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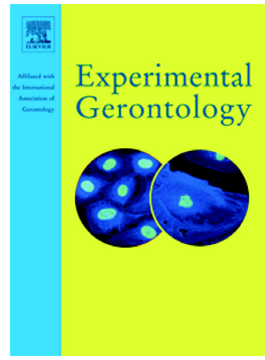

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Tai Chi is an effective form of exercise to reduce markers of frailty in older age.

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Running title: Tai Chi to reduce frailty in older age

Abstract

Frailty affects the quality of life of older age adults by limiting mobility, reducing physiological reserve and reducing independence. The frailty phenotype is typically characterised by exhaustion, loss or lack of physical activity, weight loss and weakness, although more recently there have been proposals to extend the frailty criteria to include physiological characteristics such as inflammation, oxidative stress and vascular function. Exercise has the potential to prevent, delay or even reverse frailty, but not all exercise is perceived as suitable for an older age population. The purpose of this study was to test Tai Chi and Zumba Gold® as exercise interventions in older age adults (65 to 75 years old) to improve characteristics related to the frailty phenotype. Muscle strength and flexibility (functional fitness as a measure of weakness), cardiorespiratory fitness, blood pressure, vascular function (FMD), markers of oxidative stress (total antioxidant capacity, malondialdehyde, 8-isoprostane, protein carbonyl), inflammation (CRP) and aspects of wellbeing related to exhaustion were assessed at baseline (pre-), 6 weeks (mid-) and 12 weeks (post-intervention). Both Tai Chi and Zumba Gold® improved systolic blood pressure, vascular function, and functional fitness following the 12 week intervention to a similar extent. Furthermore Antioxidant capacity was significantly increased (303±15.56 vs. 336±18.82 µm; p=0.0028) and lipid oxidation significantly reduced (36.41±6.4 vs 13.49±2.5 pg/ml; p=0.0042) after 12 weeks of Tai Chi compared to baseline. Anxiety, physical and mental fatigue decreased in both groups, with a greater decrease in mental fatigue in the Tai Chi group. Taken together, these changes suggest that Tai Chi has the potential to reduce outcomes related to the extended frailty phenotype in older age adults.

Keywords: physical activity; ageing; vascular function; redox; wellbeing

Introduction

Frailty is considered by some as a disease of old age and as such, can have a direct impact on the independence and health-related quality of life of older adults (Clegg, Young et al. 2013). Fried, Tangen et al. (2001) first depicted frailty as a phenotype based largely on four characteristics, namely: exhaustion, loss or lack of physical activity, weight loss and weakness. However, more recently there have been proposals to extend the criteria of frailty to encompass physiological characteristics such as inflammation, oxidative stress and vascular function (Deepa, Bhaskaran et al. 2017). This is due to growing evidence around the links between frailty and cardiovascular disease, as several studies have reported that markers of oxidative stress and inflammation, which are known to contribute to vascular dysfunction (Wadley, Veldhuijzen van Zanten et al. 2012) are related to frailty (Wu, Shiesh et al. 2009, Ingles, Gambini et al. 2014, Liu, Wang et al. 2016).

Exercise has the potential to reduce frailty (de Labra, Guimaraes-Pinheiro et al. 2015). There is ample evidence that exercise can improve health-related quality of life, depression, anxiety and fatigue (Mochcovitch, Deslandes et al. 2016, Rhyner and Watts 2016), which are all factors in exhaustion. Exercise can improve strength , improve functional fitness, reduce inflammation (Liberman, Forti et al. 2017) and oxidative stress (Gomez-Cabrera, Domenech et al. 2008), and improve vascular function (Wadley, Veldhuijzen van Zanten et al. 2013) in older adults. The evidence is heavily based on moderate intensity exercise and therefore moderate exercise is usually considered to be the most effective in achieving these health benefits. However, the majority of older adults are not physically active enough to achieve these health benefits (Piercy, Troiano et al. 2018), and there is evidence that exercise at lower intensities can also have health benefits especially in those with lower levels of fitness (Matthews, Moore et al. 2015, Dillon, McMahon et al. 2018)

Whereas physical limitations can be a barrier to exercise in older adults (Franco, Tong et al. 2015), enjoyment and the way exercise is delivered can enhance exercise behaviour (Devereux-Fitzgerald, Powell et al. 2016). Therefore, to facilitate the uptake and maintenance of exercise in older adults, it is important to develop exercise programmes which are suitable and appropriate for this population. Low to moderate intensity exercise is perceived as more feasible by older age adults (Muller and Khoo 2014). Tai Chi involves low impact and low velocity movements and is an exercise mode with a low risk for falls (Lan, Lai et al. 1998) and as such it is a mode of exercise that may be appealing to older age adults. Tai Chi is an ancient Chinese exercise that has been practiced for hundreds of years in China (Li, Yuan et al. 2014). However, Tai Chi is now frequently practised in most Western countries (Lan, Lai et al. 2002) and has recently been included in the UK Chief Medical Officers' Physical Activity Guidelines (Davies 2019), yet surprisingly little is known about its health benefits.

The slow movements within Tai Chi combined with deep diaphragmatic breathing are believed to not be only beneficial to physical, but also to mental health. A meta-analysis revealed that Tai Chi can improve fatigue in clinical populations to a similar extent as more intense exercise such as fast walking (Xiang, Lu et al. 2017). Musculoskeletal strength improves by increasing the neuromuscular response in the lower extremities during the slow movements (Hass, Gregor et al. 2004, Wu, Liu et al. 2004), and specifically for older adults there are reports of a reduced risk for falling and improvements of functional fitness (Rogers, Larkey et al. 2009). Benefits for cardiovascular health have also been reported, most consistently for blood pressure in both people with cardiovascular disease (Wang, Pi et al. 2016) and apparently healthy older adults (Rogers, Larkey et al. 2009). However, less is known about the benefits of Tai Chi on vascular function, which is a risk indicator for cardiovascular events. There is preliminary evidence that Tai Chi can improve vascular function (Wang, Lan et al. 2002, Shin, Lee et al. 2015), but other studies reported no such benefit (Suksom, Siripatt et al. 2011). There is also preliminary evidence that Tai Chi can be effective in perturbing redox status and reducing inflammation (Palasuwan, Suksom et al. 2011, Huang, Eungpinichpong et al. 2014, Mendoza-Nunez, Arista-Ugalde et al. 2018). Rosado-Perez, Santiago-Osorio et al. (2012), reported that daily Tai Chi training for six months significantly increased total antioxidant status (TAS), and the antioxidant enzymes superoxide dismutase (SOD) and glutathione peroxidase (GPx) in healthy older adults. Lipid peroxidation was decreased (as measured by malondialdehyde -MDA) post exercise training, compared to the no-exercise control group. Similar results using a shorter 8 week intervention also resulted in increased TAS and GPx concentration in both pre and post-menopausal women (Palasuwan, Suksom et al. 2011). In studies to date, the comparison data either comes from baseline (Palasuwan, Suksom et al. 2011), walking exercise (Rosado-Perez, Ortiz et al. 2013), or no exercise control (Rosado-Perez, Santiago-Osorio et al. 2012). However, many studies have proven that exercise is effective in improving frailty (Chin, van Uffelen et al. 2008), and thus the more pertinent question relates to the value of Tai Chi compared to other forms of aerobic exercise. Hence in this study we chose to compare Tai Chi to a form of aerobic dance.

