). European Code Against Cancer 4th edition: physical activity and cancer. *Cancer Epidemiol.* 39 Suppl 1:S46–S55.

Locher, J. L., Ritchie, C. S., Roth, D. L., Baker, P. S., Bodner, E. V., & Allman, R. M. (2005). Social isolation, support, and capital and nutritional risk in an older sample: Ethnic and gender differences. *Social Science and Medicine*, 60(4), 747-761.

Luo Y, Hawkley LC, Waite LJ, Cacioppo JT. (2012). Loneliness, health, and mortality in old age: A national longitudinal study. *Social Science & Medicine.* 74:907–914. doi: 10.1016/j.socscimed.2011.11.028.

Mahale P, Engels EA, Koshiol J. (2019). Hepatitis B virus infection and the risk of cancer in the elderly US population. *Int J Cancer.* 144(3):431-439. doi:10.1002/ijc.31643.

Mahale P, Torres HA, Kramer JR, Hwang LY, Li R, Brown EL, Engels EA. (2017). Hepatitis C virus infection and the risk of cancer among elderly US adults: A registry-based case-control study. *Cancer.* 123(7):1202-1211. doi:10.1002/cncr.30559.

Mahase E. (2019). Cancer overtakes CVD to become leading cause of death in high income countries. *BMJ.* Sep 3;366:l5368. doi: 10.1136/bmj.l5368.

Mahendran R, Liu J, Kuparasundram S, Simard S, Chan YH, Kua EH, Griva K. (2020). Fear of cancer recurrence among cancer survivors in Singapore. *Singapore Med J.* Jan 28. doi: 10.11622/smedj.2020007.

Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. (2011). Projections of the cost of cancer care in the United States: 2010-2020. *J Natl Cancer Inst.* Jan 19;103(2):117-28. doi: 10.1093/jnci/djq495.

Masi CM, Chen HY, Hawkley LC, Cacioppo JT. (2010). A meta-analysis of interventions to reduce loneliness. *Personality and Social Psychology Review.* 15:219–266. doi: 10.1177/1088868310377394.

Murphy CC, Gerber DE, Pruitt SL. (2017). Prevalence of prior cancer among persons newly diagnosed with cancer: an initial report from the surveillance, epidemiology, and end results program. *JAMA Oncology.* doi:10.1001/jamaoncol.2017.3605.

National Center for Chronic Disease Prevention and Health Promotion (US) (2014). Office on Smoking and Health The Health Consequences of Smoking: 50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: Centers for Disease Control and Prevention.

Nausheen B, Carr NJ, Peveler RC, Moss-Morris R, Verrill C, Robbins E, Nugent KP, (2010). Relationship between loneliness and proangiogenic cytokines in newly diagnosed tumors of colon and rectum. *Psychosom Med.* Nov;72(9):912-6. doi: 10.1097/PSY.0b013e3181f0bc1c.

Nausheen B, Gidron Y, Peveler R, Moss-Morris R. (2009). Social support and cancer progression: a systematic review. *J Psychosom Res.* 67(5):403-415. doi:10.1016/j.jpsychores.2008.12.012.

Nersesian PV, Han HR, Yenokyan G, Blumenthal RS, Nolan MT, Hladek MD, Szanton SL. (2018). Loneliness in middle age and biomarkers of systemic inflammation: Findings from Midlife in the United States. *Soc Sci Med.* Jul;209:174-181. doi: 10.1016/j.socscimed.2018.04.007.

Netz Y, Goldsmith R, Shimony T, Arnon M, Zeev A. (2013). Loneliness is associated with an increased risk of sedentary life in older Israelis. *Aging Ment Health.* 17(1):40-7. doi: 10.1080/13607863.2012.715140.

Noone AM, Howlader N, Krapacho M, et al. (2008). SEER cancer statistics review, 1975-2015 Bethesda, MD: National Cancer Institute.

