FIT SURVIVOR: A MULTICOMPONENT HEALTH INTERVENTION FOR ADOLESCENT AND YOUNG ADULT CHILDHOOD CANCER SURVIVORS

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ABSTRACT OF THE THESIS

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Adolescent and Young Adult (AYA) childhood cancer survivors (CCS) exhibit an increased risk for chronic disease states. Poor lifestyle behaviors characterized by lack of physical activity and unhealthful nutrition practices may further exacerbate this risk. This necessitates a need to develop interventions to prevent the manifestation of this delayed disease risk. **PURPOSE:** To evaluate the efficacy of a multicomponent 12-weel intervention, Fit Survivor, which combined 8-weeks of supervised resistance exercise (RE) and health education, a smartphone application, wearable activity monitor, and social media on strength, body composition, quality of life (QoL), and body-esteem. **METHODS:** A randomized controlled trial was conducted for 12-weeks with assessments performed pre and post intervention. Participants were randomized into experimental (EXP, N=9) or control (CON, N=10). Assessments included body fat percentage (BF%), bench press (BP), leg press (LP), quality of life (QoL), and body-esteem measures. EXP were provided the smartphone application, Fit Survivor with social media integrated into it, and a Fitbit Charge. EXP participated in 8-weeks of supervised resistance-band exercise and health education sessions. The EXP group was encouraged to continue using Fit Survivor for rest of the 12-week intervention. An analysis of variance was conducted with an alpha level of 0.05. Effect sizes were represented by Cohen's *d*. **RESULTS:** A non-significant ($p>0.05$) increase was observed in CON for BF% and FM, but not in EXP. EXP demonstrated a non-significant ($p>0.05$) increase in FFM. EXP increased BP (CON: d=0.06, EXP: d=0.30) and LP (CON: d=0.13, EXP: d=0. 52) to a greater degree than CON. Most QoL and body-esteem measures were non-significantly reduced over the intervention. **CONCLUSION:** The intervention improved strength and potentially prevented an increase in BF%. However, QoL and body-esteem were shown to non-significantly decrease possibly due to an unintended burden caused by the intervention or a high psychosocial baseline functioning which caused a regression to the mean. Overall, Fit Survivor was shown to have beneficial effects with regards to body composition and strength with more research needed to elucidate its effects on psychosocial markers.

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Childhood Cancer Survival

Advances in treatment allow for more childhood cancer patients to survive into adulthood. Although this provides immediate benefit with regards to remission, it can increase risk for chronic disease states. This risk can be exacerbated by poor lifestyle behaviors which necessitate the need to implement health interventions. These behaviors are best established early in life before the chronic diseases manifest. Furthermore, health interventions should be integrated with technology as an avenue to engage with this cohort due to the high prevalence of smartphone ownership. However, many smartphone applications are not theory-based which may yield questionable efficacy in outcomes. This highlights the need to develop a theory-based smartphone application which is able to engage with younger survivors of childhood cancer and establish beneficial lifestyle behaviors. Overall, this necessitates the investigation of methods to advance the long-term health of childhood cancer survivors (CCS).

Childhood cancer survival rates are rising annually within the United States and increased from nearly ~83% in 1995 to ~88% in 2009.[1] Although the population of CCS is increasing, many are still at risk for delayed negative health outcomes due to treatments involving chemotherapy (CTH), radiation therapy (RTH), and surgery.[2,3,4,5] CTH and RTH target cancer cells, as well as healthy cells, which can pose long-term health risks for tissues with a limited regenerative capacity.[2] These effects are prevalent due to many CCS having received CTH, RTH, or a combination of both.[6]

There are several types of CTH drugs including anthracyclines, alkylating agents, antimetabolites, antimicrotubular agents, monoclonal antibodies, and tyrosine kinase inhibitors.[7] These agents have the potential to induce adverse cardiovascular effects such as bradycardia, various arrhythmias, myocardial ischemia, left ventricular dysfunction, and congestive heart failure.[2] Furthermore, CTH may also induce acute myeloid leukemia, renal and liver dysfunction, urinary tract abnormalities, peripheral motor and sensory neuropathy, reduced bone mineral density, and neurocognitive impairment among others.[8] Anthracyclines are primarily used to treat the most common form of childhood cancer, acute lymphoblastic leukemia,[2,9] and are believed to insult cardiac tissue which causes an increased risk for cardiovascular disease (CVD).[4,10,11] Higher doses of anthracyclines exhibited the greatest increased risk for congestive heart failure, pericardial disease, and valvular disease.[12] This was potentially due to iron-mediated free oxygen radicals, yet the complete mechanistic effects are not entirely elucidated.[7]

RTH also causes health complications independent of CTH. RTH treatment may induce physiological changes that are not readily apparent with site of radiation dictating the effects. CCS who have received cranial RTH exhibited an increased body fat percentage (BF%),[13] low self-reported physical activity (PA) levels,[14] and decreased total energy expenditure.[15] These effects were possibly due to altered hypothalamus, pituitary, or thyroid function.[13,16] Also, chest-directed RTH increased risk for cardiovascular mortality,[17] myocardial infarction, congestive heart failure, valvular heart disease, and arrhythmias.[18] RTH was believed to induce myocardial damage through interstitial fibrosis with smaller vessels more vulnerable to radiation, however the integrity of the endothelium of the larger vessels were also reduced over time.[2] Together, these alterations may cause physical limitations and impair the activities of daily living in CCS. This was demonstrated as survivors who received brain and chest radiation exhibited a 2-fold increase in physical limitations,[5] suggesting that radiation exposure may contribute to decreased PA, greater BF%, and physical limitations in CCS. In addition, an increased risk for negative health outcomes was observed in CCS who received both anthracyclines and RTH compared to either alone.[4] Thus, CTH and RTH, either alone or in combination, can produce severe health complications in CCS.

The current CCS population is growing due to improved treatment success. However, surgery, CTH, and RTH may contribute to long-term negative health effects. These adverse health effects may not manifest to disease states until later life which necessitates the implementation of preventative measures. Taken together, the increased survival rates in conjunction with cancer-related treatment effects increase the likelihood of disease risk in CCS.

Disease Risk

CCS have an increased risk for endocrine disorders,[16,19] CVD,[4,10,11] diabetes,[20,21,16] subsequent cancers,[22] fatigue,[23,24,25,26] altered psychosocial status,[27] and reduced quality of life (QoL).[28,29,30] The specific risks will vary depending on treatment and time since diagnosis.[31] In addition, Hudson et al.[3] examined the health status of CCS through the utilization of a sibling comparison group and observed that survivors displayed an increased risk for the development of poor general and mental health, functional impairments, activity limitations, and adverse health status outcomes in any domain. Furthermore, CCS may exhibit a different physiological profile. Slater et al. reported CCS to have increased low-density lipoprotein-cholesterol, and lower insulin sensitivity and carotid cross-sectional dispensability compared to controls.[32] Together, this suggests that CCS have an increased risk for the development of various negative health outcomes including endocrine abnormalities, CVD, and subsequent cancer with type of treatment and time since diagnosis influencing degree of risk.

Endocrine Abnormalities

The increased disease risk may be partially attributed to alterations within the endocrine system as 44% of CCS exhibited at least one, 16.7% exhibited at least two, and 6.6% exhibited three or more endocrine abnormalities.[16] CCS who were treated with alkylating agents or radiation to an endocrine organ were particularly susceptible as 62% of these survivors developed endocrine disorders.[31] Furthermore, the cumulative incidence of endocrine disorders rose with increased time since cancer diagnosis.[33] This indicates that the degree of risk in the development of endocrine abnormalities was dependent on the type of treatment and time since diagnosis.

Cranial radiation would be particularly hazardous due to the large impact of the pituitary gland in hormonal regulation. CCS who were treated for brain tumors demonstrated a 4-fold increased risk in the development of an endocrine disorder.[33] Additionally, radiation ≥18 Gy to the hypothalamus-pituitary-axis (HPA) resulted in 56.4% of CCS having reported a HPA deficiency which includes reductions in growth and pubertal progress, insulin-like growth factor-I, serum cortisol, luteinizing hormone, follicle stimulating hormone, estradiol, testosterone, thyroid stimulating hormone, and free thyroxine.[31] Even if acute endocrine effects are not readily apparent, long-term changes can still present a significant problem, particularly given the notable rise in endocrine abnormalities with increased time since diagnosis.[33] Furthermore, radiation to other areas such as the abdomen, neck, and reproductive system influenced the prevalence of disease states including diabetes mellitus (DM), hypo- or hyperthyroidism, thyroid nodules, thyroid cancer, primary ovarian failure, male germ cell dysfunction, and Leydig cell failure.[16,31] Overall, CCS who received RTH to an endocrine organ are susceptible to hormonal abnormalities.

Although these disorders have multiple mechanisms, CCS exhibit an increased risk due to the potential of an altered hormonal state. CCS exhibited greater insulin resistance compared to age and body mass index (BMI) matched controls suggesting an increased risk for complications with glucose regulation among CCS.[2] This was supported by the fact that cancer survivors demonstrate a 60% increased risk for the development of DM compared to sibling controls.[20] Meacham et al.[34] reported CCS who received total body irradiation displayed the greatest risk (relative risk (RR): 12.6; 95% CI: 6.2-25.3) followed by those diagnosed with acute myeloid leukemia (RR: 5.7; 95% CI: 3.1-10.6) suggesting that DM risk varied based on cancer type and treatment. In addition, CCS demonstrated a 2-fold increased risk for DM with a BMI over 25 (OR: 2.0; 95% CI: 1.3-3.0) and a 4-fold increased risk observed with a BMI over 30 (OR: 4.3; 95% CI: 2.9-6.4) when compared to CCS with a BMI between 18.5 and 24.9.[34] HPA radiation was attributed to the increased prevalence of obesity in CCS and, thus may also impact

DM risk.[31] Taken together, this illustrates that CCS have an increased risk for the development of DM and obesity with non-modifiable factors such as treatment and time since diagnosis influencing the degree of risk.

Cardiovascular Disease

Cancer survivors have a 2-fold increased risk for the development of CVD.[11] Gudmundsdottir et al.[10] reported 26.9% of CCS were admitted to the hospital for CVD by the of age 50 with the mean age of CVD diagnosis in survivors being 7 years younger than the non-cancer comparison group. Furthermore, CCS were found to have an increased risk for all 10 diagnostic CVD categories with the greatest risk seen for heart failure (RR: 5.2: 95% CI: 4.5-5.9), valvular disease (RR: 4.6: 95% CI: 3.5-5.5), cerebrovascular disease (RR: 3.7: 95% CI: 3.4-4.1), and pulmonary heart disease (RR: 3.5: 95% CI: 2.9-4.3).[10] However, CVD risk in survivors may display a downward trend with age as CVD decreased from a 19-fold increased risk in early life to a 1.3-fold increased risk above the age of 60.[10] This finding was most likely due to age-dependent increases in CVD among the general population.

The increased risk among CCS may be partially due to cancer-related treatments. Mulrooney et al.[12] demonstrated a positive linear relationship between average cardiac radiation dose and risk for congestive heart failure, myocardial infarction, pericardial disease, and valvular abnormalities which can include valvular thickening and stenosis. CTH treatment demonstrated similar adverse outcomes with an increased risk for congestive heart failure, pericardial, and valvular disease.[12] Furthermore, the combination of RTH and anthracycline administration may increase the incidence for heart failure compared to those who received either in isolation.[18] This suggests that cancer-related treatments, especially chest-directed RTH, increase the risk for adverse cardiac events.

Subsequent Cancer

CCS have a 9-fold increased risk in the development of secondary sarcomas.[22] Furthermore, the risk may increase with increasing time since diagnosis. The cumulative incidence of a secondary malignant cancer rose from approximately 0.8% at 10 years' to approximately 4.5% after 25 years' post-diagnosis in CCS.[35] In addition, 14.8% of CCS were found to have a secondary cancer before the age of 40 with this percentage rising to 34.6% by age 55.[36] Together, this suggests that increased time since diagnosis raises the likelihood of the development of subsequent cancer with risk varying among cancer types ranging from 3-fold in those diagnosed with non-Hodgkin's lymphoma to almost 10-fold diagnosed with Hodgkin's disease.[35] The increased risk in CCS was associated with a higher dose of anthracyclines, alkylating agents, family history of cancer, and history of secondary malignancies suggesting that cancer-related treatments and potentially hereditary factors influence subsequent cancer risk.[22]

CCS have benefited from increased treatment success, yet exhibit an increased risk for endocrine abnormalities, CVD, and subsequent cancers. The type of cancer, treatment, and time since diagnosis have shown to influence disease risk. Yet, many of the potential disorders that are prone to manifest in CCS may be preventable through the implementation of beneficial lifestyle behaviors. In short, CCS may exhibit an inherent risk for disease, however steps can be taken to alter lifestyle factors and diminish risk for disease development.

Lifestyle Risk Factors

Beyond the influence of cancer treatment, lifestyle factors contribute to disease risk. Sedentary time and poor dietary habits are associated with an increased risk for CVD[37] with low PA levels and increased body fatness associated with an increased cancer risk in the general population.[38] Additionally, 32.5% of male and 31.0% of female CCS exhibited metabolic syndrome, a combination of hypertension, hyperglycemia, hypertriglyceridemia, low high-density lipoprotein-cholesterol, and obesity.[39] Thus, the management of PA levels and body composition may be particularly important for younger individuals as obesity in young adulthood increased risk for CVD in adulthood.[40]

Beyond their influence on CVD, lifestyle factors such as body fatness, PA, and dietary intake also contribute to cancer risk. Zhang et al.[41] performed a meta-analysis and found an association between obesity and brain tumors in a middle-aged healthy population. CCS may have an inherent risk in the development of a subsequent cancers, yet this demonstrated that lifestyle factors also contribute to cancer risk. Taken together, the risk for subsequent cancer was increased in CCS with time since diagnosis, treatment, cancer type, and lifestyle factors potentially influencing the degree of risk.