Functional fitness tests such as The Senior Fitness Test (SFT) are designed to assess fall risk and weakness (Jones & Rikli, 2002; Purath, Buchholz, & Kark, 2009). Functional fitness testing is common in studies that wish to assess the risk of fall after surgery (McIsaac, Jen et al. 2017), mobility related disability in disease (Tonet, Maietti et al. 2018) or in studies to assess the success of intervention (Stathi, Withall et al. 2018). Studies have shown that functional fitness is related to sedentary time and physical activity, independently of each other (Sardinha, Santos et al. 2015). Older adults who spend more time being physically active and less time in sedentary activities have an improved functional fitness and are more able to undertake the activities of daily living successfully (Santos, Silva et al. 2012, Sardinha, Ekelund et al. 2015) The range of movements in Tai Chi, combined with the shift in weight from foot to foot suggest it would be an excellent mode of exercise to improve physical function.

In sum, Tai Chi may represent an exercise mode that is acceptable for older age adults to engage in, that can reduce risk of falls and improve functional fitness. Given that Tai Chi also has the potential to improve physiological health by reducing inflammation, increasing antioxidant capacity and improving vascular function, it is feasible that Tai Chi could represent a mode of exercise that can enhance healthy ageing. Zumba gold® was used in this study as an exercise control. It is an aerobic form of moderate intensity exercise (Domene, Moir et al. 2016), and the benefits of aerobic exercise have been very well characterised in older age adults. As such, Tai Chi was assessed in comparison to group aerobic exercise. The present study investigated the potential for Tai Chi to improve both physiological and psychological factors associated with frailty in older age adults.

Materials and Methods

Participants (aged between 65 and 75, non-smokers, no history of cardiovascular disease, undertaking less than 1h hour structured exercise per week and independent in their daily living activities) were recruited to this study via poster advertisements in the local community. Prior to starting the study, participants received a participant information sheet, and gave written informed consent for participation. The study received ethical approval from the institutional Science, Technology, Engineering and Mathematics Ethical Committee. The study design is shown in figure 1.

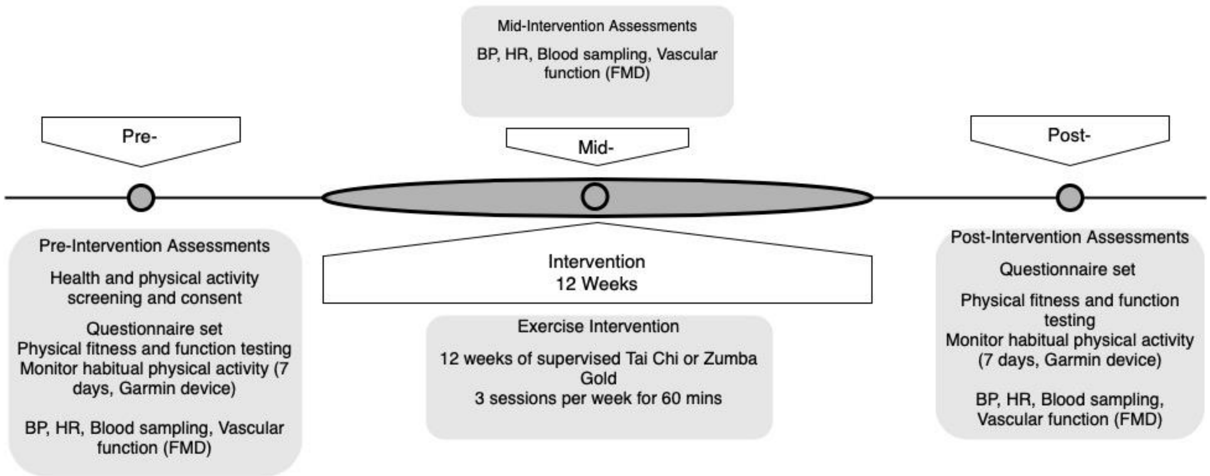


Figure 1. Schematic representation of the study and measurements taken at baseline, 6 weeks (mid) and 12 weeks (end) intervention. Blood withdrawal, ultrasound, and blood pressure were measured at pre, mid and end-intervention. Physical fitness and function was measured at baseline and 12 weeks (end-intervention). Questionnaires to assess physical activity and wellbeing were assessed at baseline and end-intervention.

Protocol

Participants were randomized into either Tai Chi or Zumba Gold exercise intervention using a randomization sequence on randomization.com (Wichmann 1982, McLeod 1985). Outcome measures were taken at baseline (pre-, 0 weeks), mid-study (6 weeks) and end-study (post-, 12 weeks). At each assessment point, participants attended two laboratory visits. One visit was completed following an overnight fast, and included measurements of height and weight, flow mediated dilation, and a blood draw for markers of oxidative stress and inflammation. During the second visit, physical fitness and function were assessed. At baseline and end of intervention, participants were also asked to complete a questionnaire pack to measure markers of health-related quality of life and wellbeing.

Outcome measures

Flow Mediated Dilation

Flow mediated Dilation (FMD) was measured according to the method of Harris (2010). During the FMD measurement, participants rested in a semi-supine position with their right arm extended and immobilized using a foam arm rest. A standard 3-inch size cuff was positioned around the arm, 2 inches below the antecubital fossa. To assess the FMD response, the image of brachial artery was scanned using B-mode ultrasound (Philip EnVisor, Andover, USA) and a high-frequency linear array transducer (10 MHz). The baseline diameter of the brachial artery was recorded for 2 minutes before the cuff was inflated to 50 mm Hg above the systolic pressure for 5 minutes. Following cuff deflation, images were recorded for a further 3 minutes. The diameter of the brachial artery was captured at 25 images per second, using an Online Vascular Imaging Analysis software (VIA), and further offline analysis was conducted using Spike software (CED). FMD was calculated as difference between peak diameter and baseline diameter, expressed as a percentage relative to baseline diameter. The site of the transducer was marked to ensure standardization between scans.

Baseline blood pressure

Participants rested semi-supine at 22-24^{o}C in low light for at least 20 minutes prior to assessment. Brachial blood pressure was taken using an automatic blood pressure machine (Omron M2 Basic, Kyoto, Japan). All measurements were made in triplicate with 5 minute intervals between measurements, and the mean value was calculated.

Physical Fitness

Physical fitness was assessed by an incremental treadmill (HP cosmos, Germany) test until participants reached 75% of their maximum predicted heart rate (maximum heart rate was estimated using the equation adapted from Tanaka, Monahan et al. (2001), adjusted for older age adult populations (HR max= 208-0.7 x age)). Start speed (1.5kph) was increased by 0.5kph every minute. The duration of walking was recorded at 55%, 65% and 75% of max HR, and perceived exertion was asked using the Borg Scale of perceived exhaustion (Borg 1982) every 2 minutes. A breath by breath measurement system (Oxycon Pro, Jaegar, Germany) was used to continuously measure oxygen uptake (VO_2) and Carbon dioxide production (VCO_2).

Physical Function

Participant's physical function was assessed using four tests from the Senior Fitness Test (SFT) battery (Rikli and Jones 2013). Lower body muscular strength was assessed by 30 second chair stand, lower body flexibility was assessed by chair sit and reach, upper body flexibility was assessed by back scratch test and dynamic balance/agility was assessed by timed up and go.

30 seconds chair stand

Participants were required to sit on a chair at a height of 17 inches with their feet flat on the floor, arms crossed with the wrists on the chest. Participants were asked to stand to full rise and return to fully seated posture repeated this procedure as many times as they could for 30 seconds. Participants were reminded to perform this testing using their own preferable speed and capability.

Chair sit and reach

Participants were asked to sit on the front edge of a chair at a height of 17 inches with one leg extended forward and another leg bent, with their foot on the floor flexed at 90 degrees. During exhalation, participants placed their hands on top of each other and slowly bent forward to the extended leg and tried to reach the toes. Participants were instructed to stay static in that position while the researcher took the measurement from the tip of middle finger to the top of the shoes. This procedure was repeated with the other leg, and an average of the two was taken to indicate overall flexibility.

