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Using a Cultural Dance Program to Increase Sustainable Physical Activity for Breast Cancer Survivors – A Pilot Study

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Abstract

Background.—Studies have shown that physical activity can reduce the risk of mortality for female breast cancer patients and improve quality of life, reduce weight, and alter circulating biomarker levels. We conducted a pilot trial to determine the feasibility of increasing physical activity through a cultural dance intervention to achieve similar benefits.

Methods.—Conducted a pilot trial implementing a cultural dance intervention to increase and sustain physical activity for breast cancer survivors, which consisted of a six-month group-based intervention of Hula Dance. Anthropometric measures, fasting blood draws, and self-reported questionnaires to assess physical activity, mood, and quality of life, were completed at baseline, at the end of the 6-month intervention (time point month-6), and at two additional post-intervention time points at month-12 and month-24 to assess sustainability.

Results.—A total of 11 women with a median age of 63 years were enrolled in the intervention trial. Eight of the 11 (73%) completed the trial to month-12 and demonstrated an overall significant increase in weekly moderate exercise. There were no significant changes in intra-individual body mass index (BMI). However, there was a sustained post-intervention reduction in waist circumference and significant changes in circulating biomarker levels. For the self-reported

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Conflict of Interest

L. Loo declares that she has no conflicts of interest. K. Nishibun declares that she has no conflicts of interest. L. Welsh declares that she has no conflicts of interest. T. Makolo declares that she has no conflicts of interest. C. Chong declares that she has no conflicts of interest. I Pagano declares that she has no conflicts of interest. H. Yu declares that she has no conflicts of interest. E. Bantum declares that she has no conflicts of interest.

Ethical Approval

This article does not contain any studies with animals performed by any of the authors.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individuals included in the study.

measures, there was a significant increase in vigor/activity ($p < 0.001$; Profile of Mood States-Short Form).

Conclusion.—Our intervention pilot trial demonstrated that a cultural dance program could achieve a sustainable increase in physical activity for breast cancer survivors, with potential to improve quality of life, increase vigor, and decrease levels of circulating cytokines associated with obesity and inflammation.

Keywords

survivor; breast cancer; physical activity; Hula Dance; biomarker

Background

There are over 3 million female breast cancer survivors in the U.S., and the number of survivors continues to rise with improved prevention and treatment strategies (www.cancer.org; American Cancer Society. *Cancer Facts and Figures 2018*. Atlanta, GA: American Cancer Society; 2018.) In addition, there have been increasing efforts to reduce the risk of recurrence and improve the quality of life (QOL) for individuals following breast cancer diagnosis and treatment.

Multiple studies have established that physical activity can reduce the risk of mortality for female breast cancer patients^{1–8}. A meta-analysis reported that physical activity after diagnosis was associated with a 34% lower risk of breast cancer-specific mortality, 41% lower risk of all-cause mortality, and 24% lower risk of breast cancer recurrence for breast cancer survivors⁹. The American College of Sports Medicine (ACSM) recommends that cancer survivors engage in MVPA for at least 150 min/wk^{10, 11}. However, only an estimated 35% of individuals with breast cancer are achieving this level of physical activity after their diagnosis^{10–12}. It is a critical challenge to provide support to breast cancer survivors to maintain, or adopt, a physically active lifestyle to meet these recommendations.

Exercise interventions to increase physical activity have been implemented with overall positive efficacy for breast cancer survivors^{13–16}. Some of the demonstrated benefits of physical activity interventions for breast cancer survivors include, a decrease in body weight and insulin resistance, improvements in physical function and QOL, and reduction of depression, anxiety, and fatigue^{14, 17–24}. In addition, studies have demonstrated that physical activity can prevent cognitive decline^{25, 26}, with dance having more cognitive impact than other forms of conventional physical activity regimens (e.g. walking, jogging, and gym-based exercise)^{27, 28}.

Increasing evidence indicates that obesity and inflammation have key roles in cancer biology^{29–31}. As obesity negatively influences disease prognosis for women with breast cancer^{32–34}, effective lifestyle modifications (e.g. increasing physical activity) to reduce the negative effects of obesity-related factors that contribute to mortality are critically needed for breast cancer patients. The beneficial effects of physical activity for cancer survival have been attributed to reducing systemic inflammation by altering circulating levels of inflammatory cytokines^{15, 16, 35}. In addition, physical activity can alter circulating levels of

hormones (i.e. estrogen, androgen, leptin, adiponectin), insulin, insulin-like growth factors (IGF), and IGF binding proteins (IGFBP))^{14, 31, 36–41}.