Lifestyle factors may influence psychosocial outcomes as well. Poor PA levels and a high BMI were found to be significantly associated with reduced global QoL, physical and cognitive functioning, body image, and increased fatigue in adult survivors.[28] However, the attainment of adequate PA levels and a healthy body composition can prevent the onset of these psychosocial outcomes. Together, adequate

PA and a healthy body composition can have holistic effects that are associated with decreased disease risk and improved psychosocial measures.

Body Composition and Obesity

Obesity is a national concern, especially in youth because of an increased risk for the development of subsequent disorders. The prevalence of obesity was 17% in 2011-2014 for individuals aged 2-19[42] with research suggesting obesity tracking into adulthood.[40] A major contributor to obesity may be a low energy expenditure due to low levels of PA. This can be deleterious for CCS due to a greater prevalence of reduced PA compared to sibling controls[32,28] in conjunction with an increased risk for CVD.[4,10,11] In addition, obesity was associated with an increased risk for high LDL-C, low HDL-C, hypertension, and diabetes,[43] which may predispose individuals to the development of CVD.[2,38]

CCS demonstrate a poorer body composition when compared to healthy individuals.[13,32,44] Poor body composition among CCS may initially present itself during cancer diagnosis and treatment as childhood cancer patients demonstrated an increased BF% and reduced lean mass upon beginning cancer treatment.[45] Additionally, childhood cancer patients exhibited an increase in adiposity over the treatment period with no change in fat free mass (FFM).[46] This lack of change in FFM but increase in fat mass (FM) may be a contributor to the underestimated BMI that was observed in CCS.[2,13] Together, this suggests that FM growth was greater than FFM growth in childhood cancer patients. Thus, the increased adiposity and reduced skeletal muscle mass exhibited in CCS begins during treatment and was never resolved.

The mechanisms for adiposity increases may be due to cancer treatment resulting in leptin receptor and concentration abnormalities,[2] hypothalamic-pituitary axis dysregulation due to cranial radiation,[2] and energy intake dysregulation due to glucocorticoid therapy.[47] In addition, BMI may underestimate the prevalence of obesity among CCS due to the lower FFM and increased FM exhibited by this population.[2,13] Blijdorp et al. conducted a long-term CCS study in the Netherlands, and demonstrated that BMI underestimated obesity by 39%.[13] Furthermore, 52% of survivors were misclassified as non-obese based on BMI, however met the obesity criteria based on BF%.[13] This underestimated BMI exhibited by CCS can be problematic due to the increased disease risk. Shea et al.[48] reported a high BF%, but normal BMI was significantly correlated with increased waist circumference, triglycerides, LDL-C, glucose, insulin, and insulin resistance. This suggests that BMI does not accurately predict health risk in CCS due to the increased adiposity and reduced lean body mass observed.

CCS have an increased risk for obesity compared to the general population with cancer and treatment-related mechanisms, as well as lifestyle factors, contributing to an increased BF%. Yet, lifestyle factors may contribute to a greater degree as a lack of PA was the primary contributor to the increased BF% in childhood cancer patients.[46]

Insufficient Activity and Cardiovascular Risk Factors

Confusion occurs due to exercise and PA being used interchangeably. Exercise is a subcategory of PA which is structured, planned, repetitive, and purposeful.[49] Lahart et al.[50] demonstrated a moderate protective effect when comparing the highest to lowest PA for all-cause and breast cancer-related mortality in adult women with breast cancer. Also, the authors found that lower PA correlates with all-cause and cancer mortality, signifying the importance of PA in the adult population on longevity. This finding may be applicable to younger individuals due to PA during childhood and adolescence being predictive of PA in adulthood.[51]

The tracking of PA into adulthood creates a need to ensure youth have adequate PA levels as increased sedentary behavior displayed a positive correlation with cardiometabolic risk factors, waist circumference, triglycerides, diastolic blood pressure, and diminished high-density lipoprotein-cholesterol.[52] A reduction in PA causes a decrease in total energy expenditure and a subsequent increase in FM and, therefore weight gain. CCS of acute lymphoblastic leukemia and lymphoma were found to exhibit a -491 kilocalorie per day difference (95% CI: -686 to -295) between the gold-standard of doubly labeled water and estimated energy expenditure.[15] This difference may have been be due to the lower skeletal muscle mass [2,4,13,53,54] and reduced PA observed in CCS [28,32] which led to increased adiposity. The diminished skeletal muscle mass may have been due to cancer-related treatments and bed rest during treatment as cancer patients demonstrated muscle strength impairments compared to healthy controls.[55] Taken together, the reduced PA exhibited by CCS increased the likelihood for the development of obesity and CVD. Because childhood and adolescent PA track into adulthood, this further supports that interventions should be aimed at the younger cohorts of CCS.

The various effects of cancer treatment on CCS are not immediately evident and the negative health outcomes may not be observed until maturation. However, healthy behaviors that may have a beneficial impact on disease risk are often neglected. In a statement by the American Heart Association, 31% of CCS were found to be below the age and sex norms for exercise capacity,[2] which may exacerbate various disease states. Thus, the incorporation of health promoting behaviors into interventions may aid in decreasing the observed disease risk among CCS.

Health behaviors have also been shown to have impacts beyond physiological outcomes as low PA was significantly correlated with reduced psychosocial measures.[28] Causal assumptions cannot be made, yet this demonstrated a connection between PA and psychosocial health. Together, PA levels may exhibit impressions on both physiological and psychosocial measures.

Quality of Life and Body-Esteem

Cancer may affect the physical, social, cognitive, and emotional aspects of an individual's life. Cancer survivors were shown to exhibit a decreased QoL compared to controls. [29,30] Although there was improvement upon remission, QoL was still reduced 2 years post-treatment.[30] Furthermore, most improvements occurred during the first year, suggesting that current methods to enhance long-term QoL are insufficient. The recovery of QoL was important due to the association between low life satisfaction and risk for suicide.[56] This was relevant as childhood and adolescent cancer survivors demonstrated a 2.5-fold increased risk for suicide when compared to non-cancer indidividuals.[57] Taken together, survivors demonstrate a decreased QoL upon completion of treatment, which may be a contributor to an increased rate of suicide in adolescents.

There are several factors that may contribute to a diminished QoL. Although body image is not well studied in this population, poor physical QoL among survivors was correlated with obesity, exposure to alkylating agents, pelvic radiation, disfigurement, and walking with a limp.[58] An increased BMI in survivors was also found to be associated with a reduced body image.[28] This finding in conjunction with the increased likelihood for excess adiposity suggests an increased prevalence of poor body image among survivors. Thus, obesity may contribute to the development of disease states and a poorer QoL and body image. CCS were more likely to report poorer mental health compared to healthy controls.[59] This may be partially due to an increased time spent at the hospital and decreased at school which may lead to a reduction in social interaction with peers.[60] The worsened physical condition and negative body-esteem may also contribute to avoidance of social situations.[60] This may decrease leisure PA, and therefore may exacerbate disease risk in CCS. Taken together, cancer has effects beyond an increase in disease risk and also negatively impacts QoL and body-esteem.

It is ideal to have children be active during treatment, however the treatment-related side effects such as extreme fatigue may impair physical functioning and motivation for some patients to do so.[61] Thus, the post-treatment period may be optimal to foster positive health behaviors. Beyond childhood and adolescent PA tracking into adulthood, evidence suggests obesity in adolescence was predictive of obesity during adulthood.[62] Therefore, building healthy habits during the earlier stages of life may reduce the risk for obesity-associated diseases and poor body-esteem in adulthood. In short, CCS demonstrate an increased risk for various diseases, an altered physiological profile, reduced QoL and body-esteem, and unfavorable health behaviors suggesting that adolescent and young adult (AYA) CCS may benefit from interventions aimed at promoting healthy behaviors as they transition into adulthood.

Exercise and Physical Activity as Therapeutic Modalities

As previously elucidated, CCS have an increased disease risk due to cancer-related treatments. Fortunately, markers such as fasting plasma glucose, total cholesterol, blood pressure, and adiposity may be positively modified with the implementation of healthy behaviors and increased PA to decrease disease risk.[63] Weaver et al.[64] reported that in adult cancer survivors, 61% have discussed dietary, 68% exercise, and 62% assistance in lifestyle modification with their doctors. Yet, survivors were more likely to be overweight, obese, physically inactive, and have hypertension or diabetes compared to healthy controls.[64] This implies that survivors may be aware of the need for behavior modification, but have not implemented these activities and behaviors. Furthermore, the investigation by Weaver et al. regarding dietary and exercise behaviors was performed in adult survivors, thus cannot be extrapolated to AYA CCS who may not be knowledgeable of their overall disease risk due to their young age at diagnosis.[65] Taken together, this suggests that interventions that assist CCS in establishing beneficial behaviors may provide long-term health behavior alterations that decrease disease risk.

Exercise and Physical Activity on Disease Risk

PA has demonstrated a plethora of physiological benefits in the general population with higher intensities superior when compared to lower. The replacement of sedentary time with light PA was found to decrease CVD mortality (HR: 0.88; 95% CI:

0.81-0.95) with a greater protective effect observed with moderate-to-vigorous PA on CVD mortality (0.36; 95% CI: 0.13-0.95) and cancer mortality (HR: 0.79; 95% CI: 0.39-1.62).[66] The degree of improvement in these markers was influenced by the intensity of PA with high-intensity PA conferring greater benefit than lower intensity. Kruk et al.[67] observed an intensity threshold with moderate, vigorous, and moderate-to-vigorous PA inducing a reduction in cancer risk while light-PA yielded inconclusive findings. Furthermore, an inverse association was seen between vigorous exercise and CVD risk in a dose-dependent manner.[68] The reduced exercise capacity in CCS allows for a greater potential for improvement as cardiovascular markers have been found to improve to a greater extent in CCS than controls.[32] Thus, the replacement of sedentary behavior with PA, especially moderate-to-vigorous PA can have a significant impact on the reduction of cardiovascular and cancer mortality.

The proposed mechanisms underlying the connection between PA and reduced cancer risk include decreased weight, alterations in endogenous sex and metabolic hormones, decreased concentrations of growth factors including insulin-like growth factor-I and insulin-like growth factor binding protein I and II, reduced superoxide and hydroxyl radical formation, detoxification of chemical carcinogens, reduction of systemic inflammation, enhanced immune function, and upregulation of DNA repair.[67] Taken together, this suggests that the implementation PA interventions have the potential to improve health markers and diminish disease risk in CCS.

A distinction often not addressed due to the epidemiological nature of assessing PA was the type of moderate-to-vigorous PA. Resistance (RE) and cardiovascular (CE) exercise have beneficial effects on basal metabolism, blood pressure, serum lipid concentrations, glucose metabolism, and body composition,[69] yet lie at different ends of the exercise spectrum. Additionally, these beneficial effects are evident in adult post-treatment cancer patients as demonstrated in a meta-analysis by Fong et al.[70] Participants enrolled in RE and CE interventions and exhibited reduced insulin-like growth factor-I, BMI, and body weight, with increased peak oxygen consumption, peak power, distance walked in six minutes, bench press weight, and leg press weight.[70] Thus, this demonstrates that both RE and CE have a beneficial impact on the physiology in individuals who have undergone cancer treatment.

However, many benefits from exercise are not maintained due to poor long-term adherence to an exercise program. Bourke et al.[71] noted that although some interventions may achieve adherence rates above 75%, many have high attrition rates. Furthermore, the authors believe that 150 minutes of aerobic exercise per week for sedentary adult survivors is not a realistic goal due to poor adherence. Whether this applies to AYA CCS is unknown, yet it demonstrated that improvements are needed within exercise interventions to increase long-term efficacy.

Overall, CE and RE have demonstrated an array of physiological benefits to CCS. However, these positive adaptations may not be maintained due to poor adherence to an exercise program. As elucidated to previously, many CCS undergo a period of increased BF% in conjunction with a reduction in FFM due to cancer treatment. Together this suggests that CCS should favor RE over CE due to the ability of RE to increase FFM.[15]

Resistance Exercise

CCS exhibit an increased disease risk and thus potentially garner a greater long-term benefit from RE than the general population. Adult survivors who were physically active and participated in RE exhibited a significant decrease in all-cause mortality compared to those who did not partake in RE.[72] RE has the potential to decrease CVD risk factors, Type II DM risk,[73] and ameliorate the underestimated BMI exhibited by CCS.[74] A meta-analysis by Strasser et al.[75] in 2013 observed RE to significantly increase strength, lean body mass, and decrease BF%, yet yielded no differences in VO2max or body fat mass in adult survivors. More recent interventions further support Strasser et al.'s findings in adult survivors for increased strength,[24,76] yet no change in body composition.[76] Taken together, this suggests that RE can increase lean body mass and strength in the adult survivor population with equivocal findings with regards to body composition.

RE was also shown to provide a similar beneficial impact on youth with systemic physiological benefits. RE demonstrated positive improvements in strength (Standardized Mean Difference [SMD]: 0.90: 95% CI: 0.71-0.91) with smaller ESs for fat mass (SMD: 0.20: 95% CI: -0.01-0.41), BF% (SMD: 0.24: 95% CI: 0.9-0.39), and waist circumference (SMD: 0.36: 95% CI: 0.17-0.55) in obese children and adolescents.[77] Furthermore, muscular fitness was found to be inversely correlated with adiposity, insulin resistance, inflammatory biomarkers, all-cause mortality, CVD mortality, and positively with self-esteem and bone health in children and adolescents.[63] Together, this demonstrates the broad physiological effects of RE in youth. Exposing adolescents to RE may prove beneficial for long-term health as greater muscular strength and power was associated with a reduced risk for the development of adult metabolic syndrome.[78] This demonstrates the importance of beginning RE during adolescence to prevent disease risk in adulthood.