Back scratch test

Participants were required to stand straight during this procedure, with one hand bending toward their back and try to reach down as far as they could. Meanwhile the other hand is placed at the position of the back with palm up, and participants were instructed to try to reach the other hand. The distance from both tips of middle finger was taken and the test was repeated using hands in the opposing positions, and an average was calculated to indicate upper body flexibility.

Timed up and go

Participants were required to walk a 3 meter walk way starting from a sitting position, and go back to the sitting position to end the test. The time was taken from the signal 'go' from the tester until the participant reached their sitting position (Rikli and Jones 2013).

<u>Blood sampling</u>

Fasting blood samples (10ml) were collected into EDTA by a trained phlebotomist via venepuncture at the antecubital vein while participants were remained at semi-supine position. All blood samples were processed immediately (Centrifugation: 10 minutes, at 3500 rpm, 4^{o}C). Plasma samples were stored at -80^{o}C until further analysis.

Total antioxidant capacity (TAC)

Total antioxidant capacity was measured using the ferric reducing ability of plasma (FRAP) assay, as described by Benzie and Strain (1999). Plasma samples (10µl) or ascorbic acid standards (ranging from 0 to 1000µM) were loaded into the 96-well cell culture plate in triplicate. FRAP reagent (20mM ferric chloride, 300mM sodium acetate buffer and 10mM 2,4,6-Tris (2-pyridyl)-S-Triazine, TTPZ, pH 3.6; 300µl) was added to the plate. Plates were left at room temperature for 8 minutes before the absorbance was read at 650nm. The value of total antioxidant was expressed using the 7 point curve value calculated from the ascorbic acid standard reading.

Thiobarbituric acid reacting substance (TBARS)

The thiobarbituric acid reacting substance (TBARS) test is a non-specific test to determine the concentration of malondialdehyde (MDA), a secondary product that is formed following lipid peroxidation. Samples and standards (0 to 50 µM of 1,1,3,3-tetramothoxypropane; 100µl) were loaded into Eppendorf tubes, and mixed with TCA solution (1.23M trichloroacetic acid (TCA), 0.05M H_2SO_4; 100µl) and colour reagent (thiobarbituric acid (TBA), 200µM buthylated hydrotoluene (BHT); 800µl) before being placed in boiling water (100^{o}C) for one hour. The reaction of MDA and thiobarbituric acid forms a fluorescent red adduct and absorbance was read at 540 nm.

8-isoprostane

Plasma 8-isoprostane was measured using a commercially available ELISA kit (Caymen Chemical, USA) according to the manufacturer's instructions. Briefly, samples and standards (50µl) were added into wells pre-coated with mouse monoclonal antibody. Samples and standards were then incubated with 8-isoprostane AChE tracer and antiserum for 18 hours at 4^{0}C. After washing, Ellman's Reagent was added to the wells and the plate was incubated on an orbital shaker for 120 minutes. The plate was read at 420nm and the 8-isoprostane concentration was calculated using the standard curve plotted using log transformation.

Protein oxidation

Prior to measuring the protein oxidation, protein concentration in the plasma samples was determined using the BCA method (Smith, Krohn et al. 1985). Plasma protein carbonylation was assessed using an ELISA described by Carty, Bevan et al. (2000). Briefly, samples and standards were diluted to a final concentration of 0.05mg/ml using a coating buffer (Sodium carbonate 50 nmM, pH 9.2). Samples and standards (50µl) were loaded into 96 well Maxisorb plate (Nunc, Fisher Thermo Scientific) in duplicate and incubated for 1 hour at 37^{o}C to allow protein binding. Following washing, 2-4-Dinitrophenylhydrazine (DNPH) (1nM in 2M HCl; 50µl) was added and incubated for another 1 hour at room temperature. The plate was washed again to remove unbound DNPH and blocking buffer (0.5% TWEEN-20; 200µl) was loaded to block non-specific binding sites for 1 hour at

37^oC. Following wash, primary antibody (mouse IgG anti-dinitrophenyl, 50µl, 1:1000 dilution) was added to the wells and the plate was incubated overnight at 4^oC. The plate was allowed to return to room temperature before being washed and secondary antibody (50µl) (anti-mouse IgE horse radish peroxidase conjugate; 1:5000 dilution) was loaded in the well. Following washing, substrate (10ml 0.5M citrate phosphate buffer, pH5, 8µl hydrogen peroxide and 2 mg o-phenyldiamine tablet, 50µl) was added and the plate was incubated in the dark at room temperature. The reaction was stopped with 2M sulphuric acid (50µl) and absorbance was measured at 490nm. The concentration of protein carbonylation was determined using the standard curve calculated from the standard concentration.

Brain derived neurotropic factor (BDNF)

Brain derived neurotropic factor (BDNF) was measured using commercially available ELISA kit purchased from R&D Systems, Minneapolis, USA (DBD00). Plasma samples (50µl) were diluted with assay diluent and added into pre-coated wells (monoclonal antibody, anti-BDNF). Enzyme-linked monoclonal antibody (volume) was then added and substrate solution was added to initiate the colour changes. The intensity of colour was dependent on the amount of BDNF that was bound in the initial process. Stop solution was added absorbance was measured using spectrophotometer at 450 nm absorbance.

C-Reactive protein (CRP)

CRP was measured using enzyme-like immunosorbent assay (ELISA) method using a commercially available kit BMS288INST from eBioScience, Vienna Austria. Prior starting the assay, plasma samples were diluted 1:5000 with assay buffer according to the manufacturer instruction. Samples (10µl) were then added into wells, and incubated at room temperature for 2 hours, on a shaker. This assay used an anti-human CRP polyclonal antibody. After washing, substrate solution (tetramethyl-benzidine) (100µl) was added and incubated at room temperature without direct exposure to intense light. Colour development was monitored and stop solution was added. Plate was read at 450nm using spectrophotometer.

Health-related Quality of life and psychological wellbeing

Validated questionnaires were used to assess different aspects of quality of life and psychological wellbeing. Perceived physical and mental health was assessed using SF-12 questionnaire (Ware, Kosinski et al. 1996). Separate scores for perceived mental and physical health were derived (Gandek, Ware et al. 1998). Anxiety and depression were recorded using the Hospital Anxiety and Depression Scale (Zigmond and Snaith 1983). The Subjective Vitality Scale (Ryan and Frederick

1997) was used as a measure of positive wellbeing. General fatigue, physical fatigue, reduced activity, mental fatigue, and reduced motivation were recorded using the Multidimensional Fatigue Index (MFI-20, (Smets, Garssen et al. 1995)). Finally, sleep quality was assessed using the Pittsburgh Sleep Quality Index Questionnaire (Buysse, Reynolds et al. 1989).

Exercise intervention

Following randomization participants were invited to attend exercise sessions for 12 weeks; 3 times per week for 1 hour. Compliance with the intervention was taken as attending 80% of the sessions throughout the intervention.

Tai Chi

Participants randomised to the Tai Chi group were guided by a certified instructor registered under Tai Chi Union Great Britain (TCUGB). They were instructed in the Yang-style of Tai Chi which consisted of 10 minutes warm up, 40 minutes of Shibashi Qigong set of 18 movements, Yang style form, and 10 minutes of cool down. During the session, participants were constantly reminded to have a natural and relaxed breathing, and try to synchronize the breathing with their movements.

