Telomeres and Stress: Promising Avenues for Research in Psycho-Oncology

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ABSTRACT

A cancer diagnosis and subsequent treatment is a stressful experience with the potential for long-term health consequences for both patients and their caregivers. It is now well-established that psychological stress is associated with detrimental effects on physical health. Recent studies have investigated the link between telomeres, the protective cap at the end of chromosomes, and stress, suggesting that stress potentially impacts on cellular aging through telomere shortening, with subsequent consequences for health. This review aims to familiarize the reader with the pertinent literature exploring the relationship between telomeres and psychological and behavioral factors and propose future directions for telomere research in psycho-oncology.

Key words: Cancer, caregivers, patients, psychosocial interventions, stress, telomeres

Introduction

The impact of cancer is far reaching. Globally, 14.1 million cancer cases were reported in 2012, with this number expected to rise to 34 million by 2023.[1] As of 2012, 32.6 million people were living with cancer within 5 years of diagnosis, yet it remains a common cause of death in most developed nations.[1,2] With population growth, treatment advances and population ageing the number of people affected by cancer is rising; therefore, we need to better understand the psychosocial impact of cancer for patients and their caregivers.

Cancer can result in significant negative biopsychosocial outcomes for patients and caregivers,[3] which can be sustained over long periods.[4] Individual variations in response to cancer may be influenced by biological links between psychological and behavioral factors.[5,6] Of particular interest, is the

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potential impact of psychosocial and behavioral risk factors on biological markers, and subsequent health consequences.

Many biomarkers associated with psychosocial stress (e.g., cortisol, interleukin-6 [IL-6], and natural killer [NK] cells) have been investigated; while new research suggests telomere biology may present a promising avenue for exploring the adverse psychosocial health effects of cancer for patients and caregivers. This review provides a brief summary of the link between psychosocial stress and cancer, before examining the link between stress and telomeres; the relevance to cancer research; and highlights the potential for telomere research in the psychosocial cancer field.

Psychosocial Stress and Cancer

It is well-documented that a cancer diagnosis is very stressful eliciting a range of emotions including anger, sadness, shock, anxiety, helplessness, and guilt. People newly diagnosed with cancer are confronted with a myriad of decisions associated with their disease and treatment options. Furthermore, the treatment itself can be distressing, expensive, and disruptive contributing to stress.

The stress associated with cancer can persist long-term with significant psychosocial repercussions. Treatments can lead to permanent health impairment, disability, sexual impairment, ongoing fatigue, and pain. For some, depression and anxiety persist for years after the initial diagnosis along with social problems (e.g., inability to work, change in roles). Furthermore, preexisting vulnerabilities such as low income, younger age at diagnosis, and minimal social support can further contribute to the stressors associated with a cancer diagnosis. This highlights that cancer-related psychosocial stressors are complex and difficult to attribute to just one factor.

Although there is compelling evidence of the association between psychosocial stress and cancer diagnosis, there is considerable variation in the prevalence of stress among cancer patients. The prevalence of cancer patients with mental disorders ranges from 9.8% to 38.2% across the cancer trajectory. Henselmans et al. studied 171 women diagnosed with breast cancer, assessing their distress 5 times in the 12 months postdiagnosis. They identified four distinct distress trajectories: A no distress group (36.3%), a group that experienced distress only in the active treatment phase (33.3%), a group that experienced distress in the re-entry and survivorship phase (15.2%), and a group that experienced chronic distress (15.2%). These findings clearly indicate that not everyone diagnosed with cancer reacts in the same manner. Significant variation in psychological reaction has also been observed in patients with colorectal, prostate, ovarian cancer, and sarcoma.

Caregivers

A diagnosis of cancer not only affects the individual diagnosed with the disease, but also their caregiver. Caregivers can experience psychosocial challenges analogous to those experienced by patients, such as shock, uncertainty, and anxiety, while managing additional financial, psychosocial, and physical demands. The caregiver’s role is complex, balancing the needs of the person they are caring for with competing priorities, such as work and family, often experiencing significant changes in roles. Subsequently, previous pleasurable activities are frequently abandoned, and opportunities for accessing social support may be limited. Compounding this, caring for a person with cancer may continue for years, often with a distressing outcome.

