

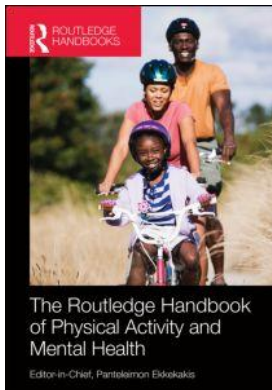
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PHYSICAL ACTIVITY AND PSYCHOSOCIAL HEALTH AMONG CANCER SURVIVORS

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and Kerry S. Courneya*

In the United States alone, approximately 1.6 million new cases of cancer (excluding skin cancer) are expected to be diagnosed in 2012 and close to 577,000 Americans are expected to die from cancer, making it the second most common cause of death in the United States after heart disease (American Cancer Society, 2012). The four most common cancers – prostate, breast, colorectal, and lung – are expected to account for approximately 50% of all new cancer cases and 50% of all new cancer deaths in 2010 (2012). The 5-year relative survival rate in the United States across all cancers and disease stages is 67% (2012). The high incidence coupled with good survival rates have resulted in nearly 12 million cancer survivors currently living in the United States (2012). Consequently, there is a growing population of cancer survivors.

Cancer and cancer treatments

Cancer consists of over 100 forms of diseases that grow at different rates and respond to different treatments. Cancer presents as either a malignant (i.e., invasive) or benign (i.e., non-invasive, encapsulated) solid tumor, or a nonsolid leukemia in the body's circulatory system (Ecsedy & Hunter, 2002). Individuals require cancer treatment that is aimed at their specific kind of cancer (e.g., breast, lung, colorectal). The most common treatment modalities for cancer are surgery, systemic therapy (i.e., chemotherapy, hormone replacement therapy), and radiation therapy. While these treatments have been shown to improve survival rates, cancer survivors are also at increased risk for many acute, chronic, and late effects of their disease and treatments, including cancer recurrence, second cancers, cardiac dysfunction, weight gain, bone loss, lymphedema, arthralgias, cognitive dysfunction, and menopausal symptoms (Shapiro & Recht, 2001).

A more immediate and often overlooked adverse consequence of cancer and its treatments is the impaired psychosocial health of survivors often experienced throughout the cancer trajectory. Data strongly suggest that survivors undergoing cancer treatment(s) often report poorer psychosocial health (Gao, Bennett, Stark, Murray, & Higginson, 2010). The adverse side-effects of cancer treatments have spurred a major research effort into strategies to alleviate and minimize treatment effects, both physical and psychosocial.

Psychosocial health and cancer

A cancer diagnosis and related treatments are often associated with increased emotional distress and reduced psychosocial health (Patrick et al., 2004). This process often leaves survivors overwhelmed, worried, depressed, and anxious, causing clinically significant and persistent psychosocial morbidity (i.e., impaired psychosocial health). These responses may arise from pain, a fear of recurrence, or treatment side-effects (e.g., nausea, fatigue) (Reddick, Nanda, Campbell, Ryman, & Gaston-Johansson, 2005). For some survivors, poor psychosocial health indicators, such as depression and anxiety, may be acute. However, for many survivors this depression and anxiety often is sustained well into survivorship (Carlson, Waller, Groff, Giese-Davis, & Bultz, 2011). Recent evidence also appears to suggest that depression may predict mortality, with recent meta-analytic data indicating a statistically significant associated risk (Satin, Linden, & Phillips, 2009).

Non-pharmacological modes by which to facilitate optimal psychosocial health profiles among cancer survivors are varied and can include group psychotherapy, educational resources, art therapy, music therapy, and individual one-on-one counseling. While data suggest that these intervention modalities have small effects on psychosocial health outcomes, they are unlikely to also address the physical and functional concerns experienced by cancer survivors. One intervention that has been found to enhance both the physical and psychosocial health of cancer survivors is physical activity. Clinically relevant and exciting evidence continues to emerge that supports the role of physical activity as a safe and effective intervention to facilitate favorable psychosocial health outcomes across various cancer survivor groups. This chapter will examine recent research on the associations between physical activity and psychosocial health among cancer survivors. Practical implications from this research will also be presented.