Zumba Gold

Zumba Gold training was given by a certified instructor. Sessions consisted of 10 minutes of warm up which included stretching and whole body movements, followed by 40 minutes Zumba Gold routines. The routines were performed using slow to fast music from the selected rhythms of merengue, salsa, cumbia, flamenco and bachata. All movements involved elements of a cardiovascular workout, balancing, and dynamic stretching. The session was closed with cooling down and stretching session for 10 minutes.

Statistical analysis

Data management and analysis were performed using SPSS 24.0 statistical package for Windows (IBM. USA). Normal data distribution was analysed using the Shapiro-Wilk's test. Not normally distributed data (for example antioxidant capacity, 8-isoprostane, CRP, protein carbonyl) were transformed using Log_{10} or square root to normalize the data. Differences at baseline between the Tai Chi and Zumba Gold group were analyses using 2 Group (Tai chi, Zumba gold) Analyses of Variance (ANOVA). Effects of the exercise interventions were analysed using 2 Group (Tai Chi, Zumba Gold®) by 3 Time (pre, mid, post) ANOVAs. Psychological wellbeing measures were only taken at baseline and post intervention, and where analysed using 2 Group (Tai Chi, Zumba Gold®) by 2 Time (pre, post) ANOVAs. Where appropriate, post hoc analyses were conducted to investigate main effects in more detail. Significant levels were set at 5% for all analyses, and variations in degrees of freedom are reflective of occasional loss of data.

RESULTS

Thirty-five participants (28 female and 7 male) were recruited to this study. Twenty one participants completed the study (16 female and 5 male). Reasons for drop out were lack of time (n=11), dislike of the exercise (n=2) and illness (n=1). Baseline demographic information of the participants is shown in table 1. There were no differences between participants in the Tai Chi vs. Zumba Gold® groups with respect to gender, age, marital status, habitual physical activity or BMI.

Table 1. Baseline demographic information of the participants**.** The gender, age, and marital status of the participants are shown for participants in each group. Data is presented as mean±SD where appropriate. Physical activity data collected via IPAQ is presented in minutes and (Met minutes per week) and BMI is presented for participants in each group.

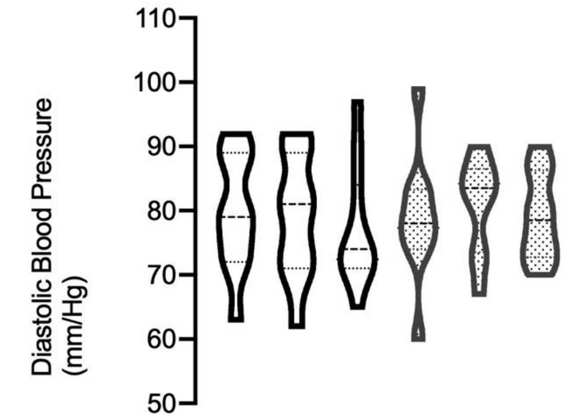
Parameters	Tai Chi	Zumba Gold®	p
Gender			
Male	4	1	
Female	7	9	
Total	11	10	0.166
Age, mean ± SD	71 ± 3.1	70 ± 3.6	.463
Marital status			
Married/Partner	5	7	
Single/Widowed	6	3	
IPAQ total (METs-minutes/week)	1908 (1327)	1555 (2919)	1.0
BMI (kg/m²)	27.4 ± 4.8	28.4 ± 3.4	.593

At 12 weeks (end of intervention) systolic blood pressure (SBP) was reduced in all participants when compared to baseline (Figure 2b). Repeated measures ANOVA yielded a significant time effect for SBP, F(2,18)= 11.37, p=.001, η^2=.558, but no group (p=.78) or group × time interaction effect (p=.24). Post hoc analyses revealed that SBP was significant lower at 12 weeks compared to both baseline and 6 weeks. Similar analyses were undertaken to determine the effect of exercise on diastolic blood pressure (figure 2a) and no significant time (p=.34), group (p=.76), or group × time interaction (p=.77) effects were observed.

Figure 2c shows the percentage of flow mediated dilation at pre, mid and end intervention in both groups. Repeated measures ANOVA found that there is a time effect, F(2,9) =9.70, p=.01, η^2=.683, but no significant group ($p=.70$) or group × time interaction ($p=.87$) effect. Post hoc analyses revealed that FMD was significantly higher at 12 weeks compared to both baseline ($p=.002$) and 6 weeks ($p=.002$).

As a specific interest was to examine the effects of Tai Chi, secondary analyses were conducted to assess the effects of Tai Chi on blood pressure and vascular function. Three time (pre, mid, post) ANAOVAs, revealed a significant time effect for SBP, $F(2,9) = 8.98$, $p=.007$, $\eta^2=.666$, no time effect for DBP ($p=.402$), and a trend towards a time effect for FMD, $F(2,4)=5.87$, $p=.065$, $\eta^2=.746$.

a)



b)

c)

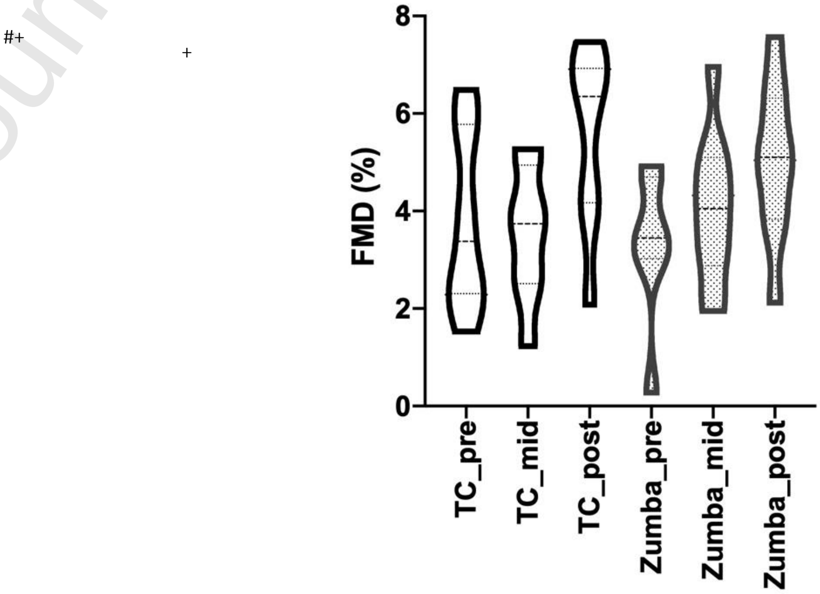


Figure 2. a) Diastolic blood pressure, b) Systolic blood pressure, and c) flow mediated dilation at baseline, mid and end intervention. Data are expressed as mean ± SE. # indicates significantly different as compared to pre training, + indicates significantly different compare to mid training

Table 2 presents data for physical fitness, as assessed by a submaximal treadmill test, at baseline and end intervention. Significant time, $F(1,17)=13.72$, $p=.002$, $\eta^2=.447$, and group x time interaction, $F(1,17)=6.56$, $p=.020$, $\eta^2=.278$, effects were found for fitness, but no overall group effect ($p=.88$). Further analysis showed that physical fitness was improved in the Zumba Gold® group with $p<.001$ following intervention, but no such change was found following Tai Chi.