Caregivers often assume the role without the preparation or consideration of whether they have the resources, skills, and knowledge required and consequently are susceptible to stress. Numerous studies have shown persistently high levels of caregiver distress with as many as 40% of caregivers affected long-term. Importantly, caregivers’ distress can have a direct impact on the patient, with two meta-analyses of psychological distress in cancer patients and their caregivers reporting moderate significant correlations between patients’ and caregivers’ distress. Other studies have found that caregivers’ distress effects patients’ long-term adjustment and is correlated with patients’ anxiety.

Theoretical framework

The transactional model of stress and coping has been widely applied as a model for understanding the impact of a cancer diagnosis and how an individual copes with the subsequent stress. Stress is defined as an interaction between the individual and their environment whereby stress results when there is an imbalance between the demands of the situation and the available resources to address or mitigate demands. Central to this model are two processes — cognitive appraisal and coping. Lazarus and Folkman describe cognitive appraisal as the individual’s evaluation of their situation, influencing their perception of control. Coping refers to the cognitive and behavioral efforts made to manage the stressful situation and serves two main functions, management of the source.
of stress, and regulation of stressful emotions.\textsuperscript{[51]} For example, if on receiving a diagnosis of cancer, the person adopts a behaviorally active, problem-focused approach to treatment, they are likely to feel as if they have some control over the situation. Alternatively, if they deny the gravity of the situation, they may not effectively manage their disease.\textsuperscript{[52]} Other factors influence appraisal and coping. For example, social support can assist with coping\textsuperscript{[53]} whereas co-morbid depression may negatively impact appraisal, leading to poorer treatment compliance.\textsuperscript{[54]} A key strength of the transactional model of coping is its recognition that both individual and environmental variables respond to coping,\textsuperscript{[51]} but a shortcoming is its failure to account for physiological mechanisms.

**Psychosocial Stress, Biomarkers, and Telomeres**

The biological link between psychosocial stress and cancer is yet to be fully understood.\textsuperscript{[7]} Psychoneuroimmunology (PNI) studies the relationship between psychosocial processes and immunological parameters\textsuperscript{[55]} and is one avenue for exploring this link. Generally, PNI research assumes that immune function is moderated through psychosocial stress via activation of the immune and nervous systems.\textsuperscript{[55]}

The link between stress and the immune system is well-established with numerous biomarkers associated with stress. For example, proinflammatory cytokines, especially IL-6, have been shown to have a significant association with depression (both in cancer and noncancer populations)\textsuperscript{[56,57]} and has also been related to the progression of disease,\textsuperscript{[58]} recurrence, and survival.\textsuperscript{[59]} Stress also influences catecholamine production, such as epinephrine, norepinephrine, and dopamine, which can significantly impact on immune function, including NK cell activity and lymphocyte proliferation.\textsuperscript{[5]} Thus, stress response and immune function are intrinsically linked, and when adaptive systems are unable to effectively resolve inflammation, the resulting inflammation can contribute to disease pathogenesis.\textsuperscript{[60]}

Caregiving in cancer has an effect on physical health\textsuperscript{[3,61]} with problems such as sleep disturbance, fatigue, pain, loss of physical strength, loss of appetite, and weight loss.\textsuperscript{[62]} However, there is a paucity of research examining the physiological mechanisms that impact on the health of cancer caregivers. Rohleder et al.\textsuperscript{[63]} studied familial caregivers in the year following a brain cancer diagnosis tracking changes in neurohormonal biomarkers (cortisol and amylose), inflammatory biomarkers C-reactive protein, IL-6, and pro- and anti-inflammatory signaling molecules (NF-kB subunits p65 and p105, 1-kB, GR-a, and GR-b) to monitor in vitro production of endotoxin-stimulated leukocytes and expression of mRNA. Despite mixed findings, possibly due to small sample (18 caregivers, 19 controls), the authors concluded that, over time, the chronic caregiving stress led to systematic changes in inflammatory markers, leaving caregivers of cancer patients vulnerable to disease.\textsuperscript{[63]}