Although RE does show beneficial impacts on body composition, the small ESs mentioned by Schranz et al.[77] demonstrate that they may not be clinically relevant. This may be due to a neglect of energy intake which would result in a minimal energy deficit and insignificant changes in body composition. However, a beneficial outcome not examined in most studies is the potential of RE to prevent fat mass gain.[79] This protective effect may be due to an increase in skeletal muscle mass as total energy expenditure was found to be positively associated with FFM ($r=0.84$; $p<0.001$).[15] Taken together, RE may potentially increase total energy expenditure through the accruement of FFM. However, due to a lack of emphasis on the creation of a caloric deficit through dietary intake, body composition changes have been minimal in RE investigations.

Participation in RE may cause reservations for parents and guardians of young CCS due to perceived safety concerns. Dahab et al. concluded RE in youth can induce muscle hypertrophy, strength gains, performance increases, and potentially reduce injury risk.[80] Furthermore, the National Strength & Conditioning Association states that RE can have beneficial effects on reducing injury from sport and recreation, improving motor skills, and enhancing bone density while having no effect on statural growth.[81] Thus, beyond the beneficial physiological effects, RE was shown to potentially decrease the risk for injury in youth. Taken together, both RE and CE are beneficial and should be incorporated into an exercise program. However, due to a reduced FFM, a greater emphasis on RE may optimize long-term health. Additionally, the restoration of FFM to levels that assist in achieving a healthy body composition may have benefits on QoL.[82]

Effects of Exercise on Quality of Life and Body-Esteem

Several investigations observed a beneficial effect for exercise interventions on QoL and body-esteem in AYA, young adult, and adult survivors.[24,29,76] However, two studies in adult survivors demonstrated null or mixed results.[83,84] The authors note that this was possibly due to sub-optimal RE loading[83] or having a high baseline QoL,[84] which suggests that exercise interventions may be optimal for survivors with a low QoL. Furthermore, lean mass was found to significantly correlate with QoL.[82] Muscular hypertrophy can still occur with the use of low loads,[85] which indicates that perhaps the intensity or structure of RE may have not been sufficient to yield results.

Both RE and CE demonstrated beneficial effects on several categories of body image, physical self-perception, and self-esteem in obese adolescents.[86] Yet, RE yielded a significant effect for global self-esteem and greater ESs for physical self-worth and appearance evaluation.[86] Furthermore, Lubans et al.[87] observed physical strength to be positively correlated with physical self-worth. However, the implementation of CE into interventions should not be eliminated as the combination of RE and CE was shown to positively impact body image, physical self-perception, and global self-esteem.[86] Together, this demonstrates that both RE and CE can elicit beneficial changes, yet an emphasis on RE may increase QoL and body-esteem to a greater degree. Furthermore, this highlights the need for research regarding the effects of exercise interventions on

QoL and body-esteem in AYA CCS as their physical and psychological responses may be different than adult survivors.

Physical Activity Interventions

Increased muscular fitness and improved health behaviors have the potential to reduce the disease risk among CCS.[78] These behaviors may be best implemented during adolescence and young adulthood due the increased independence and the potential for obesity and PA to track into adulthood.[40,88,89,90,51] Thus, interventions aimed at addressing behavior change, specifically the inadequate PA of AYA CSS, could prove beneficial in increasing long-term health outcomes in CCS.

Several interventions have emphasized increased PA[29,91,92,93,94,95,96] or weight management [97] in AYA CCS. Most interventions were shown to be at least partially successful in their outcomes through the utilization of various study designs with beneficial changes in total,[92,96] moderate[93] or moderate-to-vigorous PA[91,92,94,97]. However, not all interventions exhibited increased PA.[91] In addition, although the increase in PA may cause assumptions of increased fitness and reduced body composition, few studies examined these parameters.

In those studies that did incorporate performance/fitness measures, improvements in physical functioning or cardiorespiratory fitness were non-existent,[91] small,[29] or modest.[93,96] This was possibly due to an unsupervised training program,[91,93,96] inadequate supervision of program length,[29] or the use of inadequate intensity.[29] However, Järvelä et al.[96] showed significant improvements in mean VO_{2Peak} and physical functioning in the form of sit-up, back extensor, and full squatting tests. Although this demonstrates improvements in aerobic capacity and an individual's ability to comfortably complete tasks of daily living, it does not address alterations in strength or hypertrophy, and thus fat free mass. In addition, only Hauken et al.[29] investigated and demonstrated a small effect for strength improvement. Together, this suggests that more research is needed to develop interventions which are efficacious in the development of strength and fat free mass. Overall, the interventions demonstrated potential for improvements in physical functioning, cardiorespiratory fitness, and strength. However, conclusions regarding whole body strength and changes in fat free mass cannot be made.

As previously elucidated, PA has a minor effect on body composition. This was further supported by the studies in AYA CCS which have utilized performance/fitness measures and yielded no change in body weight.[29,94,97] However, Järvelä et al.[96] demonstrated a decreased waist circumference and BF%, but this was not clinically significant with a decrease in BF% from 27.7 ((Standard Deviation) SD: 8.3) to 26.8 (SD: 8.5) and a decrease in waist circumference from 83.9cm (SD: 11.0) to 82.2cm (SD: 11.0). Furthermore, overall conclusions regarding body composition cannot be made due to the lack of information regarding fat mass, fat free mass, and BF% in most of the studies.

Taken together, this demonstrates that PA interventions in CCS can produce beneficial changes in PA levels, fitness, and potentially body composition. However, measures of strength were assessed via handgrip strength[29] or physical functioning assessments.[96] These assessments, although valid for their purposes, do not assess the upper and lower body strength of the individual. A more comprehensive strength assessment would have the ability to elucidate the efficacy of an intervention with regards to muscular fitness.

To address the equivocal and insignificant changes in strength and body composition, the addition of a structured RE program may be an important missing component. This implementation could produce changes in fitness and perhaps body composition through an increase in skeletal muscle mass and maintenance of fat mass. Furthermore, the addition of a supervised exercise program prior to or in conjunction with a home-based program may be most beneficial for long-term adherence as supervised training was shown to be superior to unsupervised.[98] Taken together, RE interventions in AYA CCS have not been assessed and thus may prove more efficacious than PA interventions excluding RE with regards to body composition and changes in muscular fitness.

Beyond the implementation of a RE program, exercise adherence is paramount for long-term health benefits. A meta-analysis by Genugten et al.[99] highlighted that combining behavior change techniques was found to be more efficacious than utilizing one technique in isolation. Thus, appropriately applied behavior change techniques may maximize the efficacy of an intervention.

Social Cognitive Theory

Social cognitive theory (SCT) is utilized by interventions to induce behavior change with the central constructs including self-efficacy over one's health habits, knowledge of health risks and benefits of different behaviors, expected costs and benefits of different health practices, setting goals, and comprehension of factors that facilitate and/or impede behavior modification.[100] A systematic review performed by Stacey et al. evaluating SCT-based behavior change interventions on PA in adult cancer survivors reported a small-to-moderate effect (ES: 0.33) for PA interventions.[101] Although the ES was small-to-moderate, there is potential for interventions to induce meaningful improvements in PA.

Survivors reported a lack of knowledge of exercise guidelines and also displayed positive expectations in regards to the expected health outcomes suggesting that an exercise intervention would yield benefit.[102] Additionally, a large proportion of AYA CCS are not knowledgeable about their risk for late effects and strategies to mitigate against these risks. For example, 75.4% of AYA CCS were deemed “not knowledgeable” of receiving anthracycline, 54% “knowledgeable”, 33.5% “not knowledgeable”, and 12.5% “partially knowledgeable” of their risk for the effects of cancer treatment in later life.[65] This lack of awareness may be due to a young age at diagnosis and indicates that CCS may not be cognizant of their health risks. Additionally, health interventions should include an education component to address health behavior modifications aimed at decreasing disease risk for CCS. Short et al. also suggest that cancer survivor interventions should emphasize addressing knowledge gaps in regards to PA and RE, promoting PA benefits, addressing misconceptions and PA obstacles, providing encouragement, educating on goal setting and self-monitoring, and promoting social support.[102] Social support may be an especially important construct for AYA CCS as peers may not understand the hardships of cancer and treatment. The formation of in-person interventions which foster social support among AYA CCS may provide the greatest benefit with regards to establishing a healthy lifestyle. This was demonstrated in a review which observed supervised exercise interventions yielded a larger effect than unsupervised on QoL and physical functioning.[103] This highlights the importance of social support in exercise intervention settings.

The incorporation of SCT to exercise interventions is important to ensure efficacy. Yet, more research is needed with regards to the addition of technology due to its potential to further increase intervention efficacy. Technology may have the ability to increase engagement among AYA CCS and allow for a deeper integration of SCT into the intervention. Overall, SCT-based interventions demonstrated promise but can be potentially improved with the implementation of technology.

Technological Engagement

Supervised interventions optimize internal validity, yet increase intervention cost, diminish external validity, and decreases the number of participants capable of enrolling. This makes home-based and remote interventions an attractive option for researchers. Pinto et al.[104] investigated the effects of a telephone-delivered, home-based exercise intervention in breast cancer patients with the PA group self-reporting greater minutes of total PA and moderate, hard, and very-hard intensity PA per week compared to controls. Additionally, Robin et al. examined the feasibility and acceptability of a telephone-delivered PA intervention in young adult cancer survivors and observed a significant increase in moderate-intensity PA.[93] The telephone-delivered interventions were shown to be feasible and demonstrate that home-based, remote interventions may be possible to combat the delayed health risks of cancer. Furthermore, technology such as smartphones and wearable activity trackers have become more prevalent in use and can be incorporated as a medium to apply SCT. The combination of a behavior change technique, SCT, and technology may assist with engagement and behavior maintenance with AYA CCS.

Ninety-two percent of young adults aged 18-34 own smartphones which may allow intervention administrators to increase engagement with participants without increasing contact time.[105] Smartphone application (apps) interventions were shown to yield equivocal results based on reviews with regards to body composition and PA.[106,107] There may have been multiple factors that contributed to the lack of significant results. Coughlin et al.[106] noted that apps did not prescribe evidence-based guidelines. Additionally, apps included approximately 5 behavior change techniques, which may have been poorly implemented or insufficient to induce behavior change.[106] Quelly et al.[107] supported this notion that the implementation of behavioral techniques in smartphone apps needs improvement. An important consideration may have been the factors of emphasis in the apps. A coherent, comprehensive, evidence-based set of recommendations to improve the desired outcome variables (i.e., QoL, fitness, body composition, strength, etc.) would be necessary. Additionally, these reviews did not mention the potential efficacy of the incorporation of external features such as wearable activity trackers or social media. This highlights that more research is needed regarding the efficacy of interventions which utilize smartphone apps due to the various populations, behavioral techniques and theories, associated accessories utilized such as wearable trackers, and social media platforms that may be incorporated.

Several authors have developed methods to increase the efficacy of smartphone application interventions. Middleweed et al. reported that the incorporation of goal-setting, reminders, motivational features, reward system, and social media may increase engagement and thus aid in behavior modification.[108] Similarly, Semper et al. who recommended five key components for effective apps: self-monitoring, tailored goal-setting, feedback from nutritional coaches, a structured program, and social support.[109] These recommendations mirror the SCT constructs. Furthermore, a review by Wang et al. noted that apps should aim to develop comprehensive management of the intended goal and not focus on only a single aspect.[110] Therefore, PA and health behavior interventions aimed at decreasing disease risk should not solely focus on step-count but also active minutes, exercise habits, and dietary behaviors to maximize the potential benefit. Lastly, a review by Coughlin et al.[111] noted that smartphone apps are a cost-effective strategy but need to be tailored to the target-group to increase relevance. This suggests that tailoring the application to CCS, particularly AYA CCS due to the reasons elucidated previously, may maximize outcomes. Taken together, smartphone apps are promising methods for delivering PA interventions due to the incorporation of the several suggested methods to enhance the effectiveness of the intervention.

The implementation of these mentioned features can be accomplished through the process of gamification which is defined as the application of game elements to a non-game context.[112] Several features of gamification include badges, leaderboards, points and levels, challenges and quests, and social engagement loops.[113] These features can be used as a medium to implement behavior change techniques and thus, increase intervention efficacy. This was demonstrated in a review by Nour et al.[114] which showed that social media and game-based interventions were efficacious in the reduction of weight and BMI in young adults. This suggests that gamification may be used as a platform to implement SCT into an exercise intervention and increase its efficacy.

Self-monitoring and feedback may be further implemented in interventions by the use of wearable activity trackers, which have the capability to measure steps, calories, sleep, PA, heart rate, and caloric expenditure.[115] The most prominent consumer-wearable activity tracker, FitBit, was shown to be valid for steps and PA quantity, but had questionable validity with regards to energy expenditure or sleep.[116] Trackers demonstrate promise in increasing PA levels, yet the market of specific products is constantly changing with new features continuously being added.[115] The addition of new features may alter the efficacy observed from wearable trackers. This indicates that specific trackers utilized by research may not be generalizable to all trackers. This was seen in an investigation that utilized a wearable tracker and observed the comparison group lose significantly more weight (5.9kg vs. 3.5kg; p=0.02) compared to the wearable tracker intervention.[117] There have been several comments regarding the limitations of the study including the use of a discontinued wearable device which may reflect its acceptability, poor wear time as participants wore the device for a median of 4 hours per day, and a questionable user experience.[118,119,120] Furthermore, these results are counter to a review by Gierisch et al.[121] who observed that accelerometers exhibited a significant increase in PA (Standard Mean Difference: 0.26; 95% CI: 0.04-0.49). Overall, this demonstrates that more research needs to be conducted on the efficacy of wearable devices due to the variables that may affect outcomes such as device validity, location of placement, aesthetics, the ability to integrate with the smartphone, and behavioral techniques that may be incorporated.

Research may be outpaced by innovative market trends with continued exploration needed in this area. Reductionist examinations of theories, devices, and innovations are required to evaluate efficacy, yet may not elucidate effectiveness when examined holistically. Wearable activity trackers in conjunction with smartphone apps, gamification, and social media may provide additive benefits when used together. A combination of these elements in an intervention for CCS would have the ability to adequately incorporate SCT constructs and may improve health behaviors, thus decreasing disease risk.