Four measures of physical function were undertaken to provide insight into both upper and lower body flexibility (See Table 2). Measures were not different when the two groups were compared at baseline, with the exception of lower body flexibility (Chair sit and reach test). Participants in the Zumba Gold® group had better lower body flexibility $t(19)= -2.305$, $p=.033$). Following intervention, there was an improvement in lower body flexibility, with a significant time effect, $F(1,9)=5.17$ $p=.049$, and group effect $F(1,9) = 7.68$ $p=.022$, but no time by group interaction effect. A significant time effect for timed up and go, $F(1,19)=10.61$, $p=.004$, $\eta^2=.358$) showed that participants in both groups completed the task faster following the intervention period, however there were no group ($p=.156$) or group x time interaction ($p=.934$) effects. There was an increase in repetition time in the 30 seconds chair stand test at end intervention in both groups. A repeated measures ANOVA yielded a significant time effect, $F(1,19)=24.87$, $p<.001$, $\eta^2=.567$, but no significant group ($p=.553$) or group x time interaction ($p=.510$) effect. Secondary analyses in participants in the Tai Chi group only showed an significant improvement the chair stand test, $F(1,10)=7.45$, $p=.021$, $\eta^2= .427$, but no change in the timed up and go assessment ($p=.083$).

Table 2. Physical Fitness and Markers of Physical Function relating to flexibility (back scratch and chair sit and reach) and muscle strength (Timed up and go and 30 second chair stand) were assessed at baseline (0 weeks) and end intervention (12 weeks). Data are expressed as mean ± (S.E) * indicates significantly different compared to baseline.

		Tai Chi		Zumba	
		Baseline	End Intervention	Baseline	End Intervention
Physical Fitness	Submaximal test (mg/kg/min)	23.8 (2.8)	24.6 (5.4)	26.6 (2.3)	31.5 (5.0)
Physical Function	Back Scratch	-7.7 (7.4)	-7.3 (9.1)	-3.0 (7.4)	-1.0 (6.3)
	Chair sit and Reach	-2.8 (8.3)	0.5 (10.8)	6.4 (10.0)	10.6 (6.4)
	Timed up and Go	7.7 (1.7)	6.9 (1.1)	6.9 (1.4)	6.1* (1.2)
	30 Second Chair stand	13.5 (2.8)	15.9# (4.4)	14.3 (5.3)	17.4* (5.0)

Markers of oxidative stress were assessed at baseline and end intervention. At baseline the Zumba Gold® group had a lower protein oxidation (1.16 nmol/mg compared to 2.97nmol/mg) on average than those in the Tai Chi group. Total antioxidant capacity (Figure 2a) increased in both groups, whilst markers of lipid (figure 2b) and protein (figure 2c) oxidation decreased at end intervention compared to baseline.

Statistical analysis of data suggested that although there appeared to be an increase in the total antioxidant capacity over time, $F(1,18) = 6.43$, $p=.021$, $\eta^2=.263$, there were no statistically significant group ($p=.785$) or group x time effects ($p=.746$). Analysis of protein oxidation showed a time effect, $F(1,16)=9.09$, $p=.008$, $\eta^2=.362$, and a group effect, $F(1,16) = 156.84$, $\eta^2=.907$, but no group x time interaction effect ($p=.229$). For protein oxidation a group × time ANOVA revealed a significant time effect, $F(1,19)=17.01$, $p=.001$, $\eta^2= .472$, but no group effect ($p=.585$) or significant group x time interaction effect ($p=.092$). Given our specific interest in Tai Chi, when exploring the Tai Chi group only, significant changes were found for total antioxidant capacity, $F(1,10) = 5.62$, $p=.039$, $\eta^2=.360$, protein oxidation, $F(1,8)=6.35$, $p=.036$, $\eta^2=.442$, and lipid oxidation, $F(1,10) = 16.43$, $p=.002$, $\eta^2= .622$.

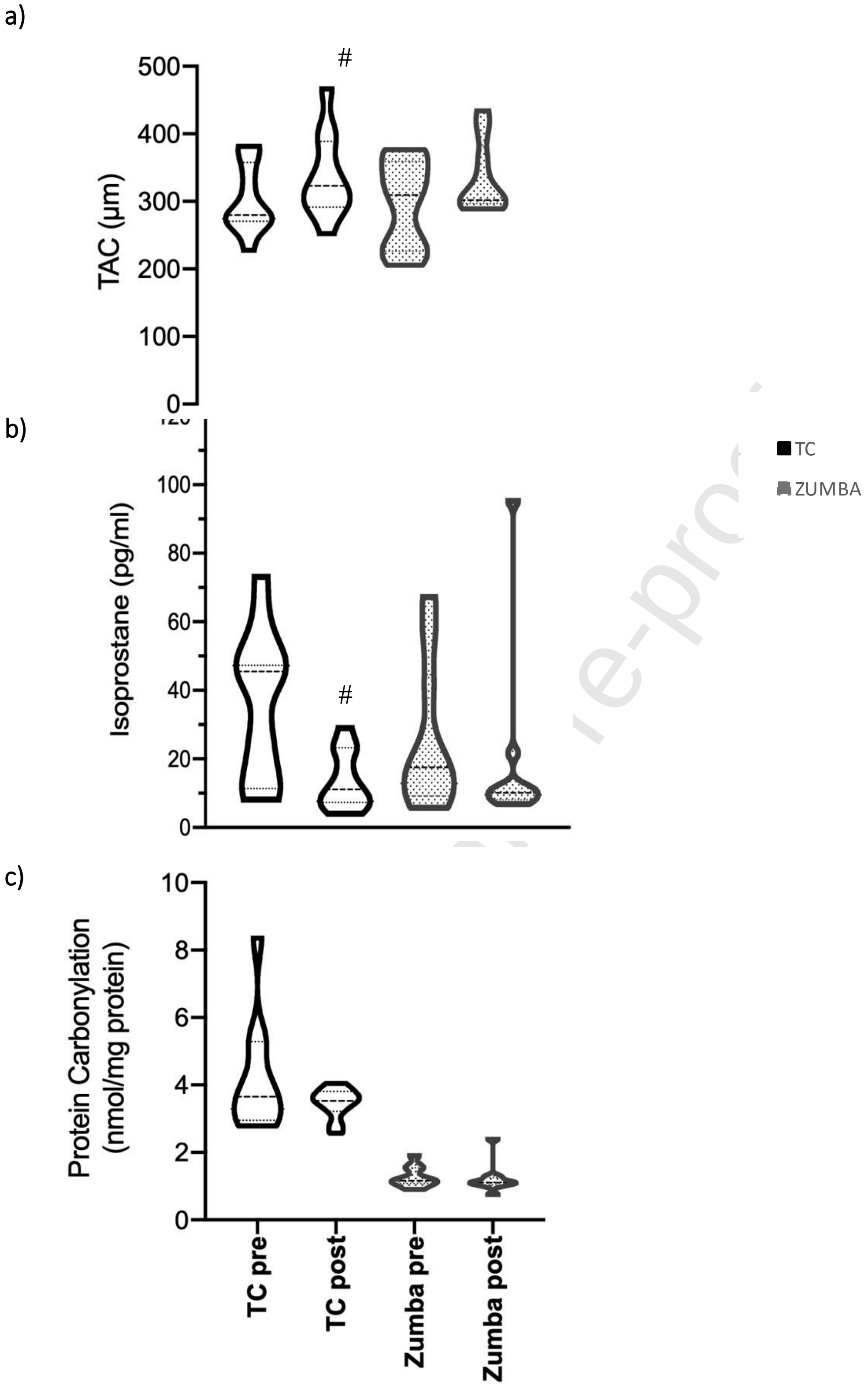


Figure 3. a) Total antioxidant capacity, **b)** Lipid peroxidation and **c)** protein oxidation assessed at baseline and end intervention. Data are expressed as mean ± SE. # indicates significantly different relative to pre training.