Physical activity and psychosocial health among cancer survivors

Among the general population, physical activity is a useful tool in both the prevention and treatment of anxiety (Conn, 2010a; Herring, O'Connor, & Dishman, 2010) and depression (Conn, 2010b), and improved positive affect (Reed & Buck, 2009). Given elevated levels of anxiety, depression, and distress among cancer survivors, researchers have attempted to understand the associations and effects of physical activity on psychosocial health outcomes across the cancer trajectory. Systematic reviews, as well as both cross-sectional and experimental studies in the cancer context, have demonstrated significant associations and effects between physical activity and several psychosocial health outcomes such as anxiety, stress, depression, self-esteem, and mood.

Conn and colleagues' recent meta-analysis of physical activity interventions for cancer survivors is one of the few to include a well-being component other than health-related quality of life – mood (Conn, Hafdahl, Porock, McDaniel, & Nielsen, 2006). Dependent on the instrument used to measure mood, indices of psychosocial health including stress, anxiety, and depression can be assumed. The results indicated small positive effects on well-being outcomes. For two-group comparisons there was a modest positive effect size for mood (0.19), although effect sizes were larger for single-group pre-post design studies. This meta-analysis clearly highlights the heterogeneity across the literature. The analyses also found that there were more favorable mood outcomes for interventions delivered after treatment compared to during, and improvement in mood was only found in the physical activity trials done after treatment completion. This is an important consideration when looking for potential benefits of physical activity on the psychosocial health outcomes in cancer survivors.

Research in the field of physical activity and cancer is now starting to examine the effects of exercise on specific psychosocial indicators. For example (and most recently) Craft and colleagues (Craft, Vaniterson, Helenowski, Rademaker, & Courneya, 2012) conducted a systematic review and meta-analysis to determine the antidepressant effects of exercise among cancer survivors. Studies included (N=15) were randomized controlled trials comparing exercise interventions to usual care using a self-report inventory or clinician rating to assess depressive symptoms. There was a significant overall effect size (-0.22) suggesting that exercise may have modest positive effects on depression symptoms.

Future well-designed studies are required to further our understanding of the role of physical activity for the psychosocial health of cancer survivors, on or off treatment. Clearly, a number of limitations are highlighted by the physical activity and cancer reviews, including most specifically the relatively sparse focus on the psychosocial health in relation to physical activity. Additional limitations include the heterogeneity across studies [intervention characteristics – duration, type and intensity, cancer type, treatment status (on/off)] and small sample size. The discord between the qualitative and quantitative findings regarding potential benefits from a physical activity intervention reflects the need to interpret the findings with caution until additional interventions confirm the findings. Finally, there has also been a lack of intervention work in cancer based on a needs-based approach (i.e., targeting individuals based on their need for improvement on a desired psychosocial health outcome).

Cross-sectional evidence

A more in-depth look at some specific studies may help to explain or elucidate the inconsistencies noted in the above reviews. In the cross-sectional literature, studies across several tumor groups have reported significant and beneficial relationships between physical activity, depression, anxiety, and self-esteem (Belanger, Plotnikoff, Clark, & Courneya, 2011; Faul et al., 2011; Jones et al., 2004; Penttinen et al., 2011; Rogers, Markwell, Courneya, McAuley, & Verhulst, 2011). For example, in a recent study of 192 mixed cancer survivors beginning chemotherapy (Faul et al., 2011), weekly metabolic equivalents (METs) were significantly associated with lower levels of anxiety and depression. Weekly METs were also associated with lower psychosocial composite scores on the SF-36. In a second study of 483 rural cancer survivors who were post-treatment, Rogers et al. found that those survivors who reported no leisure time physical activity had significantly higher depression scores compared to those survivors who were accruing at least 500 METs per week, the equivalent of 150 minutes per week of at least moderate-intensity physical activity (Rogers et al., 2011). This study also explored the associations between sitting time and depression. While a positive trend between sitting time and depression symptoms was apparent, there were no statistically significant relationships. It is important to note that this finding is not unique to cancer, as numerous cross-sectional studies in the general population have also reported no significant associations of physical activity with psychosocial health, depression, and self-esteem (Mosher et al., 2009; Taylor, Nicholls, et al., 2010).