Delivery of behavior change techniques can be facilitated through the use of social media given that 90% of young adults reported having at least one social networking account.[122] Thus, social media may be implemented into interventions to encourage behavior modification while decreasing in-person contact time. This can be beneficial as coordinating schedules is a practical and financial burden for intervention administrators and participants. A meta-analysis by Mita et al.[123] examined the use of social media interventions to reduce risk factors of non-communicable diseases and observed a small effect favoring interventions (SMD: -0.12, 95% CI: -0.29 to 0.05). This was in support by a systematic review by Maher et al.[124] which found a positive but small ESs in 9 of 10 interventions on health behavior outcomes. Additionally, Maher et al. reported that 50% of participants failed to adhere to the intervention for its duration.[124] Taken together, social media interventions may lead to long-term health behavior modification and improve cost-effectiveness of current PA interventions, but methods to increase retention should be implemented.

The most efficacious method to promote health behaviors in AYA CCS may be the utilization of an online platform in which many currently participate. Facebook is the most utilized form of social media and may be the most suitable for interventions.[122] A Facebook intervention by Valle et al.[94] yielded non-significant, but trending, improvements in self-reported minutes per week of light-PA ($p = 0.07$) and body weight ($p = 0.083$). The potential differences compared to the control group appeared to be due to the self-monitoring behaviors and behavioral feedback produced by the intervention. This demonstrates that Facebook is a potentially feasible vehicle to deliver behavior change material.

Further supporting the efficacy for the utilization of social media was a study by Maher et al.[125] who investigated the feasibility of a social networking PA intervention via Facebook in adult survivors. Both control and intervention groups increased their moderate-to-vigorous PA with only the intervention group displaying significantly increased overall PA (ES: 0.39; 95% CI: 0.01, 0.76) and walking time (ES: 0.69; 95% CI: 0.30, 1.07) at 8 weeks but not at week 20.[125] In short, there is support for the use of Facebook in PA interventions.

However, engagement is variable in these interventions. Valle et al.[94] reported that more than half of the participants never posted or only posted once in both groups. Additionally, Maher et al.[125] noted that participants posted to Facebook a mean of 2.7 (SD: 3.4) times in a group of 3-8 individuals over a 50-day period. Together, this demonstrated that there was minimal interaction through Facebook and necessitates that future interventions take steps to foster greater engagement. The lack of engagement may have been due to weak relationships between participants which may have led to decreased interaction. This may suggest that the incorporation of an in-person component would lead to greater engagement on Facebook and thus generating social support among participants.

Overall, the use of smartphone applications, wearable trackers, and social media are pervasive among AYAs. These mediums can be utilized to further engage with this cohort which may lead to greater social support, increased adherence to the intervention protocols, and decreased participant burden through decreased contact time with intervention administrators. Additionally, previous studies demonstrated low engagement among participants potentially due to weak relationships. Stronger relationships would theoretically yield greater social support which suggests that interventions should foster in-person communication between participants to generate long-term adherence.

Conclusion

The prevalence of obesity in 2011-2014 for the general population was 17% for individuals aged 2-19 [42] with several studies suggesting that CCS exhibit increased adiposity [13,32,44,53,54] and an underestimated BMI[13] when compared to the general population. Although not harmful in isolation, obesity especially in youth may lead to subsequent disorders including hypertension, elevated serum triglycerides, and diabetes.[126] An increased risk for obesity among CCS may be compounded with a greater prevalence of CVD,[4,10,11] endocrine abnormalities,[19,16] increased risk for diabetes,[20,21,16] fatigue,[23,24,25,26] and subsequent cancers.[22] This suggests that health behavior interventions should be implemented to decrease disease risk. An emphasis on RE may be most beneficial to CCS due to it's potential to increase skeletal muscle mass thus ameliorating the underestimated BMI exhibited in this population.

Interventions may be best implemented during adolescence and young adulthood when CCS are healthy enough to participate in strenuous PA. Furthermore, targeting AYA due to the modest tracking of PA and obesity into adulthood may improve long-term health. Yet, paramount for continued health improvements is adherence to exercise interventions. SCT was shown to be effective in generating behavioral change with social media and smartphone apps granting intervention administrators the potential for greater engagement with participants. Additionally, the use of wearable trackers may further augment intervention effectiveness by providing the individual with increased feedback. PA interventions integrating SCT, social media, a smartphone app, and wearable activity trackers aimed at improving fitness, PA levels, and health behaviors may have additive effects to maximize the efficacy of an exercise intervention in AYA CCS.

Chapter 2: Multifaceted Intervention Investigating the Role of Exercise, Education, Facebook, and a Smartphone App to Improve and Maintain Fitness in Childhood Cancer Survivors: Pilot Randomized Controlled Trial

Introduction

Incidence of childhood cancer has increased since 1975 by 0.6% per year,[127] however the survival rate has correspondingly improved from approximately 83% in 1995 to nearly 88% in 2009.[1] This improvement demonstrates that the population of childhood cancer survivors (CCS) is growing. Despite the increase in survival rate, the path to remission can be a difficult one. Cancer treatment that involves chemotherapy (CTH) and/or radiation therapy (RTH) puts CCS at risk for delayed negative health outcomes.[2] CTH may result in negative long-term effects including, but not limited to, adverse cardiovascular events, renal and liver dysfunction, peripheral motor and sensory neuropathy, reduced bone mineral density, and neurocognitive impairment,[2,8] while the delayed effects of RTH are influenced by the site of radiation. Cranial RTH is associated with increased body fat percentage (BF%),[13] reduced physical activity (PA) levels,[14] and a diminished total energy expenditure.[15] These outcomes are possibly due to altered hypothalamus, pituitary, or thyroid function from RTH.[13,16] In addition, chest-directed RTH increases the risk for adverse cardiac events.[18] However, the treatment with both CTH and RTH was shown to increase the risk for negative health outcomes to a greater extent than either alone.[4] Taken together, cancer treatment increases the risk for adverse conditions in CCS during and after treatment, and into adulthood.

CCS demonstrate an increased risk for cardiovascular disease (CVD),[10] diabetes,[20] metabolic syndrome,[128] endocrine disorders,[16] altered psychosocial status,[27] and a reduced quality of life (QoL) in adulthood.[28] This increased disease risk may be exacerbated by lifestyle factors. CCS exhibit a greater prevalence of excess adiposity,[13] low skeletal muscle mass,[13] and low PA levels.[32] Together, these aspects may contribute to an underestimated body mass index (BMI) exhibited by CCS[13] and may cause obesity to be underreported. Thus, CCS exhibit poor health behaviors, which may exacerbate their already elevated disease risk due to cancer treatment.

Moreover, cancer and cancer treatment have impacts beyond an increase in disease risk. CCS demonstrate a reduced QoL compared to healthy individuals that persists 2-years post-treatment.[30] Poor physical QoL in survivors was associated with exposure to alkylating agents, pelvic radiation, and disfigurement.[58] Additionally, the reduced physical QoL experienced by CCS may lead to the avoidance of social situations such as exercise and PA.[60] Together, this demonstrates the multiple impacts cancer has on the individual with both physical and psychosocial aspects affected.

However, modifiable factors may reduce the adverse health effects experienced in this population suggesting that actions could be taken to mitigate this risk. The negative health and psychosocial outcomes may be ameliorated through an increase in skeletal muscle mass and reduced BF% with exercise and PA. Both resistance (RE) and cardiovascular (CE) exercise have been shown to improve basal metabolism, blood pressure, serum lipid concentrations, glucose metabolism, and body composition.[69] However, the increased prevalence of low skeletal muscle mass and an underestimated

BMI among CCS suggests that RE should be emphasized. Furthermore, physically active adult survivors who participated in RE exhibited a decrease in mortality compared to those who did not.[72] An emphasis on RE can improve body composition and diminish the risk for the delayed adverse effects experienced by CCS.

RE should be implemented early in the treatment process to produce the greatest impact in CCS as the risk for disease development rises with increased time since diagnosis.[3] Although exercise interventions implemented during treatment show promise,[129] cancer-related fatigue and motivation may limit participation in childhood cancer patients.[61] Thus, the next opportune moment is upon remission in adolescent and young adult (AYA) CCS. Additionally, adolescence and young adulthood are transition periods characterized by increased independence from parents and guardians with obesity and PA tracking into adulthood.[40,51] Thus, interventions aimed at AYA CCS may provide the greatest reduction in long-term disease risk. There have been several investigations in AYA CCS that emphasize PA or weight management.[29,91-97] Although each utilized a different study design, most demonstrated beneficial changes in total,[92,96] moderate[93] or moderate-to-vigorous PA.[91,92,94,97] However, an increase in PA does not directly translate into increased physical performance as fitness improvements were absent,[91] insignificant,[29] or modest.[93,96] The lackluster improvements may have been due to a lack of training supervision,[91,93,96] insufficient length of supervision,[29] or the use of inadequate training intensity.[29] Furthermore, many of these studies are underpowered to detect differences. The majority of these interventions also yielded null or clinically insignificant results with regards to body composition.[29,94,96,97] This illustrates the need for continued examination of potentially efficacious RE interventions for this population.

Although exercise has the potential to produce a variety of beneficial outcomes, adherence is needed for improvements in exercise interventions. A systematic review by Kampshoff et al.[130] indicated decreased adherence in PA interventions, which included RE, CE, and other modes of exercise, from an average of 87.6% during the first three weeks to 58.14% in the last three weeks. To remedy the decrease in adherence, social cognitive theory (SCT) has been utilized to elicit and sustain behavior modification.[100] A meta-analysis of SCT-based PA interventions has demonstrated success with a small-to-moderate ES for PA outcomes.[101] Furthermore, a randomized controlled trial of a PA intervention in young adult CCS which incorporated SCT showed a significant increase in moderate-intensity PA and aerobic capacity.[93] Together, this demonstrates that SCT can be used to guide the development of interventions with CCS.

There are several mediums by which SCT can be implemented into an intervention. Approximately 90% of young adults utilize social media and 92% own smartphones,[105,122] which makes these platforms a convenient medium to implement SCT. For example, the use of social media in interventions was found to exhibit a small but favorable effect in the reduction of risk factors for non-communicable diseases.[123] However, smartphone application usage demonstrated equivocal results with regards to PA.[106,107] This may have been due to a failure to prescribe evidence-based guidelines and the ineffective implementation of behavioral techniques.[106,107]

SCT may also be implemented with the use of wearable technologies. A review by Coughlin et al.[106] suggests that participants have a preference for immediate feedback with regards to metrics (e.g. steps taken) and applications that coach and/or motivate them. The incorporation of a wearable activity monitor which has the capability of measuring steps, calories, and PA may be used to elicit increases in PA. However, wearable devices that are placed in unfavorable locations such as the upper arm may contribute to a poor user experience and not contribute to increased PA.[117] This suggests that wearable devices need to provide a positive user experience to be beneficial with regards to PA. Together, a wearable activity monitor in conjunction with a smartphone application may be incorporated together to increase the effectiveness of a PA intervention. Yet, these methods would not address any potential knowledge gaps CCS have with regards to modifiable lifestyle factors.

An education component can be implemented into PA interventions to address exercise, cancer, and nutrition-related knowledge gaps. This is supported by a meta-analysis which demonstrated a larger effect on body composition for the addition of nutritional counseling to exercise interventions.[131] Additionally, treatment-related education may increase awareness of the health risks as 75.4% of AYA CCS were “not knowledgeable” of their treatment with anthracycline or its side-effects.[65] The addition of an education component may enhance the efficacy of wearable trackers through a greater understanding of the benefits of healthful lifestyle factors. This would strengthen the implementation of SCT and increase intervention effectiveness.

To the author’s knowledge, there have been no investigations that integrate these components into a RE intervention for AYA CCS. The primary aim of this pilot study was to investigate if a multicomponent intervention that integrated supervised group RE sessions, a smartphone application, wearable activity monitor, and social media can improve strength, body composition, QoL, and body-esteem in AYA CCS. A secondary aim included whether the multicomponent intervention can maintain improved fitness.

Methodology

Research Design

A randomized, wait-list control pilot trial for AYA CCS was conducted for 12 weeks. Assessments were conducted at weeks 0 (T1), 8 (T2), and 12 (T3). They consisted of body composition, strength, QoL, and body-esteem questionnaires. T2 excluded body composition, QoL, and body-esteem assessments. Rutgers Biomedical and Health Sciences Institutional Review Board approved all methods and procedures.

The research design utilized constructs of SCT facilitated through supervised group exercise and educational sessions which included a private Facebook group that was only accessible to the participants and investigators, a smartphone application (FitSurvivor), and a wearable activity monitor (Fitbit Charge, Fitbit Inc., San Francisco, United States). The participants were provided tutorials on the Fitbit Charge and FitSurvivor app to ensure familiarity with the device and smartphone application.

Recruitment, Randomization, and Retention

Participants were recruited through a local cancer survivor registry of the Rutgers Cancer Institute of New Jersey (CINJ) Long-term, Information, Treatment effects, and Evaluation (LITE) program. Further recruitment was performed via physician and staff referral in the Division of Pediatric Hematology/Oncology by mail, phone call, and in clinic approach. Flyers were also posted in relevant areas such as community support centers for AYA CCS.

Eligibility for the investigation included the following criteria: diagnosed with cancer prior to the age of 21, currently 13-25 years old, complete remission for at least 6 months, and provided informed consent if ≥18 years of age. If < 18 years of age, parental consent was obtained in addition to participant assent. Exclusion for enrollment included any of the following criteria: medical contraindication to exercise, non-English speaking, pregnant, significant developmental delay as reported by participant, parent, or physician's report, or exceeded PA recommendations by the Center for Disease Control and Prevention guidelines.[132] The guidelines state that children and adolescents should obtain at least 60 minutes of PA per day with the majority coming from CE followed by muscle and bone strengthening exercise. In addition, at least 3 days per week should be dedicated to vigorous-intensity PA.