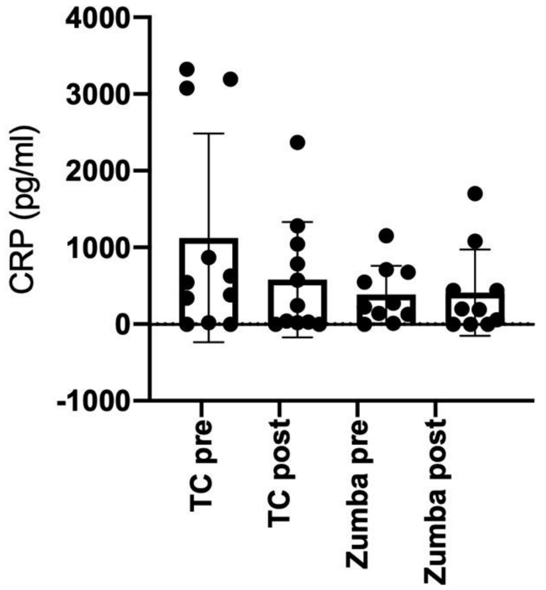


Figure 4. CRP assessed at baseline and end intervention. Data are expressed as mean ± SE.

Figure 4 shows the plasma concentration of CRP. ANOVAs revealed no group, time, group × time interaction effects for these inflammatory markers. In the Tai Chi Group a Wilcoxon matched pairs analysis showed a trend to decreased CRP post Tai Chi (p=0.09).

Table 3 presents the wellbeing data for both groups at baseline and post-intervention. There were baseline differences in some fatigue-reated outcomes, with general, physical and mental fatigue as well as reduced motivation higher in people allocated to the Tai Chi group. Group by time ANOVAs revealed a time effect for anxiety, $F(1, 19) = 8.44$, $p=.009$, $\eta^2=.308$, indicating a reduction in anxiety post intervention. There were also significant time effects for physical fatigue, $F(1,19) = 9.76$, $p=.006$, $\eta^2=.339$, and mental fatigue, $F(1,19) = 4.94$, $p=.039$, $\eta^2=.206$, with the markers of fatigue lower post-intervention compared to baseline. The Group by Time interaction effect for mental fatigue, $F(1,19) = 5.72$, $p=.027$, $\eta^2=.231$, revealed that the reduction in mental fatigue was greater following Tai Chi compared to Zumba Gold. Finally, group effects were evident for physical fatigue, $F(1,19) = 7.50$, $p=.013$, $\eta^2=.283$, mental fatigue, $F(1,19) = 4.57$, $\eta^2=.194$, and reduced motivation, $F(1,19) = 8.88$, $p=.008$, $\eta^2=.319$, which were all significantly higher in Tai Chi compared to Zumba Gold. No significant time, group or group by time interaction effects were found for perceived mental or physical health. In addition, a significant time effect was evident for sleep quality, $F(1,19) = 14.71$, $p=.001$, $\eta^2=.436$. Given the specific interest in the Tai Chi intervention, additional analyses were conducted to explore the effects in the Tai Chi group only. This revealed a significant improvements in physical fatigue, ($F(1,10) = 6.14$, $p = .033$, η^2=.380, mental fatiguie, $F(1,10) = 7.56$, p=.020, η^2=.431 , and sleep quality, $F(1,10)$=5.71, p=.038, η^2=.364.

Table 3. Mean (SD) baseline and post-intervention wellbeing measures for the Tai Chi and Zumba groups. ** significantly different from Tai Chi, p<.05, p-values based on Group × Time ANOVAs. PCS: Physical Health – SF12, MCS: Mental Health – SF12.*

	Baseline		Post intervention		p-values of ANOVA		
	Tai Chi	Zumba	Tai Chi	Zumba	Time	Group × Time	Group
Anxiety	4.5 (3.9)	5.3 (4.3)	3.7 (4.0)	4.1 (3.2)	.009	.485	.717
Depression	3.1 (4.2)	2.5 (2.7)	2.9 (3.1)	2.7 (3.1)	.979	.586	.780
General fatigue	10.2 (2.3)	7.5 (3.2)*	8.6 (3.4)	7.5 (3.7)	.288	.288	.124
Physical fatigue	10.3 (2.5)	7.0 (3.1)*	7.6 (2.5)	5.8 (1.9)	.006	.257	.013
Mental fatigue	9.7 (3.0)	6.4 (2.4)*	7.0 (2.1)	6.5 (2.1)	.039	.027	.046
Reduced activity	9.8 (3.5)	6.6 (4.2)	7.6 (3.3)	5.7 (2.6)	.054	.385	.067
Reduced motivation	9.6 (2.9)	6.1 (2.0)*	7.8 (2.9)	5.8 (2.6)	.143	.288	.008
Subjective vitality	4.6 (1.0)	5.1 (0.7)	4.6 (0.9)	5.2 (0.8)	.554	.554	.194
PCS	52.4 (9.3)	52.2 (9.3)	52.5 (8.9)	55.2 (6.0)	.243	.258	.724
MCS	41.4 (3.3)	43.1 (3.2)	43.0 (6.0)	44.2 (4.5)	.261	.794	.361
Sleep Quality	2.1 (0.7)	2.1 (0.7)	1.7 (0.8)	1.6 (0.5)	.001	.552	.836

Discussion

The aim of this study was to explore the potential of Tai Chi as an intervention to reduce markers of frailty. Tai Chi was compared to Zumba Gold®, rather than a resting control, in order to investigate the potential of a perceived low impact form of exercise, compared to a moderate form of exercise, to reduce markers of frailty. The most common barriers to exercise reported by older age adults are lack of interest and motivation, lack of time and fear of injury or falls (Franco, Tong et al. 2015). Therefore this study assessed Tai Chi as an exercise mode that might be appealing to older age adults, that is safe for this age group and that is undertaken as a group with an instructor. These elements were considered important to achieve a successful intervention, for example, using a trainer led group setting can motivate participants compared to an individual exercise programme (Ntoumanis, Thogersen-Ntoumani et al. 2017). Tai Chi was compared to Zumba Gold®, which was selected due to its aerobic nature and appropriateness for an older adult population (Dalleck, Roos et al. 2015). Zumba Gold® was also undertaken with an instructor as a group session and thus mimicked the group interaction of participants to the Tai Chi group.

Following 3 months of exercise training, a significant improvement in endothelium dependent dilation was observed in both the Tai Chi and Zumba Gold® groups (figure 1c). These changes suggest that both forms of exercise are beneficial in reducing risk of cardiovascular disease, which has been strongly associated with frailty (Fried, Tangen et al. 2001). The benefits of Tai Chi on cardiorespiratory health have been reported (Lu, Hui-Chan et al. 2013, Song, Xu et al. 2014, Zheng, Li et al. 2015). In line with previous studies (Lu and Kuo 2006, Lauche, Peng et al. 2017) the current study reported a reduction in blood pressure. To our knowledge, only one other study has assessed the effect of Tai Chi on vascular function using FMD (Shin, Lee et al. 2015). That study, by Shin, Lee et al. (2015) looked at the ability of Tai Chi to improve endothelial function and arterial stiffness in elderly women with rheumatoid arthritis and reported smaller improvements than those detected in the current study. Other studies have reported improvements in vascular function in response to different exercise training modes of moderate intensity using aerobic exercise (Westhoff, Franke et al. 2007, Swift, Weltman et al. 2014), a combination of aerobic and resistance exercise (Miche, Herrmann et al. 2006), and resistance exercise using hand grip (Badrov, Freeman et al. 2016). However, the current study is the first to report improvements in vascular function following a Tai Chi intervention in healthy older adults, and showed that these improvements were evident even in the absence of significant improvements in cardiorespiratory fitness.