Several cross-sectional studies demonstrate that these associations between physical activity and depression appear to be influenced by demographic and cancer treatment variables. For example, in a sample of 588 young adult cancer survivors, women demonstrated a clear dose-response relationship between different physical activity levels and depression, with only the two most active groups showing evidence of a physical activity and depression relationship (Belanger et al., 2011). These physical activity levels included (a) completely sedentary, (b) insufficiently active, (c) active within public health guidelines, and (d) exceeding public health activity guidelines. The same study also found that chemotherapy status (i.e., received chemotherapy vs.

no chemotherapy) moderated the relationships of physical activity level with depression, stress, and self-esteem. That is, for young adult survivors who received chemotherapy, it is likely that even smaller amounts of physical activity may be beneficial, where for survivors that did not receive chemotherapy, it appears that achieving physical activity guidelines may be required for benefits related to depression, self-esteem, and stress. In another study of cancer survivors beginning chemotherapy (Faul et al., 2011), weekly METs accounted for a significant portion of the variance in both anxiety and depression after controlling for BMI and age. In other words, physical activity was independently associated with lower anxiety and depression scores.

Experimental evidence

Several randomized controlled trials with cancer survivors have demonstrated significant and positive effects on depression, anxiety, overall psychological distress, self-esteem, and happiness outcomes (Courneya et al., 2003, 2007, 2009; Midtgaard et al., 2011; Morey et al., 2009; Noble, Russell, Kraemer, & Sharratt, 2012; Ream, Richardson, & Alexander-Dann, 2006; Sprod, Hsieh, Hayward, & Schneider, 2010). In one randomized controlled trial examining aerobic activity in 122 lymphoma survivors (Courneya et al., 2009), survivors in the aerobic group reported significantly higher ratings of happiness and significantly lower depression symptoms compared to those in a usual care control group. Courneya and colleagues have also published two randomized controlled trials in the breast cancer context (Courneya et al., 2003, 2007). In the START trial (Supervised Trial of Aerobic and Resistance Training During Chemotherapy) (Courneya et al., 2007), data suggested that those in the resistance-training group reported significantly higher self-esteem compared to those in the usual care control group. Among a sample of post-treatment (post-menopausal) breast cancer survivors, Courneya and colleagues (Courneya et al., 2003) reported significant changes in both happiness and self-esteem ratings compared to the control group. In one of the largest studies to date, Morey and colleagues randomized 641 older, overweight, long-term cancer survivors to either a home-based physical activity program or a wait-list control group (Morey et al., 2009). Data indicated that survivors in the intervention group reported significantly higher scores on the psychosocial health composite component of the SF-36 compared to the control group.

While these aforementioned studies are all positive, the evidence from other randomized controlled trials reports conflicting results. For example, a trial by Midtgaard and colleagues found significant effects on depression, but not anxiety, in a sample of 209 patients undergoing chemotherapy (Midtgaard et al., 2011). Further, Basen-Engquist reported no significant effects on psychosocial composite scores from the SF-36 after a 6-month lifestyle intervention (Basen-Engquist et al., 2006). Given the conflicting evidence, much remains to be understood. Future randomized trials need to continue to explore and elucidate the association between physical activity and psychosocial health outcomes.

Yoga, psychosocial health, and cancer

While research has primarily examined aerobic exercise, and to a lesser extent resistance training, recent research is exploring the role of other less traditional modes of physical activity. Given the permutations of developing interventions specifically designed to address psychosocial outcomes, yoga stands out as a field of interest as it consists of a low-intensity form of physical activity that may directly access mechanisms that improve patients' psychosocial health (Lin, Hu, Chang, Lin, & Tsauo, 2011; Smith & Pukall, 2009). Potential mechanisms for yoga's benefits to cancer survivors have included increased positive affect (Danahauer et al., 2009), improvements

in measures of mindfulness, best understood as a special form of non-discursive attentional regulation (Salmon, Lush, Jablonski, & Sephton, 2009), and improved regulation of the autonomic nervous system (Jerath, Edry, Barnes, & Jerath, 2006; Khattab, Khattab, Ortak, Richardt, & Bonnemeier, 2007; Sarang & Telles, 2006). Further research will elucidate the role of yoga as a means of enhancing the mental health of cancer survivors.

Mechanisms of action

Mechanisms behind physical activity-related improvements in psychosocial health are unclear, given the complexity of these relationships. Purported mechanisms are numerous and have largely been divided into psychological and physiological models. Described here are two psychological models that include the role of self-efficacy and positive affect, while two such physiological models include stress adaptation and neurobiological explanations.