Following completion of baseline assessments, participants were randomized into control (CON, n=10) and experimental (EXP, n=9) groups with an average age of 18.89 (SD: 4.18), BF% of 27.13% (SD: 10.71), and body mass index (BMI) of 24.54 (SD: 4.49). The baseline characteristics are shown in **Table 2**. No significant differences were found between CON and EXP. A total of 19 out of 29 AYA CCS completed all 3-time points of the study as seen in **Figure 1**.

Individuals were diagnosed with a form of leukemia (N=10), lymphoma (N=4), sarcoma (n=2), central nervous system tumor (n=2), and Wilms tumor (n=1). The average age at diagnosis was 10.26 (SD: 5.6) years with an age of final treatment of 12.05 (SD:

5.76) years. One individual in EXP chose not to complete the BOD POD which resulted in 18 participants analyzed for body composition changes. Four social and cognitive QoL measures were not included due to a researcher survey error. The CON group had 5 males and 5 females and the EXP had 4 males and 5 females. To prevent motivation bias, randomization was performed after the baseline assessment. EXP participated in FitSurvivor at T1, while CON was asked to maintain current activities. CON later received FitSurvivor after T3.

All participants were medically cleared for exercise. Participants were paid $20 for the completion of each assessment for a total of $60.

Measures

Anthropometrics

Participants arrived to the lab euhydrated and were at least two hours fasted. Body composition was measured by air displacement plethysmography using Bod Pod (Cosmed, Concord, CA, USA) and its companion software, in accordance with the manufacturer's instructions. The body composition assessment was performed using air displacement plethysmography (BOD POD, COSMED, Concord, CA, USA). The BOD POD was shown to be reliable and valid in adults (CV $\leq$ 4.5% and SEE $\leq$ 2.3%, respectively) and children (precision statistic = 0.83% - 0.99% and SEE = 3.3%) as a measure of body composition.[133] The Siri equation was used to compute body fat percentage from the measured body volume.[134]

Height was assessed by a stadiometer (Detecto, Webb City, MO, USA) and measured to the nearest quarter-inch. Weight was measured by the Bod Pod scale (Cosmed, Concord, CA, USA) to the nearest hundredth kilogram.

Strength Testing

A 10-repetition maximum (RM) bench press and leg press were utilized to assess upper and lower body muscular strength, respectively. Participants were instructed on proper form for the bench press and leg press according to NSCA guidelines.[135] Participants performed sets of each exercise with increasing weight over 2-5 sets until failure was reached with the aim of 10 repetitions. Rest intervals of 3-5 min were provided between sets to allow for adequate recovery. Participants were encouraged to perform at maximal effort with the completion of the test being reached upon voluntary muscular failure. To standardize data, Lander's formula was utilized to estimate 1-RM.[136]

$Lander's\ Repetition\ Max\ equation$: 1RM = (100 x load)(101.3 − 2.67123 x reps)

Quality of Life and Body-Esteem

Assessments for QoL and body-esteem were performed at T1 and T3. The PedsQL 4.0 Generic Core in adolescents[137] and young adults were utilized to examine health-related QoL.[138] The PedsQL 4.0 is a 23-item questionnaire aimed at assessing physical (8 items), emotional (5 items), social (5 items), and work/school functioning (5 items).

The Adolescent PedsQL 4.0 was used for individuals below the age of 18, while the Young Adult PedsQL 4.0 was used for individuals above the age of 18. Additionally, adolescent and young adult scales demonstrated internal consistency ($\alpha > 0.40$), reliability ($\alpha > 0.70$), and construct validity for healthy and patient populations.[137,138] Participants answered questions on a 5-point Likert scale where 1 = never a problem, 2 = almost never a problem, 3 = sometimes a problem, 4 = often a problem, and 5 = almost always a problem. The items are then reverse-scored and linearly transformed to a scale of 0-100 where 1=100, 2=75, 3=50, 4=25, and 5=0. Thus, a higher score indicates a better health-related QoL.

The evaluation of body-esteem was assessed by the Child and Youth Self-Perception Inventory, a validated 36-item questionnaire.[139] Child and Youth Self-Perception Inventory is composed of six scales: global self-worth, global physical self-worth, attractive body adequacy, sport/athletic competence, strength competence, and physical condition adequacy. Each scale was composed of six questions scored 1-4 in an alternative response format with ‘1’ indicating a low perceived competence and ‘4’ indicating a high perceived competence. The scores from each scale were averaged to yield an average scale score (range: 1-4).

Intervention

The supervised exercise-intervention lasted 8 weeks and was led by a Certified Strength and Conditioning Specialist (CSCS) from the National Strength and Conditioning Association (NSCA). Participants met with the trainer once per week in a group exercise and education session within a fitness center setting. In addition, they were instructed to perform exercise sessions from the FitSurvivor app during their own time on non-consecutive days.

Participants met once a week for an 8-week in-person RE and education intervention. The duration of each session varied between 60-90 minutes. The exercise and education portions typically lasted 50-60 minutes and 20-40 minutes, respectively. The exercise session included a 7-10 minute warm-up, 30-45 minute workout, and a 5-10 minute cool-down. Warm-up consisted of dynamic exercises to increase body temperature and range of motion of the limbs. Each workout consisted of primarily compound exercises targeting all major muscle groups performed in a circuit fashion for 2-3 sets and a repetition range of 10-20 performed with elastic bands (Thera-Band; The Hygenic Corporation, Akron, Ohio) of various tensions. An example exercise session can be observed in **Table 1**.

The Borg CR-10 scale was utilized throughout the exercise session.[140] Exertion during weeks 1 and 2 ranged from 5-7 on the RPE scale gradually increasing to 7-10 by week 8. Exercise adjustments were demonstrated to alter exercise difficulty and allow for individual modification for physical impairments. Upon completion of the workout, the cool-down was performed, which involved static stretching for all major joints and muscles held for 30 seconds for 1-2 sets.

An education session was performed before or after RE. Timing was determined based on the arrival of the participants. The education sessions were led by the trainer and investigators. Topics included goal setting, overcoming barriers, nutrition basics, ‘eating out’ nutrition, exercise myths, other healthy behaviors specific to CCS, creating an exercise program, and behavior change maintenance. Each week, one topic was discussed for 20-40 minutes and each session was designed to maximize interaction with the participants.

A 12-week home-based exercise program was provided in conjunction to the 8-week supervised sessions. In order to perform the exercises at home, the FitSurvivor app was developed for both android and iOS with the exercise program and instructions uploaded for the participant. A weekly workout was uploaded for the initial 12 weeks of the intervention that included pictures, descriptions of the exercises, sets, and repetitions mimicking the supervised session. Exercise sessions included 8-15 exercises for all major muscle groups, 1-3 sets, and 10-20 repetitions. Participants were encouraged to exercise on non-consecutive days between 2-3 times per week and to choose a resistance-band or exercise variation that would be a challenge for the prescribed repetitions. For example, the participant could progress from a lighter to higher resistance-band tension if he/she was able to complete 15 repetitions for 3 sets on the squat exercise. An example of an exercise variation would be a progression for push-ups where the participant began with their knees on the ground for a goal of 15 repetitions for 3 sets and advanced to knees off the ground upon reaching the repetition goal.

The FitSurvivor app provided additional abdominal-based and body weight exercises, moderate-to-vigorous cardiovascular workouts, and weekly RE and CE frequency goal setting. Gamification was integrated where participants could increase their ‘Fitness Level’ by having the ability to earn workout points and unlock badges.

A Fitbit Charge was given to each participant to be used in conjunction with the FitSurvivor app. Fitbit was shown to be valid for steps taken,[116,141] yet is questionable with regards to its ability to assess caloric expenditure.[55] The app allowed the participants to self-monitor daily steps, distance, active minutes, and calories burned, and view weekly workout summaries.

Social media and PA tracking were also incorporated. A social media aspect was included in the smartphone application where the participants can 'like' and comment on others' status of completed workouts. Facebook was utilized as the social media forum to further engage participants outside of the exercise session and attempt to build a greater social support network.

Statistics

A multivariate analysis of variance (MANOVA) was performed to assess differences between participants who dropped out versus adhered. Separate time x group MANOVAs with repeated measures on time were performed for anthropometric, strength, QoL, and body-esteem variables. For significant multivariate effects, univariate follow-up analyses were performed. The Huynh-Feldt epsilon was calculated for each univariate analysis to assess sphericity. If >0.75, sphericity was assumed and the unadjusted statistic was used. If the statistic was <0.75, the Huynh-Feldt statistic was utilized for significance testing. The data were analyzed at a significance level of 0.05 and reported as mean ± SD. Effect sizes (ES) were calculated for the intervention, pre & post per group, and were represented by Cohen's *d* where 0.2 - 0.5 denoted a small, 0.5 – 0.8 moderate, and ≥0.80 designated a large effect. ES was reported as Cohen's *d* ±

variance. SPSS (IBM®, SPSS® version 23, New York, NY, USA) statistical software was used for analysis.

Results

Compliance

There was a significant difference in age at diagnosis between dropouts (5.50 years ± 4.65) and those that adhered (10.26 years ± 5.67, p=0.031) to completing all assessments. No other differences were found between groups on baseline characteristics, P>0.20.

Body Composition Changes

Within subjects' analysis observed a trending significant time effect for body composition measures (p=0.068). Univariate follow-up tests for time found a significant decrease for weight from T1 to T3 (p=0.001).

BF% demonstrated no change in EXP from T1 to T3 (27.65% ± 11.87 vs. 27.56% ± 11.34) as shown in **Figure 2**. However, BF% increased non-significantly in CON from 26.71% ± 10.33 vs. 27.48% ± 9.89). Similar results were found for FM (**Figure 3**) where EXP demonstrated a minimal change (19.70 kg ± 9.39 vs. 20.04 kg ± 9.24) yet CON was found to increase (18.64 kg ± 11.54 vs. 19.55 kg ± 11.80). FFM **(Figure 3)** was shown to non-significantly increase in EXP (50.93 kg ± 10.47 vs. 52.15 kg ± 10.39) with no change observed for CON (49.71 kg ± 14.03 vs. 49.56 kg ± 13.00).

The intervention exhibited a small ES for FFM (*d*=0.22 ± 0.48) at T3 but trivial effects for all other body composition measures (**Figure 4)**. Pre-post (T1 to T3) ESs (**Figure 5**) demonstrated trivial effects for waist, weight, BF%, FM, and FFM.

Strength Changes

There were significant multivariate effects for group (p=0.028) and time (p=0.018). Yet, time x group demonstrated no significant effects. Univariate analysis showed significant time effects for BP (p=0.004) and LP (p=0.005).

Pairwise comparisons observed no significant effects between CON and EXP for BP or LP. However, significant increases were found from T1 to T2 (BP: p=0.006, LP: p=0.008) and T1 to T3 (BP: p=0.012, LP: p=0.007). However, neither group showed a significant increase from T2 to T3.

Although not significant, the intervention demonstrated greater increases for BP (**Figure 6**) from T1 to T2 for EXP (35.50 kg ± 17.41 vs. 40.68 kg ± 20.00) compared to CON (46.38 kg ± 27.06 vs. 48.02 kg ± 27.15). A similar trend was observed for LP (**Figure 6**) from T1 to T2 for EXP (194.90 kg ± 79.01vs. 236.11 kg ± 94.19) compared to CON (172.09 kg ± 55.04 vs. 179.09 kg ± 59.95). Minimal changes were seen for both groups from T2 to T3 for BP and LP.

The intervention demonstrated an increase in ES from T1 to T2 for both BP (and LP as shown in **Figure 7**. There was minimal change in ES from T2 to T3. Pre-post ESs (**Figure 8**) demonstrated trivial effects for CON (BP *d*=0.06, LP *d*=0.13) from T1 to T2 but small and moderate effects for EXP (BP *d*=0.30, LP *d*=0.52). Pre-Post ESs from T1 to T3 showed trivial and small effects for CON (BP d=0.06, LP d=0.24) and small and moderate effects for EXP (BP d=0.28, LP d=0.58).

Psychosocial Changes

Multivariate analysis found no significant effects for QoL or body-esteem. Changes in psychosocial measures from T1 to T3 can be observed in **Table 3**.

The intervention exhibited reductions in ES which can be observed in **Figure 9**. Physical condition and social QoL were the only psychosocial markers that showed potential improvement over the course of the intervention. Pre-post (T1 to T3) ES analysis (**Figure 10**) demonstrated small decrements for EXP except for physical condition and physical QoL which exhibited no change. CON showed a positive moderate ES for Physical QoL with small effects for attractive adequacy, sport competence, global physical self-worth, emotional QoL, cognitive QoL, and psychosocial QoL. Global self-worth and social QoL showed a small and moderate reduction for CON, respectively.

Discussion

This study found modest beneficial effects for strength and body composition in participants who participated in FitSurvivor. Previous interventions primarily emphasized PA or weight management, and only Hauken et al.[29] demonstrated small improvements in handgrip strength. The current investigation was novel through the examination of practical outcomes by the assessment of upper and lower body strength via bench press and leg press. Although underpowered to perform appropriate hypothesis testing given that it was a pilot study, these results are similar to those found by Schranz et al.[77] regarding the effects of RE on strength (SMD: 0.63, 95% CI: [0.46, 0.80]), BF% (SMD: 0.24, 95% CI: [0.09, 0.39]), physical QoL (SMD: -0.09, 95% CI: [-0.35, 0.18]), and psychosocial QoL (SMD: -0.11, 95% CI: [-0.35, 0.14]) in overweight and obese children and adolescents.