There have been a limited number of intervention studies involving non-conventional modes of physical activity that may be more culturally relevant to women of multiethnic populations^{42–48}. Efficacy has been observed in intervention studies involving non-conventional forms of physical activity such as Tai Chi Chuan, yoga, and dance^{42, 43, 45–47, 49}. In one study evaluating the effects of Tai Chi Chuan on breast cancer survivors, slow, fluid, weight-bearing movements combined with controlled breathing techniques resulted in changes in blood pressure, circulating levels of insulin, IGF-1, IGFBPs, inflammatory biomarkers (IL-6, IL-2, and IFN- γ), and cortisol^{43, 45, 48}. Two recent intervention studies among breast cancer survivors demonstrated that yoga led to a reduction of inflammatory signaling in survivors experiencing persistent fatigue⁴² and improved cognitive function⁴⁴. In another study, breast cancer survivors who completed a 6 month intervention of Greek traditional dance had an increase in physical function, an increase in handgrip strength, a reduction in arm volume, and a decrease in depression⁴⁶. These findings support the efficacy of culture-based, non-conventional modalities of physical activity for cancer survivors.

We conducted a pilot aerobic dance intervention study with a group-based Hula Dance program to increase physical activity for sedentary breast cancer survivors. Since the dance movements of Hula are taught in a class-based environment and involve aerobic activity, whole-body movement (engaging hands, arms and shoulders), and cognitive tasks (asymmetrical arm and leg movements and dance step memorization), the intent for implementing Hula to increase physical activity was to provide multidimensional benefits that a multiethnic population of breast cancer survivors would find sustainable.

Methods

Study Participants

Participants were recruited at participating medical centers in the Hawaii Cancer Consortium, from local breast cancer survivor groups, and through self-referrals in response to media announcements. The criteria for enrollment were: residency on Oahu, HI; female 21 years of age or older; histologically-confirmed diagnosis of primary breast cancer, disease Stage I through III; 6-60 months post-treatment completion of initial regional and systemic treatment; no current chemo- or radio-therapy; current use of hormone therapy or trastuzumab was allowed; approval for participation in the trial by attending physician; currently less than 60 minutes per week of moderate to vigorous exercise (i.e., sedentary); and physically capable of doing the hula-based physical activity. Participants were screened to determine if they met the eligibility criteria. Informed consent was obtained from all individuals included in the study.

Study Design

The pilot study was designed as an intervention trial to support a health behavior change. The study was initiated to determine feasibility and acceptability of the intervention and to

determine if a physical activity intervention with Hula Dance would be sustainable and result in changes in self-reported well-being, anthropometry, and circulating biomarker levels.

At the baseline visit, informed consent was obtained, questionnaires (QX) were reviewed for completeness, and a baseline blood draw and anthropometric measurements were taken. Blood draws, anthropometric measurements, and questionnaires were completed at four time points. The first time point was at baseline prior to the intervention program, then at three post-intervention time points, at month-6 (following the completion of the intervention), then at month-12 and 24. The protocol and informed consent were IRB-approved by the Western Institutional Review Board (WIRB) and the Clinical Trial was registered as a National Cancer Institute Clinical Trial (#).

For a total of 6 months, participants attended a 60-minute supervised Hula Dance class twice a week and instructed to complete a 15-minute home-based Hula Dance practice three times per week with the goal of at least 150 minutes of moderate to vigorous physical activity per week. Each 60-minute Hula exercise class included a warm-up (10 minutes), conditioning (40 minutes), and cool-down (10 minutes) period. During the conditioning period a target heart rate of 50-70% of maximum heart rate ($HR_{max}=220-age$) for the intended moderate-intensity physical activity during the mid-conditioning period was the goal for participants⁵⁰. Heart rate was monitored by self-measures of the number of pulses per minute taken over the radial artery, on the inside of the wrist, for each participant. Heart rate was recorded at three time points during the 60-minute class (start of class, mid-conditioning; end of class). Every Hula class was conducted by the same Hula instructor; who has extensive experience in teaching Hula Dance and knowledge of the study guidelines. Hula is a Polynesian dance form that contains dance movements (whole body) and gestures that are in alignment to the meaning of the accompanied song. The instructor would teach the dance movements to each song in segments until the entire hula dance for each song has been memorized and can be danced in entirety. The hula dance accompanying each song would be practice multiple times through each session and throughout the six-month intervention. The physical activity dance program was designed to meet the abilities of the breast cancer survivors. An attendance log was kept to record each participant's attendance. If the participant missed two consecutive Hula class meetings, the study coordinator contacted the participant with a reminder of the class schedule to encourage attendance.