Self-efficacy

Within the context of physical activity, self-efficacy refers to a person's confidence in their ability to engage in physical activity under a variety of circumstances (Pinto, Rabin, & Dunsiger, 2009). Self-efficacy influences physical activity behavior such that the stronger an individual's sense of self-efficacy, the more likely they will both respond favorably and adhere to physical activity, which subsequently further bolsters self-efficacy (Blacklock, Rhodes, Blanchard, & Gaul, 2010). Interestingly, the appraisal of physiological sensations as either positive or negative will respectively increase or decrease self-efficacy, which, in turn, also predicts adherence to physical activity (Perkins, Baum, Taylor, & Basen-Engquist, 2009).

Positive affect

A current area of clinical research interest is the study of positive affect as an independent, adaptive pathway in the cancer experience (Hou, Law, & Fu, 2010). This emerging field of research suggests both baseline positive affect and the enhancement of positive affect are important components of symptom management and cancer recovery (Lyubomirsky, King, & Diener, 2005). In general, positive affect tends to increase pre- to post-physical activity following non-exhaustive physical activity intensities and may also predict improved program adherence, further solidifying the benefits obtained through regular physical activity (Ekkekakis, Parfitt, & Petruzzello, 2011; Garber et al., 2011). This engagement in behaviors that result in greater state positive affect may, over time, result in dispositional trait-like changes and enhancement of both quality of life and psychosocial health indices (Hirsch, Floyd, & Duberstein, 2012).

Stress adaptation

In general, cancer and its treatment have far-reaching effects on the totality of physiological functioning, leading to inappropriate and sustained stress responses (Fagundes et al., 2011). While physical activity may initially further intensify these stress responses, the subsequent recovery may more appropriately down-regulate these responses (Ekkekakis et al., 2011). For example, aerobic fitness may confer stress-buffering effects to psychosocial stressors via a smaller overall stress response and more rapid recovery from stressors (Forcier et al., 2006). This shorter-duration stress response could have the effect of reducing overall wear and tear on the body (Spalding, Lyon, Steel, & Hatfield, 2004).

Neurobiology

Current research in the area of neuroscience also suggests that physical activity is responsible for a number of neurobiological changes that may impact psychosocial health (Harvey, Hotopf, Overland, & Mykletun, 2010). Ernst and colleagues suggest physical activity decreases depressive symptoms by increasing brain neurogenesis. They suggest four molecular mechanisms that could play a role in mediating the effects of physical activity on increased neurogenesis: increased levels of beta-endorphins, vascular endothelial growth factor, brain derived neurotrophic growth factor, and serotonin (Ernst, Olson, Pinel, Lam, & Christie, 2006).

An argument must be made that psychology and physiology are not discrete entities and that a psycho-physiological model may be the one that accounts for the most variance (Netz, 2009). Future research must explore the complementary psycho-physiological mechanisms by which these relationships occur and develop parsimonious explanations to better explore and describe the mediating role of physical activity in improving cancer survivor psychosocial health outcomes in general, and the antidepressive and anxiolytic effects of physical activity (Strohle, 2009). More importantly, therapies directed toward addressing the functional links between mind and body may be particularly effective in treating symptoms associated with chronic illness (Taylor, Goehler, Galper, Innes, & Bourguignon, 2010).

Mediators of change

Unfortunately, relatively few interventions have examined mediating variables that may be responsible for observed changes in psychosocial health outcomes. For example, Courneya and colleagues have reported that while physical fitness parameters (i.e., peak oxygen consumption and peak power output) may mediate changes in health-related quality of life and fatigue, no such mediation was found for self-esteem, happiness, or depression (Courneya et al., 2003, 2009). While these findings suggest that improving physical fitness outcomes may be the most effective way to realize improvements in the physical and functional aspects of health-related quality of life, these studies suggest that other aspects of physical activity programs and interventions (e.g., social support, group interaction) may be responsible for changes in psychosocial health outcomes.