Possible improvements were observed with regards to body composition following the exercise intervention. Although weight was increased in both groups, EXP exhibited no change in BF% in contrast to CON which saw an increase. This suggests that the intervention was effective in preventing FM gain. This is in line with the review by Hanson et al.[79] which found a null effect with regards to RE on body composition but a potential protective effect from FM gain in adult cancer survivors. Additionally, Schranz et al.[77] demonstrated similar results and indicated that higher training volumes (>25hrs for the whole intervention) resulted in larger negative effects for waist girth, BF%, and FM. The current intervention consisted of 8 hours of supervised training over 8-weeks, plus at home workouts provided via the FitSurvivor app to allow for more training volume. However, this investigation is unable to assess the adherence to the unsupervised training. Thus, we are unable to quantify the individual training volume of the participants. Yet, the lack of increase in strength makers from T2 to T3 likely suggests inadequate exercise stimulus. Taken together, this suggests a greater number of hours allocated towards supervised exercise would elicit superior results for body composition.

The emphasis of exercise in isolation may not be the optimal prescription to induce changes in body composition as dietary considerations need to be addressed. Exercise contributes a small role in total daily caloric expenditure compared to resting metabolic rate and non-exercise PA in the general population.[142] The participants in the current investigation were given a Fitbit Charge to encourage an increase in non-exercise PA and were provided with education sessions regarding nutrition to improve dietary behaviors. The Fitbit Charge allowed participants to self-monitor their PA, yet there was no self-monitoring technique implemented for dietary intake which has demonstrated benefit in other studies. The lack of changes in body composition suggests that nutritional education alone may be insufficient to elicit and maintain dietary behavior change. The addition of parental education may be an opportunity to improve nutrition and exercise habits in the subset of AYA who are dependent on parental support. Together, a combination of methods to increase unsupervised training volume, provide parental and AYA nutrition education, and implement self-monitoring for dietary intake may be necessary to generate significant changes in body composition.

Although the total duration of supervised training was small, changes in fitness parameters were observed with improvements in LP and BP. The moderate ES seen in the EXP group with regards to LP is in agreement with the literature.[77] However, BP exhibited a small effect for EXP in the current investigation. The difference between the mean 5.5 kg increase in EXP compared to 1.6 kg in CON over the intervention may not have been large enough to yield a statistically significant result. This may have been due to the primary use of resistance-bands and body weight during the exercise sessions, which is contrast to the free-weight BP and machine-based LP assessments. Thus, the potential fitness changes from the exercise sessions may not have directly transferred to changes in strength measures. However, the intervention emphasized exercise sessions which can be performed at home. The reliance on body weight and resistance-bands meant that higher repetitions were needed to yield a training effect. Schoenfeld and associates[143] showed that greater ($\geq$65% 1-RM) compared to lighter loads yielded enhanced strength (p=0.09) and hypertrophy (p=0.076) in untrained or recreationally trained adults. However, high-repetitions can produce increased hypertrophy and strength with the caveat being that sets are taken to muscular failure in trained individuals.[85] The increased discomfort of multi-joint high-repetition exercises may have prevented individuals from inducing sufficient muscular fatigue to yield optimal gains in strength and hypertrophy.[144] This would explain the lack of large effects for BP and LP in the current investigation. The inclusion of free weights with low repetitions (<15) would ameliorate the discomfort and still promote muscular adaptation. However, this may not have been feasible for all of our participants due to fitness center age restrictions, transportation, financial constraints, and possible physical limitations from treatment.

The current investigation found no effects of the intervention on psychosocial markers. There were several body-esteem and QoL markers that demonstrated small to moderate decrements from the intervention. This finding may have been due to random chance from our small sample size, a regression to the mean, or unintended stress from the intervention.

Our sample reported similar baseline QoL and body-esteem values as those of healthy adolescents at baseline.[87,138] Thus, exercise interventions may only provide psychosocial benefit to those with low psychosocial status.[84] The decrements were also within the baseline standard deviations which suggests an overall null effect of the intervention on psychosocial markers. Thus, it is not currently possible to elucidate the cause of the observed reductions in psychosocial measures.

It may be possible that the intervention was perceived differently among participants due to the heterogeneity of our sample. There was a difference found in individuals who dropped out versus those who adhered to the intervention. Those who dropped the intervention were diagnosed earlier in life compared to those who adhered. The memory of the cancer experience may have been perceived differently between groups as recall from 6-10 years of age is stronger than that of 1-5.[145] Additionally, cancer diagnosis during adolescence compared to early childhood was shown to conjure higher levels of post-traumatic stress and lower health-related QoL.[146] This suggests that an older age at diagnosis may be more salient than being diagnosed at a younger age and these participants may have potentially perceived the intervention to be more worthwhile as exercise was shown to have beneficial effects on post-traumatic stress.[147] Furthermore, this is in line with the finding that most AYA CCS are not knowledgeable of the treatment they received and may be unaware of the potential risks associated with cancer treatment.[65] Overall, an older age at diagnosis may have led to a greater knowledge of health risks and the expected costs and benefits of different health practices.

Approximately 34% of our sample dropped out prior to the completion of this 12-week intervention. This is in line with a systematic review of exercise adherence among cancer survivors which observed that program adherence drops from 87.6% during the initial three weeks to 58.14% in the final three weeks of an exercise program.[130] Thus, more research is needed to elucidate methods that increase exercise adherence, which would lead to further improvement in fitness and body composition markers.

Limitations

The primary limitation of the investigation was the small sample size compounded with a wide age range and the inclusion of both genders. This reduces the ability to assess the efficacy of our intervention due to the high heterogeneity of our participants. However, FitSurvivor is an on-going feasibility study with the goal of approximately 50 participants. This current investigation examined the initial cohort, and we intend to utilize the feedback from participants to implement improvements in future groups.

The second limitation is with regards to selection bias. Our sample reported similar psychosocial measures as those of healthy adolescents. This high functioning in conjunction with the inclusion criteria that excluded individuals who had severe contraindications to exercise and/or experienced developmental delays may not be a proper representation of the CCS sample. Ness et al.[5] reported that CCS with disabilities were associated with lower income levels, educational status, and rates of employment. This presents a sample of CCS that may not have access to a fitness facility and may greatly benefit from a remote intervention such as FitSurvivor. Together, this may limit the generalizability of FitSurvivor to a healthy CCS population.

A third limitation is the non-standardization of the QoL and body esteem questionnaires. The questionnaires were administered either before or after the strength assessments to decrease wait-time and thus reduce participant burden. This may have affected psychosocial measures if the participants did not reach their expectations on the strength assessments. This may explain the reductions in psychosocial measures seen in the EXP group, but further arms of FitSurvivor will further elucidate this speculation.

Future Directions

Although improvements in strength were seen, the participants were engaged in resistance-band training which may not have directly translated to an increased free-weight BP or machine-based LP 10-RM. As previously mentioned, muscular hypertrophy can be attained with higher repetitions (>15) if muscular failure is reached. However, the participants had minimal or no experience in resistance training which may have led to the self-selection of a lower repetition number than is needed to achieve muscular adaptation.[148] Resistance bands were used to allow for affordable and accessible at-home training for AYA CCS. Overall, fitness improvements were observed, but the implementation of free-weight based exercises may have produce greater increases in strength compared to the utilization of resistance-bands even when utilized at relatively high tensions.

Further benefit may be achieved through changes in resistance-band training prescriptions. The use of resistance bands for training programs is often categorized along with free-weight and machine-based modalities.[149] The resistance-band programs examined in the study utilized 1-3 sets of 8-12 repetitions, which may not have been sufficient to elicit fitness improvements in untrained individuals and exemplifies the lack of guidelines for resistance-band exercise program design. Current recommendations base repetitions per set on percentage of 1-RM which is not feasible with resistance-bands. Although there are usually varying tensions among a set of bands, there is a limited selection. This would suggest that increases in repetitions or sets may be the most practical method for progression. Additionally, high-discomfort will be present with greater repetitions which would prevent some individuals from training to failure. To accommodate for this and provide a direction for progression, a baseline number of repetitions can be established at a given resistance-band tension and then progression can be implemented through an increase in repetitions, sets, or resistance-band tension.

Conclusion

Survivorship from childhood cancer is constantly increasing, yet care does not end upon remission. Follow-up care is needed due to the increased disease risk, which may not manifest until later in life. Many of these negative health outcomes can be mitigated through improved health behaviors. Health interventions that target CCS early in life may be the optimal period to commence RE and nutritional education in order to enhance fitness and foster beneficial health behaviors, which will lead to improved health and longevity.

The current investigation is part of an on-going trial to improve health behaviors in AYA CCS. FitSurvivor demonstrated improvements in fitness and body composition, but no improvements in psychosocial measures. The high baseline functioning of the participants may have led to this finding as previous research suggests exercise has a beneficial effect on psychosocial markers. Feedback from the current cohort will be utilized to further improve the FitSurvivor program. In short, the health intervention named FitSurvivor which integrated group RE, a smartphone application, wearable activity monitor, and social media was shown to modestly benefit the fitness of AYA CCS.

Tables

Table 1. Example Exercise Session During Supervised Training				
Warm-Up	**Exercise**	**Sets**	**Reps / Duration**	**Resistance**
	Jumping Jacks	2	60 seconds	None
	Dead Bug	2	15 per side	None
	Dislocates with Band	2	15	None
	Glute Bridges	2	15	None
	Shoulder Internal & External Rotation	2	15 per side	None
Total Body	**Exercise**	**Sets**	**Reps / Duration**	**Resistance**
	Squats	2	15	Band Tension
	Row	2	15	Band Tension
	Lunges	2	15 per side	BW or Band
	Push-up	2	15	BW or Band
	Bent Pull-up	2	15	Band Tension
	Plank	2	15	BW
	Side Plank	2	15	BW
	Triceps Extension	2	15	Band Tension
	Bicep Curl	2	15	Band Tension
Cool-Down	**Exercise**	**Sets**	**Reps / Duration**	**Resistance**
	Glute Bridge	1	15	None
	Dead Bug	1	15 per side	None
	Quadricep Stretch	1	30s	None
	Hamstring Stretch	1	30s	None
	Hip Flexor Stretch	1	30s	None
	Pectoralis Stretch	1	30s	None
	Latissimus Dorsi Stretch	1	30s	None

Abbreviations: BW, body weight.
Example exercise session during supervised training.

Table 2. Baseline Characteristics

	Total		CON		EXP	
	N	Mean + SD	N	Mean ± SD	N	Mean ± SD
Age at diagnosis	19	10.3 ± 5.7	10	11.0 ± 5.8	9	9.4 ± 5.7
Time Since Treatment Ended	19	12.1 ± 5.8	10	13.0 ± 5.5	9	11.0 ± 6.2
Age	19	18.9 ± 4.2	10	19.4 ± 4.0	9	18.3 ± 4.6
Height (cm)	19	168.0 ± 10.6	10	167.0 ± 11.2	9	169.1 ± 10.4
Weight (kg)	19	69.5 ± 16.2	10	68.4 ± 21.3	9	70.8 ± 8.9
Body Fat Percentage (%)	18	27.1 ± 10.7	10	26.7 ± 10.3	8	27.7 ± 11.9
Fat Mass (kg)	18	19.1 ± 10.4	10	18.6 ± 11.5	8	19.7 ± 9.4
Fat Free Mass (kg)	18	50.3 ± 12.2	10	49.7 ± 14.0	8	50.9 ± 10.5
Bench Press (kg)	19	41.2 ± 23.1	10	46.4 ± 27.1	9	35.5 ± 17.4
Leg Press (kg)	19	182.9 ± 66.5	10	172.1 ± 55.0	9	194.9 ± 79.0
Attractive Body Adequacy	19	2.2 ± 0.7	10	2.3 ± 0.6	9	2.1 ± 0.7
Sport Competence	19	2.5 ± 0.7	10	2.6 ± 0.6	9	2.5 ± 0.9
Strength Competence	19	2.3 ± 0.5	10	2.4 ± 0.6	9	2.3 ± 0.4
Physical Condition Adequacy	19	2.5 ± 0.5	10	2.5 ± 0.4	9	2.4 ± 0.6
Global Physical Self-Worth	19	2.5 ± 0.6	10	2.6 ± 0.5	9	2.3 ± 0.7
Global Self-Worth	19	3.1 ± 0.6	10	3.3 ± 0.4	9	2.9 ± 0.8
Physical QoL	19	79.3 ± 10.5	10	80.0 ± 6.1	9	78.6 ± 14.3
Emotional QoL	19	73.7 ± 14.4	10	72.5 ± 14.7	9	75.0 ± 14.9
Social QoL	15	87.0 ± 10.8	8	86.9 ± 9.2	7	87.1 ± 13.2
Cognitive QoL	15	69.7 ± 14.7	8	70.6 ± 13.7	7	68.6 ± 16.8
Psychosocial QoL	19	76.3 ± 8.6	10	76.5 ± 7.8	9	76.1 ± 9.8

Abbreviations: SD, standard deviation; N, number of participants; CON, Control; EXP, Experimental.