Telomere length has emerged as a biological marker of interest in both cancer and psychosocial research. Telomeres are specialized DNA sequences that cap chromosomal ends, promoting chromosomal stability and preventing end-to-end fusion of chromosomes. Each time cells divide; telomeric DNA is gradually lost from the end of each chromosome, as a result of limitations in the replication machinery. Over time, telomeres shorten due to somatic cell division and exposure to oxidative stress; when they become too short the cell will initiate a DNA damage response, no longer divide, or die. Genetic factors, epigenetic regulation, and recombination can also influence telomere length.\textsuperscript{[64]} Some human cells are able to counteract natural telomere attrition by activating the enzyme telomerase, which adds the repetitive telomere sequence directly onto the chromosome ends. Telomerase is essential to the preservation of telomere length, healthy cell function, and long-term immune function.\textsuperscript{[65]}

It is well-established that telomere length is both a marker and potential mechanism of cellular ageing.\textsuperscript{[65,66]} Shortened leukocyte telomere length has been linked to numerous age-related diseases, such as increased cancer risk,\textsuperscript{[64,67]} diabetes, cardiovascular disease, and dementia.\textsuperscript{[68-70]} Variable telomere length in cancer cells and shortened telomere length in stromal cells has been associated with substantial risk of metastasis or dying from cancer.\textsuperscript{[67,71]}

The following sections examine the link between telomeres and psychosocial stress; and the impact of interventions aimed at stress reduction on telomere length in cancer and noncancer populations. Table 1 summarizes the identified studies.

**Psychological Stress and Telomeres**

Telomere research is of interest from a psychosocial perspective, as stress appears to influence both telomere length and telomerase production. Shortened telomere length and decreased telomerase activity have been associated with psychological and life stress in a number of studies.\textsuperscript{[73,74,84]} Of
| Study | Study design | Sample | Inclusion criteria | Outcome measures | Results | Methodology comments |
|-------|--------------|--------|-------------------|------------------|---------|----------------------|
| Epel et al.\(^{[72]}\) | Prospective cohort study | \(n=39\) | Female caregiver of child with a disability | Telomere length, Telomerase activity, Oxidative stress index on perceived stress, BMI | Duration of chronic stress related to shortened telomere length, lower telomerase and greater oxidative stress. Significant correlations between perceived stress and telomere length, telomerase activity and oxidative stress in both groups. | Controlled for age |
| Sible et al.\(^{[73]}\) | Prospective cohort study | \(n=36\) | Adults aged between 47 and 75 with pain or no pain | Telomere length, Graded Chronic Pain Scale, 10 item Center for Epidemiologic Studies Depression Scale, Physical exam | Telomere length differed between the pain/stress groups \((P<0.01)\). Chronic pain/high-stress group had significantly shorter telomere length as compared to the no pain/low stress group \((P=0.001)\). | Small sample |
| Abola et al.\(^{[74]}\) | Prospective cohort study | \(n=2911\) | Men and women aged 30-64 participating in the health 2000 study | Telomere length, Maslach Burnout Inventory-General Survey | Individuals with severe exhaustion had leukocyte telomeres on average 0.043 relative units shorter than those with no exhaustion \((P=0.009)\). Remained significant after adjustment for covariates \((P=0.008)\). | Controlled for covariates |
| Epel et al.\(^{[75]}\) | Within group experimental study - all participants exposed to laboratory psychological stressor | \(n=44\) | High stress/low stress | Telomere activity, Cortisol (saliva), Inventory for Depressive Symptomology Self-Rated, Cohen PSS, Threat and challenge appraisals | Across both groups telomerase activity increased by 18% 1 h after the stressor \((P<0.01)\). Telomerase activity increases were associated with greater cortisone increases. Psychological response to task-related to greater telomerase activity in controls. | Small sample |
| Daubenmier et al.\(^{[76]}\) | Randomized waitlist controlled pilot trial | \(n=47\) | Overweight/obese women | Telomere activity, Psychological distress, Eating behavior, Metabolic factors (weight, serum cortisol, fasting glucose and insulin, insulin resistance) | Both groups increased in mean telomerase activity over 4 months in intent-to-treat and treatment efficacy analyses \((P<0.001)\), nonsignificant treatment effect \((0.10)\). Changes in chronic stress, anxiety, dietary restraint, dietary fat intake, cortisol, and glucose were negatively correlated with changes in telomerase activity. | Wide confidence intervals when comparing groups over time |
| Jacobs et al.\(^{[77]}\) | RCT | \(n=30\) | Experienced meditation practitioner | Telomerase activity, Five Facet Mindfulness Questionnaire, Ryff’s Well-Being Scale (9 item purpose in life subscale), 9 item environmental mastery subscale, The Big Five Inventory (8 item Neuroticism subscale) | Telomerase activity significantly greater in retreat participants \((P<0.05)\). Increases in perceived control, mindfulness and purpose in life \((P<0.01)\). Decreases in neuroticism in retreat participants \((P<0.01)\). | No baseline telomerase activity measurement |
| Puterman et al.\(^{[78]}\) | Prospective cohort study | \(n=63\) | Postmenopausal women aged between 54 and 82 | Telomere length, 10 item PSS, Physical activity level | In nonexercisers, a one unit increase in the PSS was related to a 15-fold increase in the odds of having shorter telomeres \((P<0.05)\). | Small sample |
| Lin et al.\(^{[79]}\) | Prospective cohort study | \(n=60\) | Healthy nonsmoking women | Telomere length, PSS, Physical activity level | Physical activity buffered the negative effects of childhood abuse \((\beta_{interaction}=-0.08, SE=0.03, P=0.01)\) and accumulated life stress \((\beta_{interaction}=0.01, SE=0.00, P=0.03)\) on leukocyte telomere length, after covarying for BMI and age. | Small sample |