Ojembe BU, Ebe Kalu M. (2018). Describing reasons for loneliness among older people in Nigeria. *J Gerontol Soc Work.* Aug-Sep;61(6):640-658. doi: 10.1080/01634372.2018.1487495.

Page RM, Hammermeister J. (1995). Shyness and loneliness: relationship to the exercise frequency of college students. *Psychol Rep.* 76(2):395-398. doi:10.2466/pr0.1995.76.2.395.

Patel AV, Friedenreich CM, Moore SC, Hayes SC, Silver JK, Campbell KL, Winters-Stone K, Gerber LH, George SM, Fulton JE, Denlinger C, Morris GS, Hue T, Schmitz KH, Matthews CE. (2019). American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. *Med Sci Sports Exerc.* Nov;51(11):2391-2402. doi: 10.1249/MSS.0000000000002117.

Perlman D, Peplau LA. (1981) Toward a social psychology of loneliness. Gilmour & S Duck (Eds.) Personal relationships in disorder (pp. 31–56). London: Academic Press.

Peters-Golden H. (1982) Breast cancer: Varied perceptions of social support in the illness experience. *Social Science & Medicine* 16: 483–491.

Petrelli NJ, Winer EP, Brahmer J, Dubey S, Smith S, Thomas C, Vahdat LT, Obel J, Vogelzang N, Markman M, Sweetenham JW, Pfister D, Kris MG, Schuchter LM, Sawaya R, Raghavan D, Ganz PA, Kramer B. (2009). Clinical Cancer Advances 2009: major research advances in cancer treatment, prevention, and screening – a report from the American Society of Clinical Oncology. *J Clin Oncol* 27:6052–6069.

Pinquart M, Duberstein PR. (2010). Depression and cancer mortality: a meta-analysis. *Psychological Med.* 40:1797–1810.

Potter J, Brown L, Williams RL, Byles J, Collins CE. (2016). Diet Quality and Cancer Outcomes in Adults: A Systematic Review of Epidemiological Studies. *Int J Mol Sci.* 17(7):1052. Published 2016 Jul 5. doi:10.3390/ijms17071052.

Reiche EM, Nunes SO, Morimoto HK. (2004). Stress, depression, the immune system, and cancer. *Lancet Oncol.* Oct;5(10):617-25. doi: 10.1016/S1470-2045(04)01597-9.

Richard A, Rohrmann S, Vandeleur CL, Schmid M, Barth J, Eichholzer M. (2017). Loneliness is adversely associated with physical and mental health and lifestyle factors: Results from a Swiss national survey. *PLoS One.* 12(7):e0181442. Published 2017 Jul 17. doi:10.1371/journal.pone.0181442.

Rico-Uribe LA, Caballero FF, Olaya B, Tobiasz-Adamczyk B, Koskinen S, Leonardi M, Haro JM, Chatterji S, Ayuso-Mateos JL, Miret M. (2016). Loneliness, Social Networks, and Health: A Cross-Sectional Study in Three Countries. *PLoS One.* Jan 13;11(1):e0145264. doi: 10.1371/journal.pone.0145264.

Rock CL, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, Bandera EV, Hamilton KK, Grant B, McCullough M, Byers T, Gansler T. (2012). Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin.* 62:243–274.

Rota M. (2017). Evidence for an association between alcohol intake and an increased risk of nonmelanoma skin cancer. *Br J Dermatol.* 177(3):611-612. doi:10.1111/bjd.15790.

Rotenberg KJ, (1999). Flood D. Loneliness, dysphoria, dietary restraint, and eating behavior. *Int J Eat Disord.* 25(1).

Rudatsikira E, Muula AS, Siziya S, Twa-Twa J. (2007). Suicidal ideation and associated factors among school-going adolescents in rural Uganda. *BMC Psychiatry.* 7:67.