It has been suggested that physical activity has the potential to improve endothelial function by reducing oxidative stress and inflammation (Korsager Larsen and Matchkov 2016), as well as increases in shear stress on the vasculature during physical activity (Wilson, Ellison et al. 2015). The importance of oxidative stress and inflammation in the frailty phenotype is increasing (Liu, Lyass et al. 2016, Zhu, Liu et al. 2016) and these markers offer an opportunity to understand the potential mechanisms of action of exercise on the frailty phenotype. Indeed numerous studies have reported that moderate-intensity exercise intervention can reduce age-related increases oxidative stress and inflammation (Ji 2001, Konig, Wagner et al. 2001, Yu and Chung 2006, Ji 2008, Mendoza-Nunez, Hernandez-Monjaraz et al. 2014, Mendoza-Nunez, Arista-Ugalde et al. 2018). In line with this, markers of oxidative stress (8-isoprostane) and antioxidant capacity were significantly altered following 12 weeks of Tai Chi. The present study is the first to show that Tai Chi has the ability to alter circulating redox status.

Older age adults experiencing the early phases of the frailty phenotype commonly see a reduction in physical function and fitness which can not only cause a loss in independence, but can also contribute to increasing incidence of falls. A high risk of falls is associated with frailty and has been reported to be due to poor balance and reduced muscle strength and endurance (Lang, Michel et al. 2009), but exercise can improve both balance and muscle strength. In the present study, two functional measures of balance and strength were assessed: timed up and go test and 30 seconds chair stand. Participants in the Zumba Gold® group showed a significant improvement in these measures after 12 weeks. Looking at the nature of the Zumba Gold® routines, this is not surprising given dance routines such as Merengue and Salsa, which involve lower limb muscle movement. For participants in the Tai Chi group, improvements in these assessments were also seen, but these were only statistically significant for leg strength and movement. Even though Tai Chi involves less intense lower limb movement compared to Zumba Gold®, the improvements in the Tai Chi group are likely to be due to the 'feel the ground' philosophy in Tai Chi. Feel the ground is the basic concept of standing with your knees slightly bent, and channelling all your weight equally through both legs, which helps the development of balance and muscle strength, especially calf muscles. Both groups improved upper and lower body flexibility. Several studies have suggested that Tai Chi can improve aspects of physical functioning in older adults (Lan, Lai et al. 2002, Faber, Bosscher et al. 2006, Zeeuwe, Verhagen et al. 2006, Frye, Scheinthal et al. 2007, Chin, van Uffelen et al. 2008, Song, Zhang et al. 2014) but this is the first study to directly compare Tai Chi to a form of aerobic exercise, and to assess aspects of physical function together with outcomes of vascular, metabolic and mental health. Together these improvements in balance, muscle strength, and flexibility all contribute to enhanced functional ability to be able to conduct everyday tasks in life.

Whilst some measures of well-being such as anxiety are not part of the classical frailty phenotype, physical and mental fatigue speak to the well established exhaustion frailty criteria. In our measures of well-being, anxiety, physical and mental fatigue were lower following the exercise interventions. Interestingly, the decrease in mental fatigue was greater following Tai Chi. However, it should be acknowledged that mental fatigue was higher in the Tai Chi group at baseline, which could have contributed to this significant interaction effect. Given the improvements in physiological outcome measures, it is perhaps surprising that no other markers of positive or negative wellbeing were changed following the intervention. A potential explanation for this lack of improvement following either Tai Chi or Zumba Gold exercise, could be due to the relatively high levels of wellbeing in the participants at baseline. For example, given that a depression score of 8 or higher on the HADS can be considered as experiencing mild depressive symptoms, the average score of below 3 for the participants in the current study indicates that the participants had very low levels of depression. Therefore it is possible that there was a ceiling effect, which made it difficult for participants to improve their wellbeing. It is also possible that in order to achieve further improvements in wellbeing in those with relatively high levels of wellbeing, more intense exercise is necessary. In line with this suggestion, it has been found that in those who are not physically active, a reduction in all-cause mortailty risk can be achieved by low levels of exercise (non-exercise activity). Whereas more intensive exercise is necessary to achieve a reduction in all-cause mortailty in those who are active (Matthews, Moore et al. 2015). However, without specifically testing these hypotheses, this will remain speculation.

This study did not include a control (no exercise) group. Whilst a control group or social interaction group could have been implemented to meet 3 times a week, to mimick the exercise commitment and allow exposure to social interaction, there are already many reports about the value of social interaction for older adults (Segel-Karpas, Ayalon, & Lachman, 2018; Tiikkainen & Heikkinen, 2005). A strength of this study is that Zumba Gold® was used as an exercise control. Zumba Gold® could be considered as an aerobic form of exercise, and the benefits of aerobic exercise have been very well characterised in older age adults. This study experienced a 40% dropout during the intervention, which was higher than the anticipated 30% previously seen in studies using exercise interventions in older age adults (Farrance, Tsofliou et al. 2016). Therefore, the number of participants completing the study was lower than expected which inevitably impacted the statistical power of this study. However, exploration of the effect sizes of the non-significant findings revealed in general low effect sizes (all η^2's < .182). Therefore, it is unlikely the non-significant findings were due to low sample size.

This study presents data to show that twelve weeks of Tai Chi improved markers of physiological and psychological health which make up the frailty phenotype in older age adults. Tai Chi is capable of stimulating similar improvements in vascular function, physical function and quality of life as an aerobic mode of exercise such as Zumba Gold®, especially in strengthening leg muscles and body endurance, and thus it has the capability to reduce frailty.

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References:

Badrov, M. B., S. R. Freeman, M. A. Zokvic, P. J. Millar and C. L. McGowan (2016). "Isometric exercise training lowers resting blood pressure and improves local brachial artery flow-mediated dilation equally in men and women." Eur J Appl Physiol **116**(7): 1289-1296.
Benzie, I. F. and J. J. Strain (1999). "Ferric reducing/antioxidant power assay: direct measure of total antioxidant activity of biological fluids and modified version for simultaneous measurement of total antioxidant power and ascorbic acid concentration." Methods Enzymol. **299**: 15-27.
Borg, G. A. (1982). "Psychophysical bases of perceived exertion." Med Sci Sports Exerc **14**(5): 377-381.
Buysse, D. J., C. F. Reynolds, 3rd, T. H. Monk, S. R. Berman and D. J. Kupfer (1989). "The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research." Psychiatry Res **28**(2): 193-213.
Carty, J. L., R. Bevan, H. Waller, N. Mistry, M. Cooke, J. Lunec and H. R. Griffiths (2000). "The effects of vitamin C supplementation on protein oxidation in healthy volunteers." Biochem.Biophys.Res.Commun. **273**(2): 729-735.
Chin, A. P. M. J., J. G. van Uffelen, I. Riphagen and W. van Mechelen (2008). "The functional effects of physical exercise training in frail older people : a systematic review." Sports Med **38**(9): 781-793.
Clegg, A., J. Young, S. Iliffe, M. O. Rikkert and K. Rockwood (2013). "Frailty in elderly people." Lancet **381**(9868): 752-762.
Dalleck, L. C., K. A. Roos, B. R. Byrd and R. M. Weatherwax (2015). "Zumba Gold((R)): Are The Physiological Responses Sufficient to Improve Fitness in Middle-Age to Older Adults?" J Sports Sci Med **14**(3): 689-690.
Davies, S. A., F; McBride, M; Calderwood, C (2019). UK Chief Medical Officers' Physical Activity Guidelines. Gov.uk.
de Labra, C., C. Guimaraes-Pinheiro, A. Maseda, T. Lorenzo and J. C. Millan-Calenti (2015). "Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials." BMC Geriatr **15**: 154.
Deepa, S. S., S. Bhaskaran, S. Espinoza, S. V. Brooks, A. McArdle, M. J. Jackson, H. Van Remmen and A. Richardson (2017). "A new mouse model of frailty: the Cu/Zn superoxide dismutase knockout mouse." Geroscience **39**(2): 187-198.
Devereux-Fitzgerald, A., R. Powell, A. Dewhurst and D. P. French (2016). "The acceptability of physical activity interventions to older adults: A systematic review and meta-synthesis." Soc Sci Med **158**: 14-23.
Dillon, C. B., E. McMahon, G. O'Regan and I. J. Perry (2018). "Associations between physical behaviour patterns and levels of depressive symptoms, anxiety and well-being in middle-aged adults: a cross-sectional study using isotemporal substitution models." BMJ Open **8**(1): e018978.
Domene, P. A., H. J. Moir, E. Pummell, A. Knox and C. Easton (2016). "The health-enhancing efficacy of Zumba(R) fitness: An 8-week randomised controlled study." J Sports Sci **34**(15): 1396-1404.
Faber, M. J., R. J. Bosscher, A. P. M. J. Chin and P. C. van Wieringen (2006). "Effects of exercise programs on falls and mobility in frail and pre-frail older adults: A multicenter randomized controlled trial." Arch Phys Med Rehabil **87**(7): 885-896.
Farrance, C., F. Tsofliou and C. Clark (2016). "Adherence to community based group exercise interventions for older people: A mixed-methods systematic review." Prev Med **87**: 155-166.
Franco, M. R., A. Tong, K. Howard, C. Sherrington, P. H. Ferreira, R. Z. Pinto and M. L. Ferreira (2015). "Older people's perspectives on participation in physical activity: a systematic review and thematic synthesis of qualitative literature." Br J Sports Med **49**(19): 1268-1276.