(Continued)
| Study | Study design | Sample | Inclusion criteria | Outcome measures | Results | Methodology comments |
|-------|--------------|--------|-------------------|------------------|---------|----------------------|
| Hovatta et al [80] | Randomized, controlled intervention, multicenter study (individually tailored dietary advice, guidance to increase physical activity) | IG: Lifestyle intervention (n=667) CG: Waitlist (n=343) | Individuals with impaired glucose tolerance BMI >25 kg/m², age 40-64 years | Telomere length at 2-time points on average 4.5 years apart during the active intervention and post intervention follow-up Glucose and insulin measurements at same time points | Telomere length increased in about two-thirds of the individuals both in the intervention and in the control groups during follow-up Telomere length increased most in individuals with the shortest telomere length at the first measurement Telomere length was not associated with development of Type 2 diabetes mellitus, nor did lifestyle intervention have an effect on telomere length | Lack of a population-based control group without any intervention |
| Biegler et al [81] | Randomized, longitudinal trial | IG: Psycho social telephone counseling intervention (n=22) CG: Nil | Cervical cancer survivor | Psychological distress, measured by the Brief Symptom Inventory-18 Relative telomere length Baseline and 4 months post enrolment | Longitudinal changes in telomere length of the CD14-subset, primarily T lymphocytes, were associated with longitudinal increases in the naive T-cell population | 4 months not optimal as a longitudinal time frame |
| Ornish et al [82] | Descriptive pilot study | IG: Lifestyle intervention addressing diet, activity, stress management CG: Active surveillance only (n=10) CG=25 | Low-risk biopsy-proven prostate cancer, defined as a stage T1 or T2a tumor | Relative telomere length Telomerase activity | Men who participated in the comprehensive lifestyle intervention had significant increases in relative telomere length, whereas telomere length decreased in the controls Correlation between the degree of adherence to lifestyle changes and the extent of change in relative telomere length | Small sample, retrospective, not randomized |
| Carlson et al [83] | RCT IG: SET - 18 h contact time of emotional expression and group support MBCR: 18 h of mindfulness meditation and gentle Hatha yoga CG: Usual care plus 1 day 6 h stress management seminar (n=92) SET=36 MBCR=34 CG=18 | Distressed survivors with a diagnosis of Stage I-II breast cancer who had completed treatment at least 3 months previously | Primary outcome Measures - relative telomere length as measured by the T/S Ratio and cortisol slopes across four daily measures averaged Over 3 days, secondary outcomes - self-reported mood and stress symptoms | No significant differences between MBCR and SET groups on T/S ratios, trend effect between combined intervention group and controls (P=0.054) on telomere length Statistically significant difference in cortisol slopes (P<0.05) between intervention groups and controls. MBCR significant improvement in stress scores | Small control group Strengths - randomization and homogenous group |