For anthropometric assessments, a trained technician obtained participants' height, weight, waist circumference and hip circumference measurements at each time point. Self-reported outcomes were assessed with the completion of questionnaires at each time point, with the exception of the individuals' demographics, which was provided at the baseline visit only, e.g. information on socio-demographic and health characteristics included ethnicity, stage of breast cancer at diagnosis, treatment type, comorbidities and occupation, and family history of cancer. The Godin Exercise Questionnaire was used to assess minutes per week of exercise in the categories of light, moderate, and vigorous exercise⁵¹. This questionnaire is a self-report measure asking participants to describe how many times they engage in strenuous, moderate, or mild physical activity during a typical 7-day period. The European Organization for Research and Treatment of Cancer Quality-of-Life Core Questionnaire

(EORTC QLQ-C30) was used to assess the quality of life of cancer patient participants⁵². It contains 30 items each scored on a 4 point response scale, with three categories: global health status, functional status (physical, role, emotional, cognitive, and social), and physical symptoms. The Brief Fatigue Inventory (BFI) is a 15 item measure (scored on a 11 point response scale), assessing for the severity and impact of fatigue on daily functioning during the last 24-hour period⁵³. The Centers for Epidemiological Studies Depression Scale (CES-D) was used to assess the presence of depression⁵⁴ with 20 items (scored on a 4 point scale) that include questions that fall into nine categories of depression (sadness, loss of interest, appetite, sleep, thinking/concentration, guilt, fatigue, movement, and suicidal ideation). The Profile of Mood States-Short Form (POMS-SF) questionnaire assessed affective states by asking participants to indicate how they have been feeling related to 65 adjectives rated on a 5-point scale⁵⁵. The 15-item, 5-point Social Constraints Scale (SCS)⁵⁶ was used to measure the degree to which participants feel their social relationships are strained due to experiencing cancer.

For circulating biomarker assessments, fasting (10 hours) blood was collected by a trained phlebotomist. One 10 ml EDTA collection tube was obtained at each blood draw. Whole blood was processed for plasma and buffy coat components, then aliquoted and stored at -80°C until the three time points (baseline, month- 6 and 12) could be analyzed, to minimize batch effects. Levels of hormones, cytokines, and inflammatory markers were measured in the plasma component. To ensure reproducibility and reliability, a standard and quality control duplicates were also assayed. C-reactive protein (CRP) was assayed with the latex particle-enhanced immunoturbidimetric method using a kit (Pointe Scientific, Inc.) and a Cobas Mira Plus clinical autoanalyzer (Roche Diagnostics); insulin, IGF-1, IGFBP3, adiponectin, and leptin were assessed by double-antibody enzyme-linked immunosorbent-assays (EFISA; R&D Systems) according to the manufacturer's specifications; and biomarkers of inflammation (GM-CSF, IFN- γ , IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, TNF- α) were assayed with an immunoassay kit (Cytokine Human Magnetic 10-Plex Panel for the LuminexTM Instrument, ThermoFisher Scientific).

Statistical Analysis

To test for intra-individual differences in pre- and post-intervention for each of the self-reported assessments, least squares estimated (adjusted for covariates) means are shown. For the biomarker assessments, levels were adjusted for BMI at each time point. The mixed linear model (MIXED procedure; incorporating repeated measures) assessed the outcome changes over time, with a separate model run for each outcome⁵⁷. The SAS 9.4 software (SAS Institute Inc., Cary NC) performed all analyses.

Results

A total of 70 individuals inquired and were screened for eligibility; 45 were ineligible (generally because they were exercising more than 60 minutes per week), two were eligible but not interested after discussing the intervention parameters and requirements; 23 female breast cancer survivors were eligible and expressed an interest in participating (Figure 1). Of the 23 eligible individuals, 11 consented and completed their baseline assessments. The 11

participants had a median age of 63 years (SD=10.2 years), were diagnosed with early stage breast cancer (Stages I-II), and 2 years (median) post-diagnosis. Ten of the 11 (90%) participants self-reported as an ethnic minority (Asian/Pacific Islander).

We assessed intra-individual changes pre-and post-intervention for anthropometry, self-reported psychosocial outcomes (questionnaires), and circulating plasma biomarkers, comparing baseline assessments to time points at months 6, 12, and 24 (Figure 2). The month-6 assessment was the assessment immediately following the intervention program, and the month-12 and 24 time points were included to assess the sustainability of the intervention, and changes associated with health-related outcomes 6 and 18 months following the end of the supervised Hula Dance program.

To determine the feasibility of this study, we report that 9 of the 11 participants (82%) completed the Hula Dance program (0-6 months). The average attendance for the intervention phase of the nine participants was 84%. Eight of the 11 participants completed the study to the month-12 assessments and seven participants completed the month-24 assessments (anthropometric measures and self-report questionnaires). All seven participants who completed the month-24 assessments indicated that they continued to dance Hula regularly.

Anthropometric measures (weight, height, and waist and hip circumferences) were assessed. There was no significant change in body mass index (BMI) or hip circumference associated with the increased physical activity of the Hula intervention (Table 1), however there was a reduction in the waist circumference for the comparisons between the baseline and month-6, 12 and 24 time points. This reduction was statistically significant ($p < 0.05$) for the baseline versus month-6 and month-24 time points. In addition, the reduction in the waist/hip circumference ratio for the baseline versus month-24 comparison was highly significant ($p < 0.001$). These results suggest that the increased physical activity with the Hula Dance program led to a reduction primarily in the abdominal region, suggesting a decrease in central adiposity.