Sam Palmer, Luca Albergante, Clare C. Blackburn, T. J. Newman. (2018). Thymic involution and disease incidence. *Proceedings of the National Academy of Sciences* Feb, 115 (8) 1883-1888. doi: 10.1073/pnas.1714478115.

Samuel LJ, Dennison Himmelfarb CR, Szklo M, Seeman TE, Echeverria SE, Diez Roux AV. (2015). Social engagement and chronic disease risk behaviors: the Multi-Ethnic Study of Atherosclerosis. *Prev Med.* 71:61-66. doi:10.1016/j.ypmed.2014.12.008.

Sang Min Park, Young Ho Yun, Young Ae Kim, Minkyung Jo, Young-Joo Won, Joung Hwan Back, Eun Sook Lee., (2016). Pre-diagnosis Body Mass Index and Risk of Secondary Primary Cancer in Male Cancer Survivors: A Large Cohort Study. *Journal of Clinical Oncology* 2016 34:34, 4116-4124.

Satin JR, Linden W, Phillips MJ. (2009). Depression as a predictor of disease progression and mortality in cancer patients: a Meta-Analysis. *Cancer.* Nov 15;115(22):5349-61. doi: 10.1002/cncr.24561. PMID: 19753617.

Schmitz KH, Campbell AM, Stuiver MM, Pinto BM, Schwartz AL, Morris GS, Ligibel JA, Cheville A, Galvão DA, Alfano CM, Patel AV, Hue T, Gerber LH, Sallis R, Gusani NJ, Stout NL, Chan L, Flowers F, Doyle C, Helmrich S, Bain W, Sokolof J, Winters-Stone KM, Campbell KL, Matthews CE. (2019). Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. *CA Cancer J Clin.* 69(6):468-484. doi:10.3322/caac.21579.

Secretan B, Straif K, Baan R, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V. (2009). A review of human carcinogens—Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. *Lancet Oncol.* 10(11):1033–1034.

Seitz HK, Stickel F. (2010). Acetaldehyde as an underestimated risk factor for cancer development: role of genetics in ethanol metabolism. *Genes Nutr.* 5: 121- 128.

Seitz HK, Stickel F. (2007). Molecular mechanisms of alcohol-mediated carcinogenesis. *Nat Rev Cancer.* 7: 599- 612.

Shankar A, McMunn A, Banks J, Steptoe A. (2011). Loneliness, social isolation, and behavioral and biological health indicators in older adults. *Health Psychology.* 30(4):377–385. doi: 10.1037/a0022826.

Sheena Daniels. (2015). Cognitive Behavior Therapy for Patients With Cancer. *Journal of the Advanced Practitioner in Oncology September,* 6(1):54-6.

Shiovitz-Ezra S, Litwin H. (2012). Social network type and health-related behaviors: Evidence from an American national survey. *Soc Sci Med.* 75(5): 901–904.

Siegel RL, Miller KD, Jemal JA. (2018). Cancer statistics, CA: CancerJ Clin. 68(1):7–30.

Singh N, Baby D, Rajguru JP, Patil PB, Thakkannavar SS, Pujari VB. (2019). Inflammation and cancer. *Ann Afr Med.* Jul-Sep;18(3):121-126. doi: 10.4103/aam.aam_56_18.

Sinha R, Knize MG, Salmon CP, Brown ED, Rhodes D, Felton JS, Levander OA, Rothman N. (1998). Heterocyclic amine content of pork products cooked by different methods and to varying degrees of doneness. *Food Chem Toxicol.* 36: 289- 297.

Smith KJ, Gavey S, RIddell NE, Kontari P, Victor C. (2020). The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. *Neurosci Biobehav Rev.* May;112:519-541. doi: 10.1016/j.neubiorev.2020.02.002.

Song M, Giovannucci E. (2016). Preventable Incidence and Mortality of Carcinoma Associated With Lifestyle Factors Among White Adults in the United States. *JAMA Oncol.* Sep 1;2(9):1154-61. doi: 10.1001/jamaoncol.2016.0843.