RCT: Randomized controlled trial, SET: Supportive-expressive therapy, MBSR: Mindfulness-based stress reduction, MBCR: Mindfulness-based cancer recovery, IG: Intervention group, CG: Control group, PSS: Perceived Stress Scale, SE: Standard error, BMI: Body mass index.
particular interest, stress hormones, such as epinephrine and cortisol, have been linked with shortened telomeres and decreased telomerase activity. The most popular model proposed to explain this relationship is the dysregulated homeostasis/allostatic load model. Allostatic load is the wear and tear on a person’s body that grows when an individual is exposed to chronic stress. This model proposes chronic stress influences the regulation of the HPA axis, by increasing cortisol secretions, contributing to allostatic load, and in turn impaired telomere maintenance.

Seminal research by Epel et al. found that caregivers of disabled children experiencing high levels of perceived stress over time exhibited lower telomerase activity, higher oxidative stress, and shorter telomeres. These results are consistent with other caregiver studies that have shown associations with telomere erosion. There is also evidence that people who experience poor social support, partner/ caregiver stress, or depression over long periods have shorter telomeres.

Numerous studies have explored other forms of chronic stress and telomere erosion. Exposure to childhood stress (e.g., maltreatment, divorce, parental separation) have been associated with shortened telomeres in adults, indicating the long-term effect of childhood stressors. A review of the association between early life stress and shortened telomeres suggests a dose-dependent, relationship with early-life stress.

Sibille et al. investigated the link between chronic pain, stress, and telomere length, finding that individuals experiencing chronic pain with high stress had shorter telomeres than those without chronic pain and low stress. This suggests that the combination of stress and pain accelerates immune vulnerability and cellular ageing, demonstrated in telomere shortening. These findings complement other studies that point to the cumulative effects of multiple stressors on telomere erosion. For example, Ahola et al. reported a significant link between work-related exhaustion and telomere length. Together, these studies suggest that ongoing stress places a “burden on the system,” resulting in accelerated cellular ageing and increased risk to health.

Although stressors do have an effect on telomere maintenance both in the short- and long-term, their impact is variable. A recent meta-analysis of telomere length and heritability found a high and consistent heritability component (34-82%) to telomere length. Environmental and individual factors, such as stress perception, long-term exposure to stress, lifestyle factors, and social support, are highly variable and have demonstrated effects on telomere maintenance. This highlights the potential for interventions that address stress arousal, perception, and reduction to impact on physiological mechanisms, such as telomere length.

The Impact of Interventions Targeting Stress Reduction in Noncancer Populations on Telomerase Activity and Telomere Length

A growing literature suggests that management of stress may have beneficial effects for the telomere maintenance system. As a supportive therapy, mindfulness-based stress reduction (MBSR) has been shown to be effective in psychosocial outcomes in a number of settings. For example, Daubenmier et al. examined the effects of MBSR addressing eating behaviors on telomerase activity in peripheral blood mononuclear cells. Pre- and post-intervention analysis of telomerase activity found no reported effect of the intervention on telomerase activity; however, correlations between improvements in distress, eating behavior, and metabolic health were associated with creases in telomerase activity. The authors suggested that telomerase activity may, in part, be regulated by both psychological and metabolic stress, which would indicate the potential for MBSR as an intervention influencing telomerase production.

Other forms of meditation have also been investigated, with Jacobs et al. investigating telomerase activity and concentrative meditation for approximately 6 h/per day during a 3-month residential retreat. Participants had significantly greater telomerase activity compared to matched waitlist controls. While baseline telomerase activity was not measured, the authors argued the between-group difference was due to meditative practice increasing perceived control and decreasing negative affectivity, thereby contributing to increased telomerase activity.