Established questionnaires were used to assess self-reported outcome measures. The questionnaires were intended to identify changes in exercise levels, QOL, depression, and mood associated with participation in the Hula Dance intervention trial (Table 2). Based on the Godin Exercise Questionnaire results, participants significantly increased the amount of moderate exercise engaged in (increase in minutes of this type of intensity of exercise) during the supervised Hula intervention and sustained this increase for more than one year post-intervention ($p < 0.001$). The majority of the measures from the EORTC QLQ-C30 assessment tool did not indicate statistically significant changes in QOL for the study participants. However, we did observe a trend of increasing global health status, although it was not statistically significant. There was also a sustained reduction in dyspnea and diarrhea ($p=0.02$), as measured by the self-reported EORTC scale. The POMS-SF questionnaire used to determine changes in mood associated with the intervention, there was a highly significant increase in vigor/activity ($p<0.001$), indicating an improvement in the participants' mood or a decrease in mood disturbances⁵⁵. Interestingly, this questionnaire

detected a marginally significant increase in the level of confusion/bewilderment in the comparison between baseline versus month-24.

We also observed significant changes in the levels of circulating biomarkers associated with the Hula Dance intervention when we compared levels at baseline versus month- 6 and 12 (Table 3). Assays were not performed on the month-24 plasma samples, so there are no circulating biomarker data for this time point. A decrease in circulating IGFBP-3 levels was the only significant change observed for the baseline to month-6 comparison, and levels of IGFBP-3 were further reduced at the month-12 time point. There were multiple biomarkers with significant changes for the baseline versus month-12 comparison. In addition to IGFBP-3, we observed a reduction in the levels of IGF-1 as well as multiple inflammatory cytokines (IL-1B, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, GM-CSF, IFN- γ , and TNF- α). These results support the observation that physiologic changes, as measured by changes in circulating IGF-1 and its binding protein, IGFBP-3, and biomarkers of inflammation, were associated with increased physical activity through participation in this cultural dance program.

Discussion

It is established that formalized exercise interventions to increase physical activity have been implemented with overall positive efficacy for breast cancer survivors. However, cancer survivors of minority populations were observed to be less likely to meet physical activity recommendations, more likely to be obese, and generally had poorer health-related QOL^{12, 58–61}. The poor breast cancer outcomes for some minority groups may be related to the lack of adherence to physical activity and weight control recommendations, highlighting a need for physical activity intervention strategies to increase interest and adherence for women of minority populations who are generally not meeting recommendations. Hawaii is one of the most racial and ethnically diverse places in the world, according to the U.S. Census Bureau, with approximately 75% of the population comprised of minorities. The racial/ethnic composition of our study participants reflected the high percentage of minorities in the population. In addition, breast cancer incidence is relatively high in Hawaii, ranking 6th in the nation (2018; statecancerprofiles.cancer.gov). Therefore, there was great motivation to initiate a study to increase physical activity through a modality that is culturally sensitive for a population with high breast cancer incidence.

Prior studies have demonstrated that increasing physical activity with a dance program has multiple benefits such as good adherence to physical activity, and improved QOL, vigor, and physical function^{46, 62}. Our pilot trial to examine the psychosocial and biological effects of increasing physical activity using a supervised six-month cultural dance intervention demonstrated that this approach has the potential to increase and sustain moderate physical activity for previously sedentary breast cancer survivors. The intra-individual levels of moderate physical activity increased significantly during the six-month intervention and were sustained for more than one year after the completion of the intervention. In addition, we observed multidimensional effects (e.g. anthropometric, circulating biomarker levels, physical functioning, and psychosocial) associated with the completion of the trial. To our

knowledge, this is the first intervention study utilizing Hula Dance to increase physical activity and improve QOL for breast cancer survivors.

This pilot intervention trial demonstrated that a cultural dance program could be implemented to sustain moderate physical activity for the intervention period and even post-intervention. We were particularly encouraged because 7 of the 11 participants that started the trial continued to practice their Hula Dance well past (>1 year) the completion of the intervention portion of the trial. Maintaining healthy behavior changes is challenging, especially when there are many competing demands following diagnosis and treatment for cancer survivors. To facilitate sustaining the participants' increased physical activity through Hula Dance, the Hula classes continued to be available to the participants following the intervention portion of the trial. Our study demonstrated that sedentary breast cancer survivors can increase their levels of physical activity and maintain a lifestyle change to include moderate-intensity physical activity. Additional studies with larger sample sizes will be important to confirm the efficacy in these findings.

While there are numerous effective physical activity interventions, long-term maintenance and follow-up is rarely conducted and assessed for many studies. For example, a report evaluating the maintenance of intervention outcomes, found that only 16% (10 of 63 trials) of physical activity and/or dietary interventions trials for breast cancer survivors did a post-intervention assessment (3 months) ⁶³. Of the 10 trials, only four (40%) observed maintenance of the intervention outcomes. These results support the importance of post-intervention study follow-ups and a better understanding of the factors that contribute to a sustainable physical activity modality.