Limitations and future directions

Despite the aforementioned studies demonstrating several characteristics that are indicative of well-conducted, high-quality research (e.g., large sample sizes, targeted samples, randomized controlled trial methodology), several limitations remain that should be mentioned. First, while several studies have reported physical function as a primary outcome, no studies have developed a physical activity intervention specifically for alleviating psychosocial outcomes such as depression and anxiety symptoms, or improving self-esteem. Psychosocial health outcomes are most often included within a secondary analysis and are largely exploratory. Thus, the randomized controlled trials published to date are not statistically powered to detect specific changes in psychosocial health outcomes. Future studies should be designed with specific psychosocial health outcomes as the targeted outcome, and thus be appropriately powered to detect such changes.

Issues also remain with the assessment of physical activity. In all of the (associative) studies in the cancer context, physical activity was assessed via self-report. Across these studies, the self-report tools used varied considerably. While the limitations of self-reported physical activity are well documented (e.g., over-reporting, difficulty with recall), future research should make use of the recent technological advances in physical activity measurement. For example, step pedometers and accelerometers are two methods that provide a more objective index of physical

activity behavior. While pedometers primarily capture walking activities, accelerometers (considered the gold standard of physical activity measurement) provide information relating to the intensity of the movement/activity being performed and may be particularly useful within the cancer context (Rogers, 2010). Accelerometers are able to provide information not just related to light, moderate, and vigorous physical activity, but also information related to time spent being sedentary. Using more objective indicators of physical activity may provide more detailed insight into the physical activity (and the emerging science of sedentary behavior), and psychosocial health relationship.

Across the studies, psychosocial health outcomes were also assessed in a variety of ways. While depression is the most commonly reported outcome across the studies, several assessments of depression symptom frequency are used (e.g., Center for Epidemiological Studies – Depression Scale, Hospital Anxiety and Depression Scale). The most common depression assessment used is the Center for Epidemiological Studies – Depression Scale (CES-D) (Kohout, Berkman, Evans, & Cornoni-Huntley, 1993; Radloff, 1977). The CES-D is a measure of depressive symptom frequency. Across studies, data suggest that the mean depression symptom frequency is actually quite low. For example, CES-D baseline mean are typically <10 on a 0–30-point scale (Belanger et al., 2011; Courneya et al., 2009). Therefore, it seems reasonable to suggest that physical activity interventions are simply able to reduce already somewhat low frequencies of depression symptoms. Future large-scale trials should determine whether physical activity interventions are able to reduce the actual clinical occurrence of depression, rather than simply mean symptom frequency, which is documented to be relatively low. To do so, future research must utilize more appropriate and clinically relevant assessments of depression. For example, the Patient Health Questionnaire – 9 (Kroenke, Spitzer, & Williams, 2001) asks individuals, “Over the last 2 weeks, how often have you been bothered by any of the following problems?” for each of the 9 DSM-IV criteria, which included such items as “Feeling tired or having little energy” and “Feeling down, depressed, or hopeless.” Response options are “not at all,” “several days,” “more than half the days,” and “nearly every day.” Major depression is diagnosed if five or more symptoms are present, including depressed mood or anhedonia (i.e., inability to experience pleasurable emotions). Other depression is diagnosed if two to four depressive symptoms are present, including depressed mood or anhedonia (Kroenke et al., 2001).

Implementation

This chapter has highlighted the largely positive associations and effects observed in studies examining physical activity and psychosocial health outcomes. The evidence supports the role of physical activity across the cancer context and across tumor groups for facilitating some psychosocial health outcomes such as depression and self-esteem. Given the low rates of physical activity among a variety of tumor groups, clearly the challenge of facilitating physical activity behavior in this population remains. Several currently ongoing randomized controlled trials are exploring the effects of physical activity on a range of psychosocial health outcomes across a variety of tumor groups (Jones et al., 2010; Kampshoff et al., 2010; Persoon et al., 2010). These studies will add to the literature by providing critical information about the effects of physical activity on psychosocial health by examining different tumor groups and exploring different doses of physical activity. Research into factors that help cancer survivors engage in lifelong physical activity may not only result in more optimal psychosocial health profiles, but also reduce the risk of recurrence and facilitate longer survival for millions of cancer survivors. Staging these efforts within a theoretical framework appears to be one effective way to encourage and facilitate the adoption and maintenance of physical activity behavior in various cancer survivor groups

(Vallance, Courneya, Plotnikoff, & Mackey, 2008). While new trials continue to explore the physical activity and psychosocial health relationship among cancer survivors, resulting data should be used to develop physical activity behavior change trials and population health campaigns designed to facilitate the psychosocial health of this population.