Spiegel D. (2012). Mind matters in cancer survival. *Psychooncology.* 21(6):588-593. doi:10.1002/pon.3067.

Steed L, Boldy D, Grenade L, Iredell H. (2007). The demographics of loneliness among older people in Perth, Western Australia. *Australas J Ageing.* 26:81–6.

Steinmetz KA, Potter JD. (1996). Vegetables, fruit, and cancer prevention: a review. *J Am Diet Assoc.* 96:1027–1039.

Stickley A, Koyanagi A, Leinsalu M, Ferlander S, Sabawoon W, McKee M. (2015). Loneliness and health in Eastern Europe: findings from Moscow, Russia. *Public Health.* 129(4):403-410. doi:10.1016/j.puhe.2014.12.021.

Stickley A, Koyanagi A, Roberts B, Richardson E, Abbot P, Tumanov S, McKee M. (2013). Loneliness: its correlates and association with health behaviours and outcomes in nine countries of the former Soviet Union. *PLoS One.* 8(7):e67978. Published 2013 Jul 4. doi:10.1371/journal.pone.006797.

Swiatoniowska N , A Szymanska-Chabowska , J Gajek , B Jankowska-Polanska. (2019). Determinants of non-pharmacological compliance in patients with heart failure, Poster Presentation.Heart Failure. 6th World Congress on Acute Heart Failure. 25 - 28 May, Athens – Greece.

The 2018 Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: Department of Health and Human Services; 2018.

Thun M, MS Linet, JR Cerhan, CA Haiman, D Schottenfeld, eds. (2017). Cancer Epidemiology and Prevention. 4th edn. New York: Oxford University Press.

Tiwari SC. (2013). Loneliness: A disease?. *Indian J Psychiatry.* 55(4):320-322. doi:10.4103/0019-5545.120536.

Torress HL, Gore-Felton C. (2007). Compulsivity, substance use, and loneliness: the loneliness and sexual risk model (LSRM) *Sexual Addiction & Compulsivity*. 14(1):63–75.

Tso FY, Sawyer A, Kwon EH, et al. (2017). Kaposi's Sarcoma-Associated Herpesvirus Infection of Neurons in HIV-Positive Patients. *J Infect Dis*. 215(12):1898–1907. doi:10.1093/infdis/jiw545.

Usta YY. Importance of social support in cancer patients. *Asian Pac J Cancer Prev*. 2012;13(8):3569–3572. doi:10.7314/apjcp.2012.13.8.3569.

Valtorta, N. K., M. Kanaan, S. Gilbody, and B. Hanratty. (2018). Loneliness, social isolation and risk of cardiovascular disease in the English Longitudinal Study of Ageing. *European Journal of Preventive Cardiology* 25(13):1387–1396.

van Tilburg TG, Fokkema T. (2018). Hogere eenzaamheid onder Marokkaanse en Turkse ouderen in Nederland: Op zoek naar een verklaring [Stronger feelings of loneliness among Moroccan and Turkish older adults in the Netherlands: A search for an explanation]. *Tijdschr Gerontol Geriatr*. 49(6):263–273. doi:10.1007/s12439-018-0269-1.

Vancampfort D, Lara E, Smith L, Rosenbaum S, Firth J, Stubbs B, Hallgren M, Koyanagi A. (2019). Physical activity and loneliness among adults aged 50 years or older in six low- and middle-income countries. *Int J Geriatr Psychiatry*. 34(12):1855–1864. doi:10.1002/gps.5202.

Vehling S, Kissane DW. (2018). Existential distress in cancer: Alleviating suffering from fundamental loss and change. *Psychooncology*. 27(11):2525–2530. doi:10.1002/pon.4872.

Victor CD, Scambler SJ, Bowling A, Bondt J. (2005) The prevalence of and risk factors for loneliness in later life: A survey of older people in Great Britain. *Ageing & Society*. 25:357–375.