The self-report assessments indicated a significant increase in vigor during the intervention and post-intervention. This would be expected, as previous studies have demonstrated exercise and group support have been related to increased vigor ⁶⁴⁻⁶⁸. The Hula Dance intervention was conducted in a group-based setting, likely fostering social support among the participants. However, the increase in bewilderment and confusion for the baseline to months- 6, 12, and 24 time point comparisons was unexpected. It is possible that it reflects a change in the participants' perception of cognitive functioning since the task of learning and memorizing the Hula Dance steps for each song may have been challenging. Because of the small sample size, we are limited in our interpretation and assessment of the impact of these differences.

Obesity is a risk factor of breast cancer ^{5, 69}. Increased circulating levels of insulin and IGF-axis proteins are strongly associated with obesity and breast cancer ⁷⁰⁻⁷². Insulin and IGFs are growth factors that can promote proliferation in mammary cells, potentially initiating breast cancer development and recurrence. Levels of biologically active IGFs are regulated by IGF-binding proteins; IGFBP-3 is the binding protein that regulates the bioavailability of IGF-1. Previous studies have examined the association between increasing physical activity and a reduction in circulating IGF-1 and IGFBP-3 levels, but the results were mixed. Irwin et al. found a significant decrease in insulin, IGF-1, and IGFBP-3 levels for postmenopausal breast cancer survivors participating in a six-month, moderate-intensity aerobic exercise intervention trial ¹⁴ However, McTieman et al. observed a marginal, non-significant decrease

in IGF-1 and IGFBP-3 levels in a 12-month moderate-intensity exercise trial ⁷³. A 12-week physical activity intervention with moderate intensity Tai Chi Chuan for breast cancer survivors did not result in a reduction of IGF-1 or IGFBP-3 ⁴⁵. In our study, we observed a statistically significant decrease in IGF-1 and IGFBP-3 levels associated with the Hula Dance program. Interestingly, IGF-1 levels demonstrated a decreasing trend from baseline to months- 6 and 12, with the most marked decrease by month-12. It is possible that sustained physical activity (6 months) is important for a significant decrease in IGF-1 levels. There was also a decreasing trend in IGFBP-3 levels, with the most significant change in month-12. Moreover, IGFBP-3 levels have been shown to be positively related to central adiposity ⁷⁴; although there was not a significant reduction in weight for our study participants, we did observe a significant reduction in waist circumference and WHR. These results suggest that increasing moderate physical activity with the Hula Dance intervention resulted in a reduction in central adiposity and a concomitant decrease in circulating IGFBP-3 levels.

Inflammation plays a role in the development and progression of cancer ⁷⁵. Elevated circulating levels of inflammatory cytokines (e.g. CRP, TNF- α , IL-6) have been observed in breast cancer patients ^{76, 77}, and physical activity has been shown to modulate these levels ^{45, 78–80}. However, results across studies have been inconsistent. Some studies have indicated significant changes in CRP, or TNF- α , IL-6 levels associated with exercise, and others have found no significant changes in these levels. Interestingly, CRP and IL-6 were two cytokines that did not significantly decrease with our physical activity intervention. In fact, IL-6, although not significant, demonstrated an increasing trend in levels between baseline and months-6 and 12. Janelins et al. also observed an increase in IL-6 levels associated with their Tai Chi Chuan intervention ⁴⁵. In our study, we observed a significant decrease in the circulating levels of multiple inflammatory cytokines at month-12 (IGF-1, IGFBP3, IL-1B, IL-2, IL-4, IL-5, IL-10, GM-CSF, IFN- γ , and TNF- α). The majority of these cytokines were not significantly different at month-6, which is the time point at the completion of the intervention. It is possible that sustained physical activity (6 months) is important in significantly decreasing the levels of these inflammatory biomarkers. However, Schmidt et al. observed a decrease in the levels of inflammatory cytokines (IL-2, IL-4, IL-5, IL-10, IL-12, IL-13, GM-CSF, IFN- γ and TNF- α) associated with increased physical activity (walking) for one week and the effects were more pronounced in obese participants ⁴⁹.

Although this was a small pilot study and there are limitations in the conclusions that can be made from it, the study demonstrates the feasibility to increase physical activity with a cultural dance program. A larger wait-list controlled study should be implemented to confirm our findings, that the increased physical activity through the Hula Dance intervention can result in an improvement in the QOL, a reduction in waist circumference, as well as changes in the levels of circulating biomarkers associated with the IGF-axis and inflammation. Self-efficacy is important to continued maintenance of physical activity ⁸¹. Therefore, fostering dissemination of culturally relevant physical activity interventions is critically important, especially for minority populations that are generally not meeting the physical activity recommendations. In addition, sustainability of the increased physical activity is important for long-term impact of these types of interventions.