Puterman et al. examined the buffering effect of exercise on chronic stress finding that, in nonexercisers, a 1 unit increase in the perceived stress scale was related to a 15-fold increase in the odds of having shorter telomeres. In exercisers, perceived stress was unrelated to telomere length, suggesting exercise acts as a buffer in terms of telomere length. In a separate study of the same cohort, they found that women with histories of childhood abuse had shorter leukocyte telomeres than women with no reported childhood abuse. However, this relationship disappeared.
in women who exercised vigorously at least 3 times/week; demonstrating that exercise buffered the negative effects of childhood abuse and accumulated life stress on leukocyte telomere length.\textsuperscript{[79]} Although these studies did not involve a direct exercise intervention, the results are promising in terms of utilizing exercise interventions to target telomere maintenance in populations with high stress. A review of exercise interventions in cancer patients by Galvão and Newton\textsuperscript{[101]} found evidence for physiological and psychological benefits when exercise is undertaken during or after treatment for cancer.

While the aforementioned studies are promising, other results are mixed. Hovatta et al.\textsuperscript{[80]} examined the effects of a lifestyle intervention on patients with impaired glucose tolerance. They found increases in telomere length in approximately two-thirds of both the intervention and control groups over an average of 4 years, suggesting that the healthy lifestyle education provided to both groups was effective; despite only the intervention group receiving intensive counseling and monitoring.\textsuperscript{[80]} The authors concluded that the lifestyle intervention had no effect on relative telomere length, but that leukocyte telomere length can increase with time in at-risk populations.\textsuperscript{[80]}

Cancer, Psychosocial Stress, and Telomeres

There is a paucity of studies on the associations between telomere length and chronic psychosocial stress in the cancer population, with only three intervention studies with cancer patients and none involving cancer caregivers. Biegler et al.\textsuperscript{[81]} retrospectively examined the associations between telomere length and psychological distress among cervical cancer survivors. They found an association between decreased distress and increased telomere length.\textsuperscript{[81]} While the authors acknowledged that the sample size was small with a relatively short longitudinal time frame, they concluded that telomere length is potentially modifiable through psychosocial interventions aimed at reducing distress, in turn reducing the chronic stress response.\textsuperscript{[81]} As such, they argue for the inclusion of telomere length measurement in the biobehavioral paradigm in the cancer population.\textsuperscript{[81]}

The second study by Ornish et al.\textsuperscript{[82]} investigated the long-term effects of a lifestyle intervention in 35 men identified as having low-risk prostate cancer undergoing active surveillance. Telomere length was significantly increased in the 10 men who participated in the comprehensive lifestyle intervention and significantly decreased in the 25 control subjects. Importantly, the degree of adherence to lifestyle changes was significantly correlated with the extent of change in relative telomere length.\textsuperscript{[82]} Although this was a small pilot study with no comparison to men without a diagnosis of cancer, the results are promising in terms of the potential for the intervention having a positive effect on relative telomere length in patients with early stage cancer. While the results from both of these studies are encouraging, larger, randomized, controlled trials exploring the impact of interventions on telomere length in the cancer population are needed before any firm conclusions are drawn.

Finally, Carlson et al.\textsuperscript{[83]} explored the effect of group mindfulness-based cancer recovery or supportive-expressive group therapy, in comparison to usual care, on distress and telomere length in breast cancer survivors. Women in the usual care group showed a shortening of telomeres over the period from baseline to follow-up (3 months) while telomere maintenance was reported for the intervention groups. There were no associations noted between changes in telomere length and changes in mood or stress scores over time.\textsuperscript{[83]} The authors acknowledged that the interpretation of the results was difficult, yet still promising, in terms of interventions having an effect on telomere length.\textsuperscript{[83]}

Methodological Considerations

Although most of the studies report promising results with regard to telomere length or telomerase activity and psychosocial factors, there are methodological weaknesses. Many of the studies were retrospective, cross-sectional in design, with small samples, making it difficult to draw causal influences. There is substantial variability in relative telomere length in humans due to genetic and nongenetic factors, therefore large samples are required to increase the potential generalizability of reported effects and the confidence around reported correlations between telomere length/telomerase activity and psychosocial variables. Furthermore, only one study\textsuperscript{[83]} was a randomized, controlled trial, the accepted gold standard for effectively testing an intervention effect. Hence, there is increased risk of potential bias present in the remaining studies. In addition, the follow-up time for most studies was relatively short; longer-term follow-up is desirable to establish whether interventions have a meaningful effect on telomere maintenance over time.