Victor CR, Bowling A. (2012). A longitudinal analysis of loneliness among older people in Great Britain. *J Psychol*. 146(3):313–331. doi:10.1080/00223980.2011.609572.

Walker E, Ploubidis G, Fancourt D. (2019). Social engagement and loneliness are differentially associated with neuro-immune markers in older age: Time-varying associations from the English Longitudinal Study of Ageing. *Brain Behav Immun*. 82:224–229. doi:10.1016/j.bbi.2019.08.189.

Warren GW, Cartmell KB, Garrett-Mayer E, Salloum RG, Cummings KM. (2019) Attributable Failure of First-line Cancer Treatment and Incremental Costs Associated With Smoking by Patients With Cancer. *JAMA Netw Open*. 2: e191703 10.1001/jamanetworkopen.2019.1703.

Watters JL, Park Y, Hollenbeck A, Schatzkin A, Albaneset D. (2010) Alcoholic beverages and prostate cancer in a prospective US cohort study. *American Journal of Epidemiology*. 172(7):773–780.

Wells M, Kelly D. (2008). The loneliness of cancer. *European Journal of Oncology Nursing*. 12(5):410–411. doi: 10.1016/j.ejon.2008.11.003.

Whisman MA. (2010). Loneliness and the metabolic syndrome in a population-based sample of middle-aged and older adults. *Health Psychol*. 29:4.

Wiedmann M, Brunborg C, Lindemann K, Johannessen TB, Vatten L, Helseth E, Zwart JA. (2013). Body mass index and the risk of meningioma, glioma and schwannoma in a large prospective cohort study (The HUNT Study). *Br J Cancer* 109:289–9427,28.

Williams JB, Pang D, Delgado B, Kocherginsky M, Tretiakova M, Krausz T, Pan D, He J, McClintock MK, Conzen SD.. (2009). A model of gene-environment interaction reveals altered mammary gland gene expression and increased tumor growth following social isolation. *Cancer Prev Res (Phila)*. 2(10):850-861. doi:10.1158/1940-6207.CAPR-08-0238.

Wilson C, Moulton B. (2010). Loneliness among older adults: a national survey of adults 45+. Prepared by Knowledge Networks and Insight Policy Research. Washington, DC, AARP.

Wilson RS, Krueger KR, Arnold SE, Schneider JA, Kelly JF, Bennett DA. (2007). Loneliness and risk of Alzheimer disease. *Archives of General Psychiatry*. 64:234–240. doi: 10.1001/archpsyc.64.2.234.

Yang F, Zhang J, Wang J. (2018). Correlates of loneliness in older adults in Shanghai, China: does age matter? *BMC Geriatr*. 18(1):300. Published 2018 Dec 4. doi:10.1186/s12877-018-0994-x.

Yang KM, Victor C. (2011). Age and loneliness in 25 European nations. *Ageing Soc*. 31:1368–88. doi: 10.1017/S0144686x1000139x.

Yu S, Yang CS, Li J, You W, Chen J, Cao Y, Dong Z, Qiao Y. (2015). Cancer Prevention Research in China. *Cancer Prev Res (Phila)*. Aug;8(8):662-74. doi: 10.1158/1940-6207.CAPR-14-0469.

Zhong BL, Liu XJ, Chen WC, Chiu HF, Conwell Y. (2018). Loneliness in Chinese older adults in primary care: prevalence and correlates. *Psychogeriatrics*. 18(5):334-342. doi:10.1111/psych.12325.

Zilioli S, Slatcher RB, Chi P, Li X, Zhao J, Zhao G. (2017). The impact of daily and trait loneliness on diurnal cortisol and sleep among children affected by parental HIV/AIDS. *Psychoneuroendocrinology*. 75:64-71. doi:10.1016/j.psyneuen.2016.10.012.

Copyrights

Copyright for this article is retained by the author(s), with first publication rights granted to the journal. This is an open-access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/4.0/>).