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Highlights:

- Physical activity can reduce risk of cancer recurrence, improve quality of life, lower body mass index, reduce inflammation, and alter levels of circulating biomarkers associated with obesity.
- We demonstrate the feasibility of a cultural dance program to increase and sustain physical activity in previously sedentary breast cancer survivors.
- We observed a significant reduction in waist circumference, changes in levels of circulating biomarkers of obesity and inflammation, and an increase in vigor/activity based on self-reported measures through questionnaires.

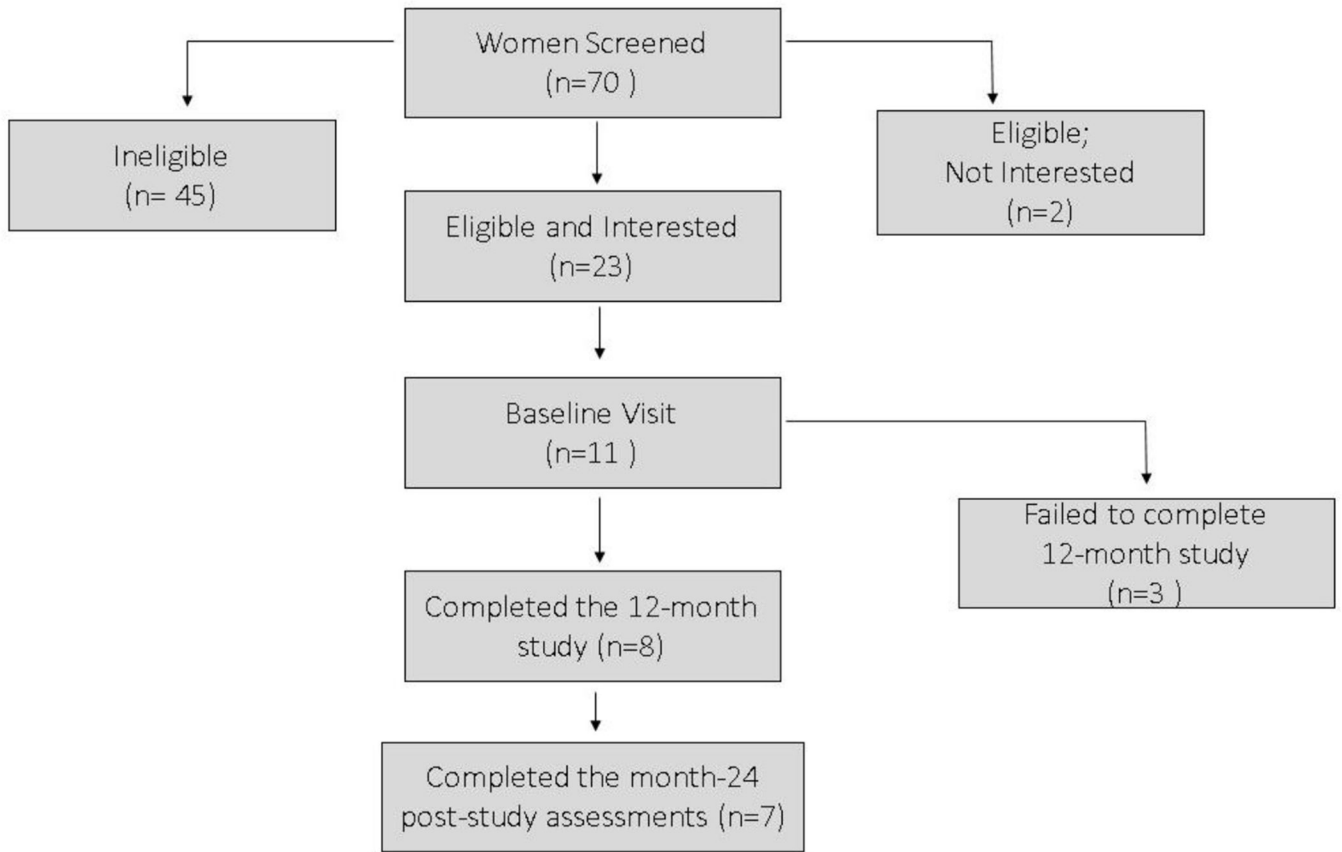


Figure 1. Flow chart of Hula Study participant recruitment and retention.

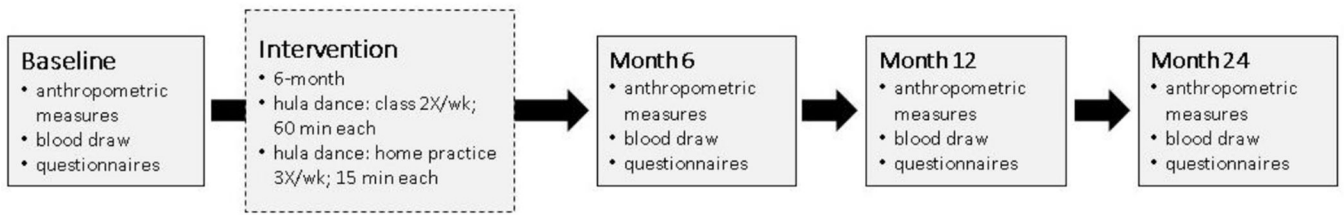


Figure 2.
Diagram of Hula Dance intervention time points and assessments.