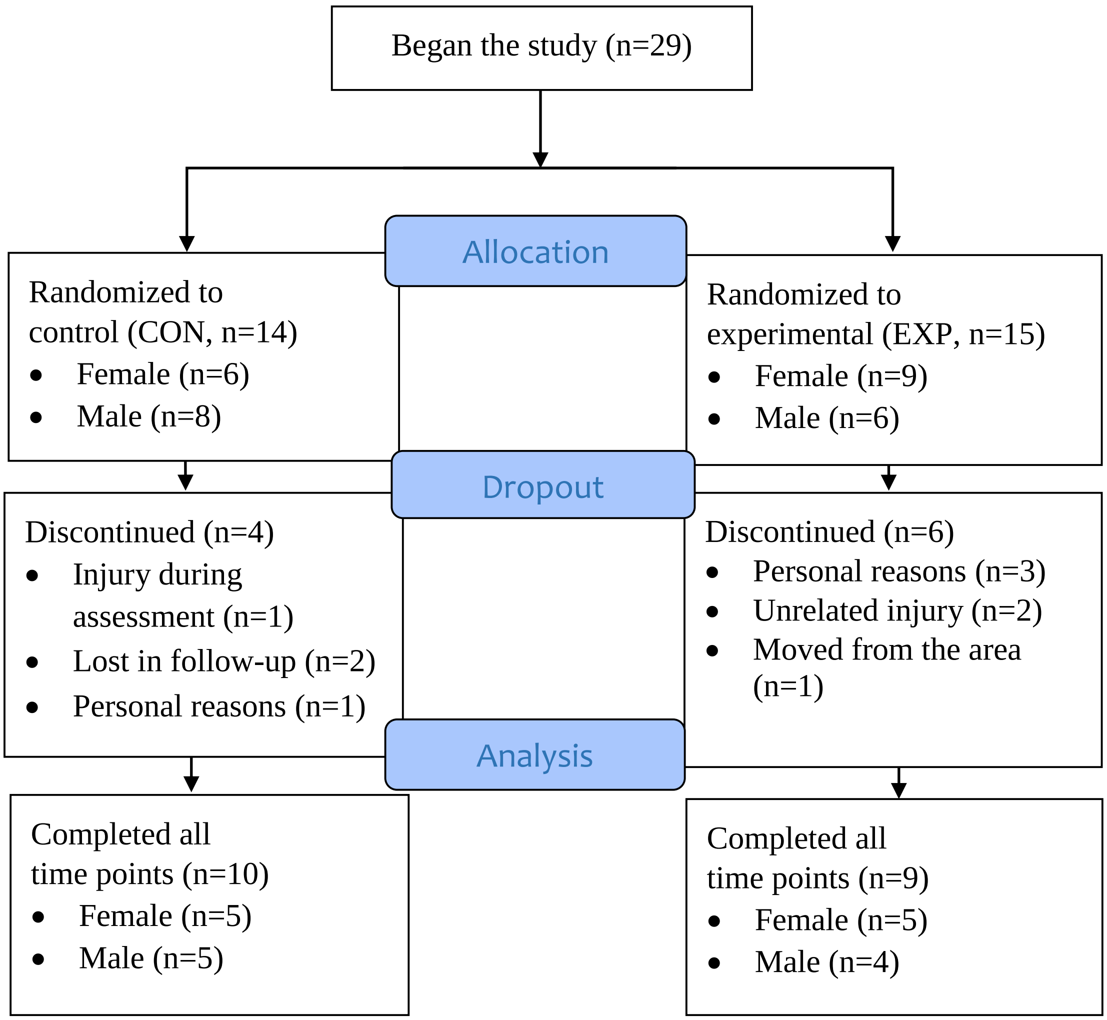
Table 3. Change Psychosocial Status

	CON	EXP		
	T1	T3	T1	T3
	Mean + SD	Mean + SD	Mean + SD	Mean + SD
Attractive Body Adequacy	2.27 + 0.53	2.42 + 0.41	2.03 + 0.83	1.72 + 0.77
Sport Competence	2.65 + 0.69	2.73 + 0.65	2.39 + 0.66	2.36 + 0.88
Strength Competence	2.19 + 0.42	2.4 + 0.54	2.22 + 0.42	2.03 + 0.85
Physical Condition Adequacy	2.52 + 0.4	2.48 + 0.29	2.25 + 0.47	2.33 + 0.94
Global Physical Self-Worth	2.44 + 0.33	2.67 + 0.36	2.25 + 0.81	2.08 + 0.81
Global Self-Worth	3.27 + 0.41	3.04 + 0.34	2.67 + 0.82	2.56 + 0.78
Physical QoL	80.36 + 6.61	83.93 + 8.75	76.79 + 14.77	76.79 + 23.77
Emotional QoL	72.92 + 16.06	76.04 + 12.15	75.69 + 17.76	65.28 + 24.95
Social QoL	86.88 + 9.23	81.88 + 15.8	89.17 + 13.2	85.83 + 13.93
Cognitive QoL	70.63 + 13.74	75.00 + 12.25	66.67 + 17.51	61.67 + 17.22
Psychosocial QoL	76.85 + 8.52	78.55 + 8.53	76.52 + 9.33	72.16 + 16.62

Abbreviations: T1, Time point 1, T3, Time point 3, QoL, Quality of Life.
T1 and T3 values for body-esteem and QoL.

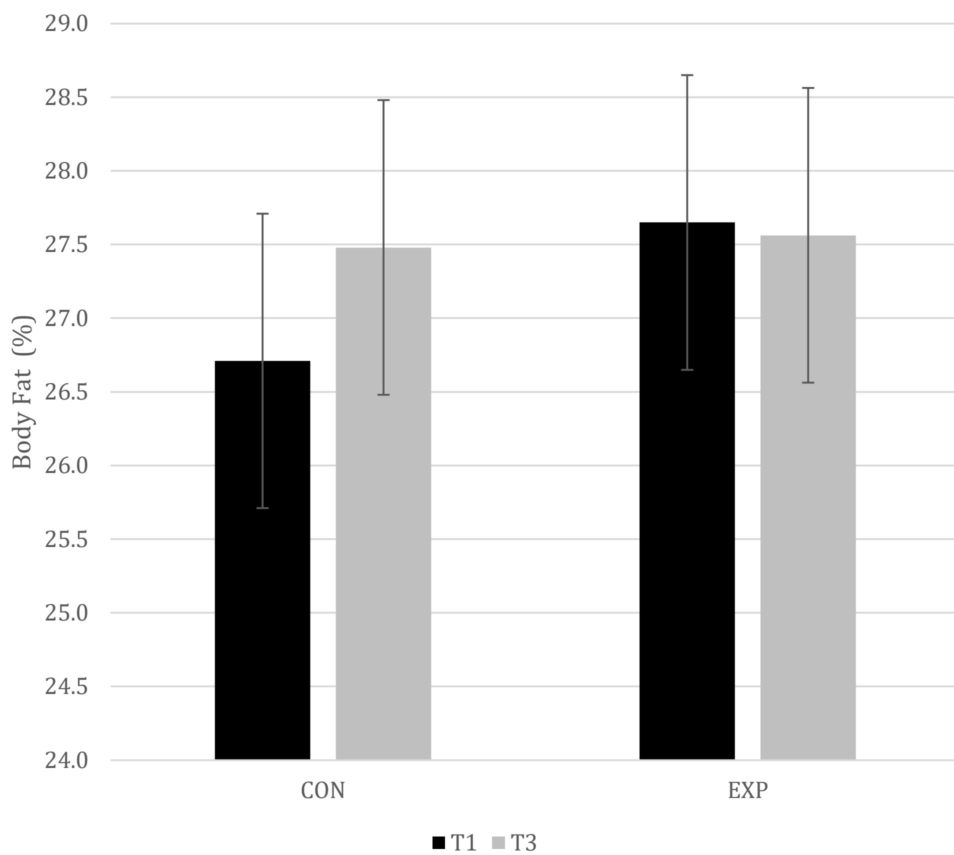
Figures

Figure 1. Research Design



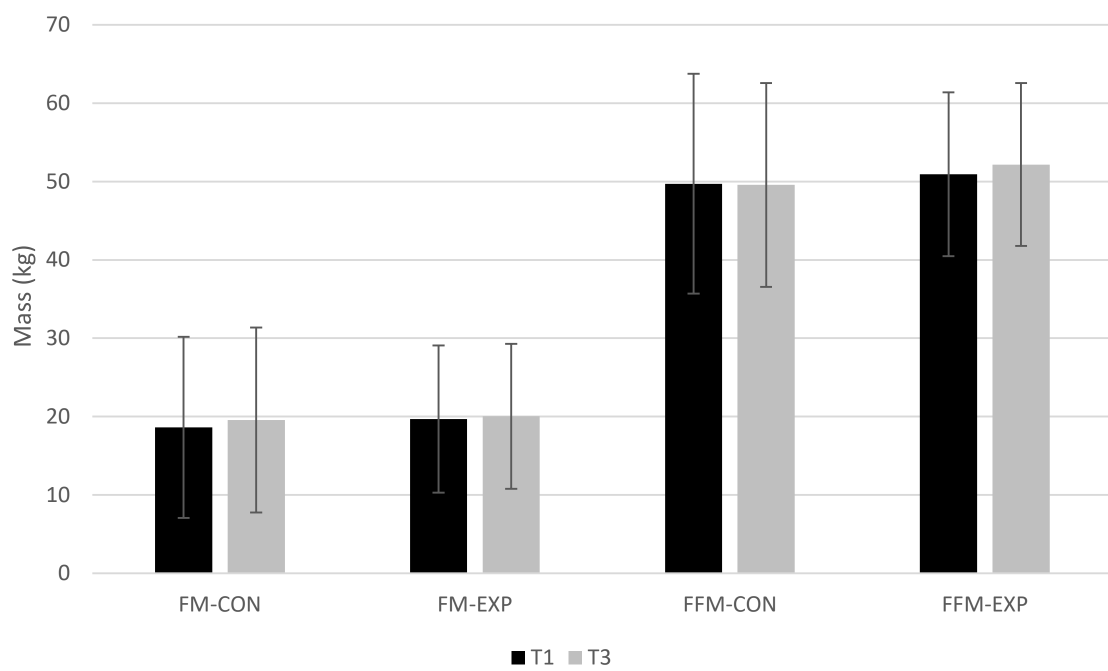
Research design diagram.

Figure 2. Changes in Mean Body Fat Percentage



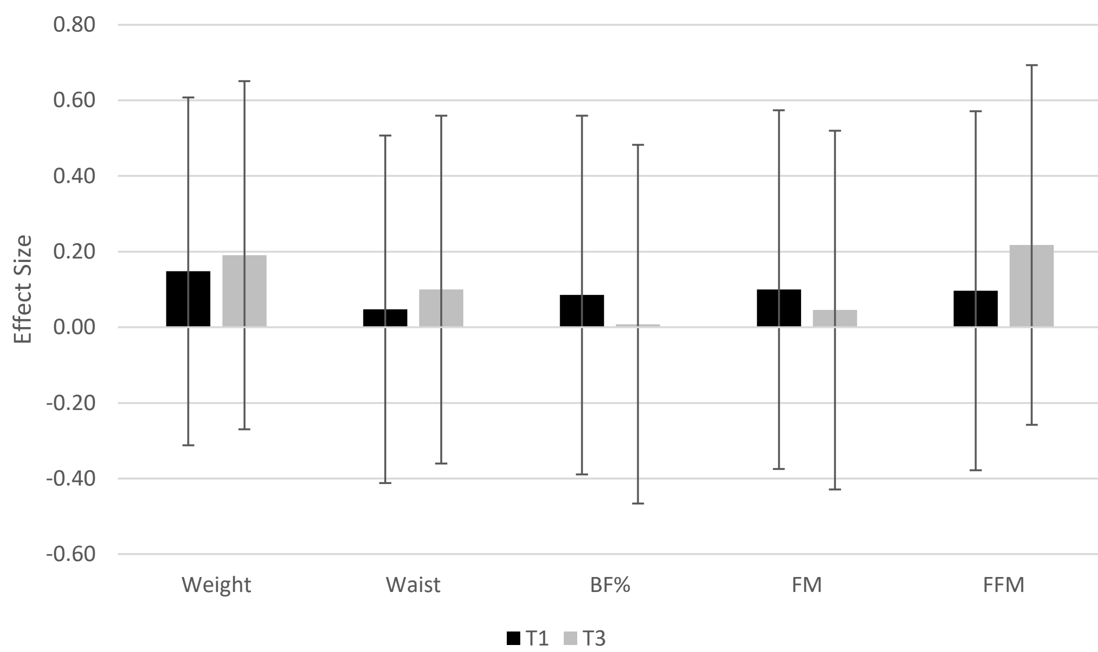
Abbreviations: T1, Time Point 1; T3, Time Point 3.
There was no significant time x group effect for mean body fat percentage over the intervention from T1 to T3.

Figure 3. Changes in Mean Fat Mass and Fat Free Mass



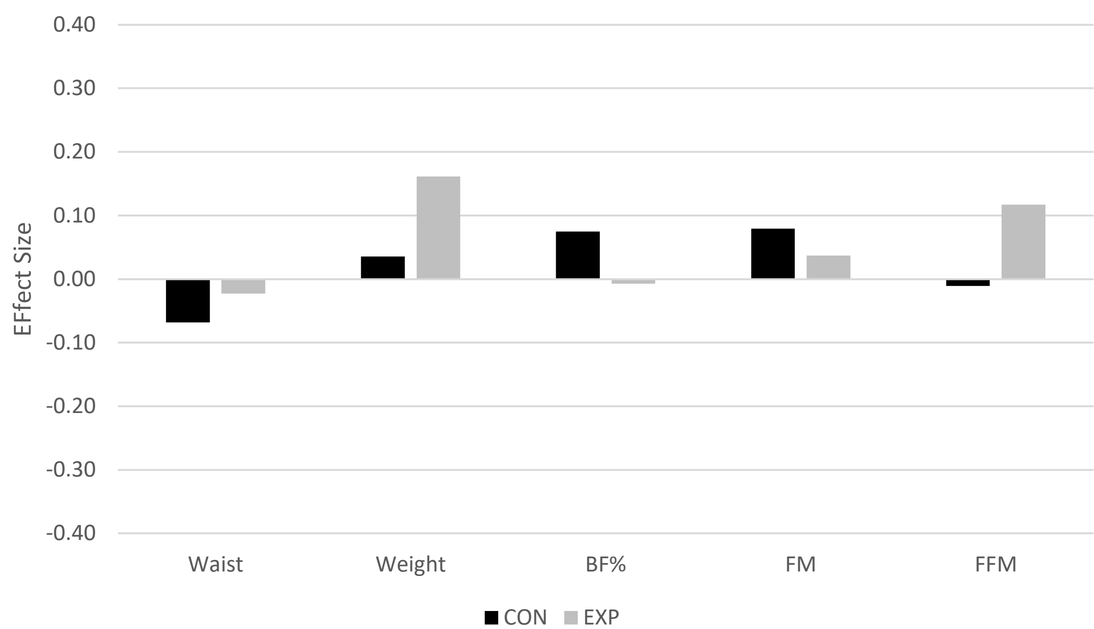
Abbreviations: FM, Fat Mass; FFM, Fat Free Mass.
There was no significant time x group effect for mean FM or FFM over the intervention.