The recent ACSM roundtable on “Exercise guidelines for cancer survivors” (Schmitz et al., 2010) concluded physical activity is safe both during and after cancer treatments, resulting in improvements in physiological, physical, and psychosocial health outcomes across several cancer survivor groups. Current recommendations suggest an overall volume of weekly activity of 150 minutes of moderate-intensity physical activity, or 75 minutes of vigorous-intensity physical activity, or an equivalent combination (Schmitz et al., 2010). Suggested strength training recommendations are to perform two to three weekly sessions including physical activities for all major muscle groups. Flexibility guidelines suggest stretching on days other physical activities are performed. These guidelines are embedded within the proviso that physical activity programs must be adapted for the individual on the basis of their health status, treatments, and anticipated disease trajectory.

Research indicates the timing of these interventions may also be important. It is suggested that although regular physical activity may improve outcomes during treatment, it may provide greater benefits during the survivorship phase (Courneya & Friedenreich, 2007; Doyle et al., 2006). However, this reported enhanced physical activity benefit post-treatment may be a reflection of survivors’ treatment completion and lessening of medical demands, creating additional time and energy for cancer survivors to devote to and benefit from physical activity. ACSM roundtable guidelines suggest that cancer survivors, regardless of where they are in the treatment continuum, should avoid inactivity and that any level of physical activity carries with it some benefit (Schmitz et al., 2010).

The goals of the physical activity program and unique psychosocial health needs of cancer survivors should guide the development of tailored physical activity prescription. Research has strongly encouraged these programs to be as prescriptive as possible to meet survivors not only where they are in the cancer trajectory but also based on a host of other concerns, which may well include psychosocial health (Hacker, 2009). Deciding on the best approach for people with cancer requires detailed knowledge of the individual’s current abilities, past physical activity experience, specific cancer, cancer treatment and recovery, and co-morbid conditions to best tailor the physical activity intervention program. It has been further suggested interventions should include multiple options based on preferences of targeted cancer-specific subgroups (Rogers, Markwell, Verhulst, McAuley, & Courneya, 2009).

To be prescriptive, survivors are best served by highly knowledgeable health and fitness professionals who have not only cancer-specific training but also understand the intricacies of prescribing physical activity for psychosocial health and wellness. To this end, the recent Cancer Exercise Specialist (CES) initiative by ACSM is a critical addition to cancer-specific physical activity testing and prescription. The potential for this professional designation, along with more established designations of Clinical Physical Activity Specialist and Clinical Physical Activity Physiologist, to serve as a springboard for better prescribing physical activity to cancer survivors for a variety of health concerns, not least for the express aim of mitigating symptoms and improving health in general with an eye toward psychosocial health, is highly warranted. In addition, as oncology in and of itself is a highly interdisciplinary endeavor, physical activity clinicians should be prepared to work with other treatment team members including physicians, nurses, and psychosocial health professionals.

Reaching this level of complexity in physical activity prescription will be contingent on state-of-science knowledge of cancer etiology and treatment as well as clinical physical activity

physiology and behavioral health interventions. This requires a health professional well versed in all three areas. In the meantime, ACSM recommendations serve as a strong starting point for most individuals that can be further broken down into activities they enjoy, feel good doing, and derive benefit from. In maintaining such a regime, the by-product appears to be enhanced psychosocial health profiles, regardless of intervention specifics.

Summary

Unfortunately, the majority of cancer survivors will not realize these aforementioned psychosocial health benefits due to overwhelmingly low physical activity participation rates (Blanchard, Courneya, & Stein, 2008). Despite the accumulating evidence documenting the associated benefits of physical activity after a cancer diagnosis, most cancer survivors are not meeting the minimal amounts of physical activity required for the accrual of health benefits (Blanchard et al., 2008; Coups & Ostroff, 2005; Courneya, Katzmarzyk, & Bacon, 2008). Cancer care professionals can expect that less than 10% of cancer survivors will engage in physical activity during treatments and between 20% and 30% will engage in regular physical activity after their treatments. Developing and evaluating strategies to assist cancer survivors in adopting and maintaining physical activity so that psychosocial health benefits can be realized are critical. These initiatives need to be developed based on current knowledge of the determinants of physical activity in this population.

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