Intra-individual changes in anthropometry comparisons between baseline and post-intervention measures

Table 1.

Anthropometric Measures	Mean Measures (n=8)		baseline vs. month 6		Mean Measures (n=8)		baseline vs. month 12		Mean Measures (n=7)		baseline vs. month 24	
	baseline	month 6	p-value	baseline	month 12	baseline	month 12	p-value	baseline	month 24	p-value	
Weight (lbs)	134.5	132.0	0.21	134.5	134.3	127.7	128.5	0.90	127.7	128.5	0.73	
Height (inches)	61.1	61.0	--	61.1	60.8	60.9	60.7	--	60.9	60.7	--	
Waist Circumference (inches)	37.6	36.2	0.05	37.6	36.9	36.3	34.1	0.30	36.3	34.1	0.006	
Hip Circumference (inches)	38.4	38.1	0.28	38.4	38.0	37.5	37.7	0.15	37.5	37.7	0.63	
Waist / Hip Circumference Ratio	0.98	0.95	0.07	0.98	0.97	0.97	0.90	0.51	0.97	0.90	<0.001	
Body Mass Index (kg/m ²)	25.3	24.9	0.31	25.3	25.5	24.2	24.6	0.70	24.2	24.6	0.45	

Table 2. Intra-individual changes in physical activity and psychosocial measures between baseline and post-intervention time points

	mean measures (n=8)		baseline vs. month 6		mean measures (n=8)		baseline vs. month 12		mean measures (n=8)		baseline vs. month 24	
	baseline	month 6	p-value	baseline	month 12	p-value	baseline	month 24	p-value	baseline	month 24	p-value
Physical Activity and Psychosocial Measures												
strenuous exercise (times per week)	0.2	0.0	0.80	0.2	1.3	0.16	0.0	0.1	0.83	0.0	0.1	0.83
moderate exercise (times per week)	0.7	3.6	<0.001	0.7	2.9	0.002	0.4	2.9	<0.001	0.4	2.9	<0.001
mild exercise (times per week)	4.6	3.3	0.18	4.6	3.1	0.10	4.8	2.7	0.01	4.8	2.7	0.01
Godin Leisure-Time Exercise Questionnaire: Total Leisure Activity Score	14.9	23.4	0.28	14.9	31.3	0.05	12.7	23.7	0.16	12.7	23.7	0.16
EORTC QLQ-30 (v3): Global Health Status / QoL	66.7	74.0	0.15	66.7	72.9	0.21	66.7	73.8	0.39	66.7	73.8	0.39
EORTC QLQ-30 (v3): Physical Functioning	86.7	87.9	0.73	86.7	85.8	0.82	85.7	83.8	0.56	85.7	83.8	0.56
EORTC QLQ-30 (v3): Role Functioning	85.4	83.3	0.75	85.4	87.5	0.75	83.3	88.1	0.48	83.3	88.1	0.48
EORTC QLQ-30 (v3): Emotional Functioning	78.1	84.4	0.08	78.1	82.3	0.23	76.2	78.6	0.50	76.2	78.6	0.50
EORTC QLQ-30 (v3): Cognitive Functioning	85.4	85.4	1.00	85.4	81.3	0.21	83.3	78.6	0.23	83.3	78.6	0.23
EORTC QLQ-30 (v3): Social Functioning	85.4	91.7	0.13	85.4	89.6	0.30	83.3	92.9	0.08	83.3	92.9	0.08
EORTC QLQ-30 (v3): Fatigue	22.2	20.8	0.79	22.2	25.0	0.60	22.2	25.4	0.55	22.2	25.4	0.55
EORTC QLQ-30 (v3): Nausea and Vomiting	2.1	0.0	0.37	2.1	2.1	1.00	2.4	0.0	0.29	2.4	0.0	0.29
EORTC QLQ-30 (v3): Pain	18.8	14.6	0.57	18.8	18.8	1.00	21.4	21.4	1.00	21.4	21.4	1.00
EORTC QLQ-30 (v3): Dyspnoea	12.5	4.2	0.27	12.5	4.2	0.27	14.3	0.0	0.07	14.3	0.0	0.07
EORTC QLQ-30 (v3): Insomnia	20.8	16.7	0.46	20.8	25.0	0.46	23.8	19.0	0.59	23.8	19.0	0.59
EORTC QLQ-30 (v3): Appetite Loss	4.2	0.0	0.21	4.2	0.0	0.21	4.8	0.0	0.14	4.8	0.0	0.14
EORTC QLQ-30 (v3): Constipation	16.7	8.3	0.15	16.7	12.5	0.46	14.3	4.8	0.16	14.3	4.8	0.16
EORTC QLQ-30 (v3): Diarrhea	16.7	12.5	0.52	16.7	0.0	0.02	19.0	9.5	0.28	19.0	9.5	0.28
EORTC QLQ-30 (v3): Financial Difficulties	20.8	16.7	0.58	20.8	12.5	0.27	23.8	14.3	0.23	23.8	14.3	0.23
Center for Epidemiological Studies Depression (CESD): Total Score	10.9	7.5	0.17	10.9	8.3	0.28	11.6	8.1	0.16	11.6	8.1	0.16
Brief Fatigue Inventory: Index	1.8	1.7	0.88	1.8	2.4	0.32	2.1	1.9	0.79	2.1	1.9	0.79
POMS-SF: Tension/Anxiety	2.0	2.9	0.27	2.0	2.5	0.52	2.1	5.1	0.09	2.1	5.1	0.09
POMS-SF: Depression/Dejection	2.0	2.3	0.78	2.0	1.8	0.84	2.3	5.3	0.08	2.3	5.3	0.08