Finally, it should be acknowledged that telomere length is controlled by multiple mechanisms, and, as such, telomerase activity alone may not explain changes in telomere length.\textsuperscript{[102]} Studies have shown inconsistent relationships between telomerase activity and telomere length leading
to some debate regarding how telomerase activity can be interpreted in regard to stress and telomere shortening. Future studies would benefit from large-scale randomized, controlled trials, and where possible, longitudinal design with telomere length, telomerase activity measurement, and expression of telomerase components, such as telomerase reverse transcriptase and/or telomerase template RNA, at multiple intervals. Greater replication of findings is also needed to add depth and certainty to the field.

**Discussion and Implications**

With ongoing advances in the detection and treatment of cancer, there are now significant declines in cancer-related death and increases in life expectancy, resulting in increasing numbers of cancer survivors. Indeed, cancer is now considered a chronic disease. Yet persistent disparities in both physical and psychological outcomes continue, which may in part be explained by the biopsychosocial mechanisms that underpin the stress process. Due to the chronic levels of stress, cancer can impose on people by cancer, stress reduction strategies are warranted. Interventions that address both the patient and the caregiver as a dyad may have a significant impact on psychological functioning and subsequent health.

Stress management techniques have been identified as one avenue to address distress in people affected by cancer. Mindfulness-based programs are now increasingly offered in cancer settings with promising results in terms of psychological and quality of life outcomes. Several studies have reported reductions in stress and cancer-related symptomatology in cancer patients participating in MBSR programs. Propose a model whereby cognitive appraisal can lead to increased arousal impacting on telomere maintenance via cognitive stress. They propose that mindfulness meditation may impact on telomere length by reducing cognitive stress and stress arousal, subsequently improving states of mind and influencing stress hormones in such a manner that promotes telomere maintenance. MBSR research that explores telomere maintenance in both cancer patients and caregivers may further our understanding of the biological mechanisms associated with stress in this population. To our knowledge, only one study exploring the effect of an MBSR intervention on telomere length in cancer patients has been undertaken. To date, it appears that the impact on cancer caregivers has not been explored.

There are many questions yet to be answered in terms of the longitudinal effects of psychosocial interventions that have an impact on telomere maintenance. It is not known if psychosocial interventions that affect telomere length are meaningful in terms of disease outcomes or for how long an effect on telomere length persists. There is a growing literature on accelerated aging in cancer survivors, and telomere length may be a biomarker for predicting such outcomes. The incorporation of telomere measurement into psychosocial interventional studies may provide insight into whether biological targets are useful in terms of measuring the effects of such studies. Psycho-oncology research traditionally relies heavily on self-reported measures of stress to examine the relationship between health outcomes and stress, therefore incorporating telomere maintenance offers an objective measure that may complement self-reported measures and further contribute to the empirical literature.

Biopsychosocial research has the potential to further our understanding of the differences in outcomes for cancer patients, and to guide psychosocial interventions that improve the quality of life, and possibly survival, of cancer patients, by providing an avenue to address the subjective experience of stress, its biological underpinnings and its consequences. With increasing numbers of programs offering psychosocial support to people with cancer, it is of interest to better understand the biological markers associated with psychosocial factors. In addition, with cancer care increasingly shifting to outpatient centers, the number of caregivers in the general community is increasing. It has been established that caregiving has an impact on telomere maintenance in some caregiver populations; however, in the cancer caregiving population, it has yet to be explored, and may further our understanding of the biological impact of caring.

The findings reviewed above provide promise for telomere measurement as a biomarker of stress in both people diagnosed with cancer and their caregivers. Within the stress and coping framework, such a biomarker has the potential to account for the effects of early life experience, future vulnerability, and efficacy of therapeutic interventions. Future research may clarify its role in exploring the adverse psychosocial health effects of a cancer diagnosis for both patients and caregivers.

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**Conflicts of interest**

There are no conflicts of interest.
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