Figure 4. Intervention Effect Sizes for Body Composition



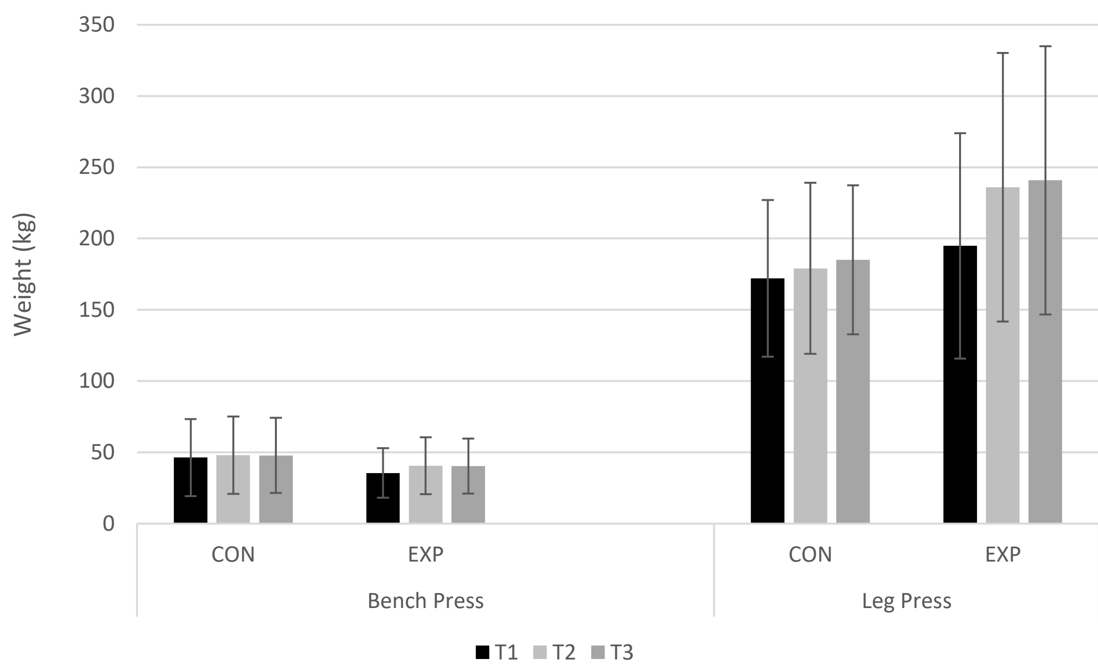
Abbreviations: T1, Time Point 1; T3, Time Point 3.
Body composition measures yielded trivial effect sizes for T1 and T3.

Figure 5. Pre-Post Effect Sizes for Body Composition



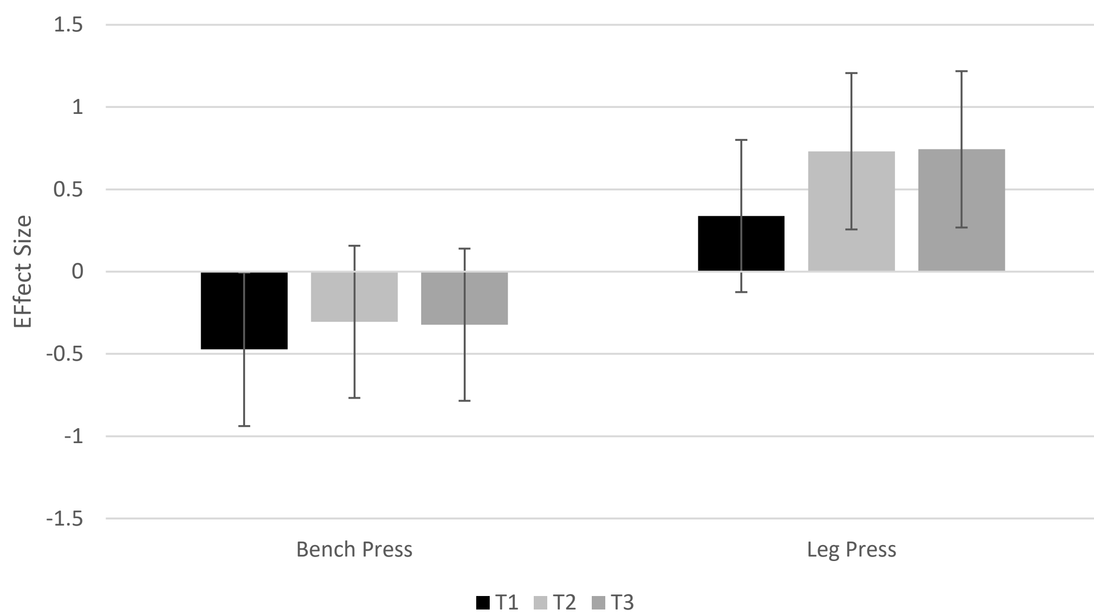
Abbreviations: T1, Time Point 1; T3, Time Point 3.
Pre-post effect sizes for CON and EXP groups for body composition from T1 to T3.

Figure 6. Changes in Bench Press and Leg Press



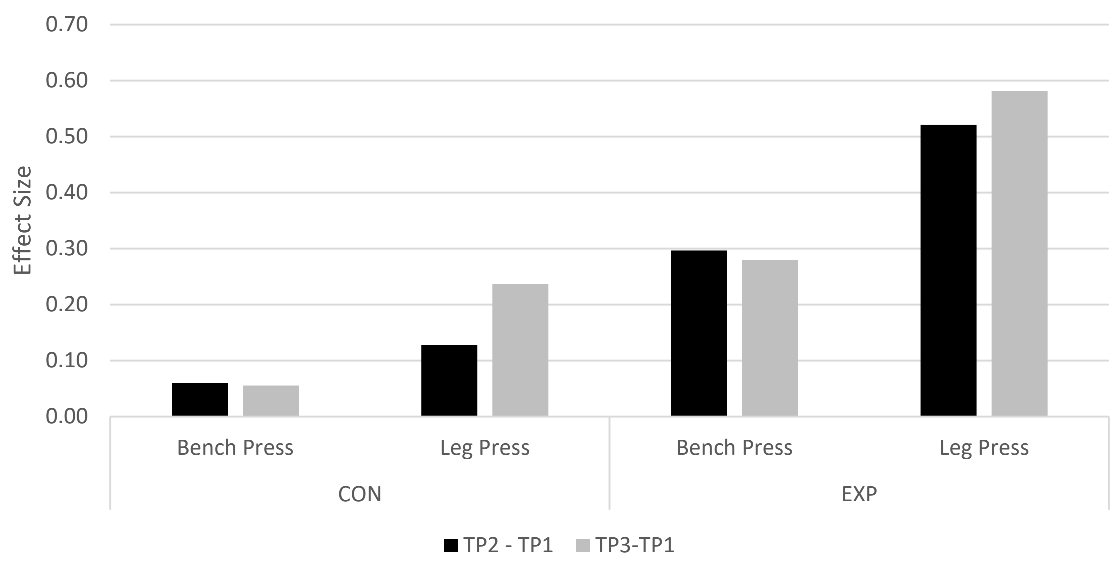
Abbreviations: T1, Time Point 1; T2, Time Point 2; T3, Time Point 3.
Changes in weight for bench press and leg press for T1, T2, and T3.

Figure 7. Intervention Effect Sizes for Bench Press and Leg Press



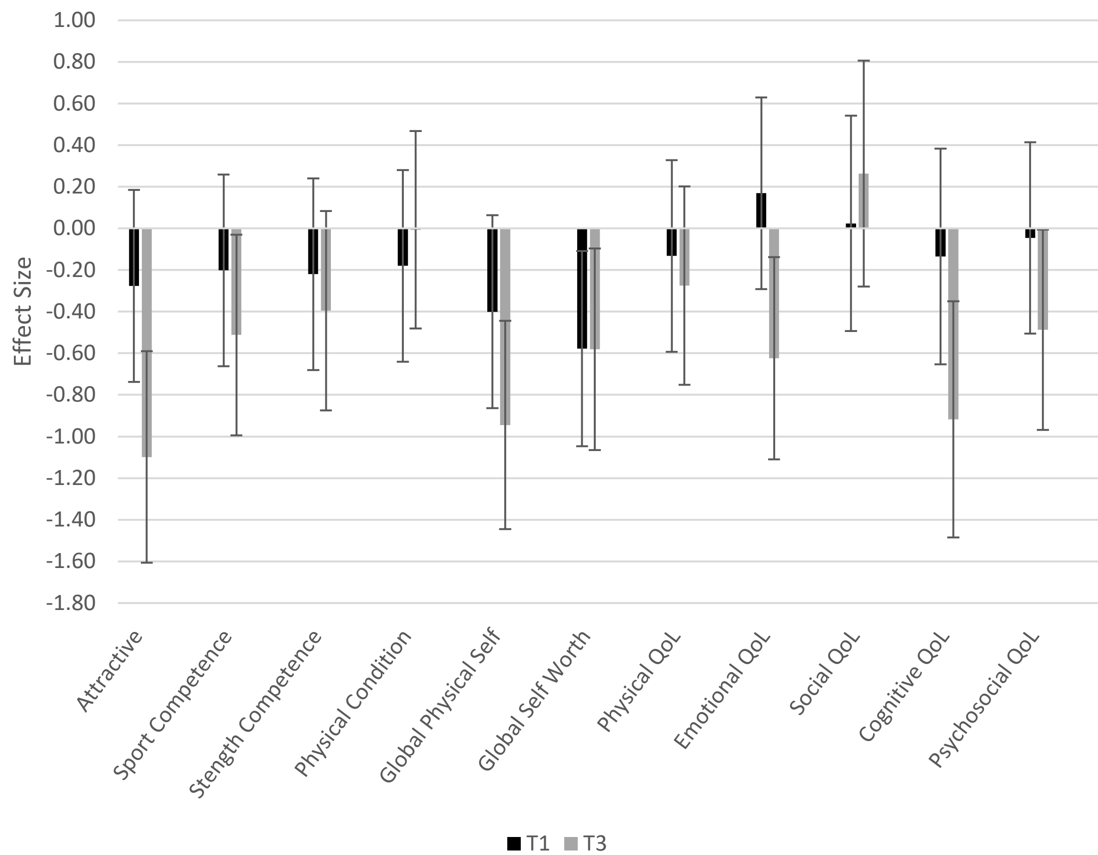
Abbreviations: T1, Time Point 1; T2, Time Point 2; T3, Time Point 3.
Bench press and leg press effect sizes for T1, T2, and T3.

Figure 8. Pre-Post Effect Sizes for Bench Press and Leg Press



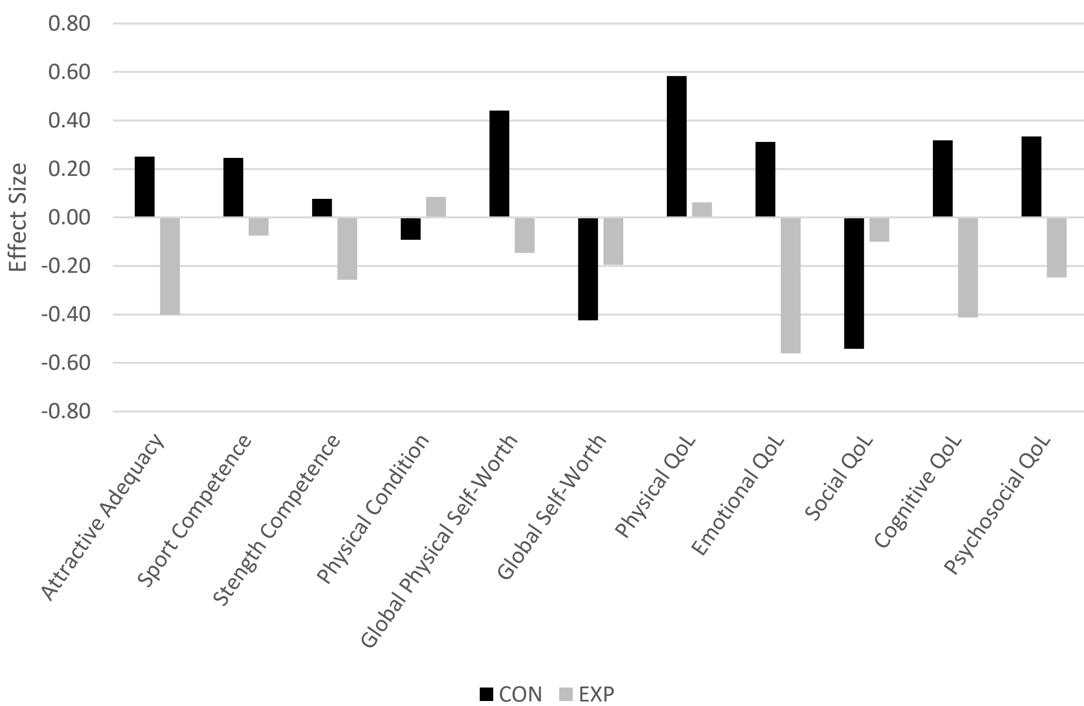
Abbreviations: CON, Control; EXP, Experimental; T1, Time Point 1; T2, Time Point 2; T3, Time Point 3.
Pre-post effect sizes for CON and EXP groups for strength measures. This table illustrates the difference from T1 to T2 and from T1 to T3.

Figure 9. Intervention Effect Sizes for Body-Esteem and Quality of Life



Abbreviations: QoL, Quality of Life; T1, T3, Time Point 3.
Body-esteem and QoL effect sizes for T1 and T3.

Figure 10. Pre-Post Effect Sizes for Body-Esteem and Quality of Life



Abbreviations: CON, Control; EXP, Experimental; QoL, Quality of Life; T1, T3, Time Point 3.
Pre-post effect sizes for CON and EXP groups for QoL and body esteem from T1 to T3.

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