Physical Activity and Psychosocial Measures	mean measures (n=8)		baseline vs. month 6		mean measures (n=8)		baseline vs. month 12		mean measures (n=8)		baseline vs. month 24	
	baseline	month 6	p-value	baseline	month 12	p-value	baseline	month 24	p-value	baseline	month 24	p-value
POMS-SF: Anger/Hostility	1.5	2.9	0.20	1.5	2.4	0.42	1.3	5.1	0.11	1.3	5.1	0.11
POMS-SF: Fatigue	4.0	4.5	0.68	4.0	4.4	0.77	4.6	6.7	0.25	4.6	6.7	0.25
POMS-SF: Confusion/Bewilderment	1.8	2.9	0.09	1.8	2.8	0.12	2.0	4.3	0.05	2.0	4.3	0.05
POMS-SF: Vigor/Activity	10.5	14.1	<0.001	10.5	13.0	0.008	10.6	14.9	<0.001	10.6	14.9	<0.001
POMS-SF: Total Mood Disturbance	0.7	1.4	0.88	0.7	0.8	0.99	1.7	11.7	0.23	1.7	11.7	0.23
SCS: Most Important Person	1.7	1.7	0.88	1.7	1.7	0.92	1.8	1.5	0.31	1.8	1.5	0.31
SCS: Other People	1.8	1.8	0.86	1.8	1.8	0.69	1.8	1.6	0.23	1.8	1.6	0.23

Table 3. Intra-individual changes in circulating biomarker levels between baseline and post-intervention time points

Circulating Biomarker Levels*	mean measures (n=8)		baseline vs. month 6		mean measures (n=8)		baseline vs. month 12	
	baseline	month 6	month 6	p-value*	baseline	month 12	month 12	p-value*
	Adiponectin (ug/mL)	8.7	9.9	8.7	0.09	8.7	9.6	8.7
Cortisol (ng/mL)	94.4	88.9	94.4	0.65	94.4	88.6	94.4	0.63
IGF-1 (ng/mL)	82.6	82.4	82.6	0.95	82.6	74.9	82.6	0.03
IGFBP-3 (ug/mL)	2.5	2.2	2.5	0.03	2.5	2.0	2.5	0.005
Insulin (uIU/mL)	5.4	4.6	5.4	0.39	5.4	4.8	5.4	0.50
Leptin (ng/mL)	18.1	17.2	18.1	0.83	18.1	17.5	18.1	0.88
Glucose (mg/dL)	129.9	133.2	129.9	0.89	129.9	106.7	129.9	0.33
CRP (mg/L)	1.2	0.8	1.2	0.33	1.2	0.9	1.2	0.46
IL-1B (pg/mL)	26.3	28.0	26.3	0.46	26.3	20.8	26.3	0.02
IL-2 (pg/mL)	38.7	38.4	38.7	0.92	38.7	28.7	38.7	0.01
IL-4 (pg/mL)	33.6	36.5	33.6	0.37	33.6	26.5	33.6	0.03
IL-5 (pg/mL)	26.8	27.0	26.8	0.94	26.8	20.9	26.8	0.02
IL-6 (pg/mL)	58.2	60.8	58.2	0.93	58.2	77.1	58.2	0.54
IL-8 (pg/mL)	111.5	132.2	111.5	0.09	111.5	93.3	111.5	0.14
IL-10 (pg/mL)	57.6	58.4	57.6	0.90	57.6	40.7	57.6	0.03
GM-CSF (pg/mL)	32.7	35.4	32.7	0.39	32.7	26.1	32.7	0.05
IFN-γ (pg/mL)	44.0	49.3	44.0	0.15	44.0	36.3	44.0	0.05
TNF-α (pg/mL)	29.6	30.2	29.6	0.81	29.6	22.3	29.6	0.02

* adjusted for BMI