Fried, L. P., C. M. Tangen, J. Walston, A. B. Newman, C. Hirsch, J. Gottdiener, T. Seeman, R. Tracy, W. J. Kop, G. Burke and M. A. McBurnie (2001). "Frailty in older adults: evidence for a phenotype." The journals of gerontology. Series A, Biological sciences and medical sciences **56**(3): M146-156.
Frye, B., S. Scheinthal, T. Kemarskaya and R. Pruchno (2007). "Tai Chi and Low Impact Exercise: Effects on the Physical Functioning and Psychological Well-Being of Older People." Journal of Applied Gerontology **26**(5): 433-453.
Gandek, B., J. E. Ware, N. K. Aaronson, G. Apolone, J. B. Bjorner, J. E. Brazier, M. Bullinger, S. Kaasa, A. Leplege, L. Prieto and M. Sullivan (1998). "Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment." J Clin Epidemiol **51**(11): 1171-1178.
Gomez-Cabrera, M. C., E. Domenech and J. Vina (2008). "Moderate exercise is an antioxidant: upregulation of antioxidant genes by training." Free Radic Biol Med **44**(2): 126-131.
Harris, R. A. (2010). "FMD, reproducibility, and acute exercise in the obese: are the results confounded?" Eur J Appl Physiol **109**(2): 357-358.
Hass, C. J., R. J. Gregor, D. E. Waddell, A. Oliver, D. W. Smith, R. P. Fleming and S. L. Wolf (2004). "The influence of Tai Chi training on the center of pressure trajectory during gait initiation in older adults." Arch Phys Med Rehabil **85**(10): 1593-1598.
Huang, X. Y., W. Eungpinichpong, A. Silsirivanit, S. Nakmareong and X. H. Wu (2014). "Tai chi improves oxidative stress response and DNA damage/repair in young sedentary females." J Phys Ther Sci **26**(6): 825-829.
Ingles, M., J. Gambini, J. A. Carnicero, F. J. Garcia-Garcia, L. Rodriguez-Manas, G. Olaso-Gonzalez, M. Dromant, C. Borras and J. Vina (2014). "Oxidative stress is related to frailty, not to age or sex, in a geriatric population: lipid and protein oxidation as biomarkers of frailty." J Am Geriatr Soc **62**(7): 1324-1328.
Ji, L. L. (2001). "Exercise at old age: does it increase or alleviate oxidative stress?" Ann.N.Y.Acad.Sci. **928**: 236-247.
Ji, L. L. (2008). "Modulation of skeletal muscle antioxidant defense by exercise: Role of redox signaling." Free Radic Biol Med **44**(2): 142-152.
Konig, D., K. H. Wagner, I. Elmadfa and A. Berg (2001). "Exercise and oxidative stress: significance of antioxidants with reference to inflammatory, muscular, and systemic stress." Exerc Immunol Rev **7**: 108-133.
Korsager Larsen, M. and V. V. Matchkov (2016). "Hypertension and physical exercise: The role of oxidative stress." Medicina (Kaunas) **52**(1): 19-27.
Lan, C., J. S. Lai and S. Y. Chen (2002). "Tai Chi Chuan: an ancient wisdom on exercise and health promotion." Sports Med **32**(4): 217-224.
Lan, C., J. S. Lai, S. Y. Chen and M. K. Wong (1998). "12-month Tai Chi training in the elderly: its effect on health fitness." Med Sci Sports Exerc **30**(3): 345-351.
Lang, P. O., J. P. Michel and D. Zekry (2009). "Frailty syndrome: a transitional state in a dynamic process." Gerontology **55**(5): 539-549.
Lauche, R., W. Peng, C. Ferguson, H. Cramer, J. Frawley, J. Adams and D. Sibbritt (2017). "Efficacy of Tai Chi and qigong for the prevention of stroke and stroke risk factors: A systematic review with meta-analysis." Medicine (Baltimore) **96**(45): e8517.
Li, G., H. Yuan and W. Zhang (2014). "Effects of Tai Chi on health related quality of life in patients with chronic conditions: a systematic review of randomized controlled trials." Complement Ther Med **22**(4): 743-755.
Liberman, K., L. N. Forti, I. Beyer and I. Bautmans (2017). "The effects of exercise on muscle strength, body composition, physical functioning and the inflammatory profile of older adults: a systematic review." Curr Opin Clin Nutr Metab Care **20**(1): 30-53.

Liu, C. K., A. Lyass, M. G. Larson, J. M. Massaro, N. Wang, R. B. D'Agostino, Sr., E. J. Benjamin and J. M. Murabito (2016). "Biomarkers of oxidative stress are associated with frailty: the Framingham Offspring Study." Age (Dordr) **38**(1): 1.
Liu, Z., Q. Wang, T. Zhi, Y. Zhu, Y. Wang, Z. Wang, J. Shi, X. Xie, X. Chu, X. Wang and X. Jiang (2016). "Frailty Index and Its Relation to Falls and Overnight Hospitalizations in Elderly Chinese People: A Population-based Study." J Nutr Health Aging **20**(5): 561-568.
Lu, W. A. and C. D. Kuo (2006). "Comparison of the effects of Tai Chi Chuan and Wai Tan Kung exercises on autonomic nervous system modulation and on hemodynamics in elder adults." Am J Chin Med **34**(6): 959-968.
Lu, X., C. W. Hui-Chan and W. W. Tsang (2013). "Tai Chi, arterial compliance, and muscle strength in older adults." Eur J Prev Cardiol **20**(4): 613-619.
Matthews, C. E., S. C. Moore, J. Sampson, A. Blair, Q. Xiao, S. K. Keadle, A. Hollenbeck and Y. Park (2015). "Mortality Benefits for Replacing Sitting Time with Different Physical Activities." Med Sci Sports Exerc **47**(9): 1833-1840.
McIsaac, D. I., T. Jen, N. Mookerji, A. Patel and M. M. Lalu (2017). "Interventions to improve the outcomes of frail people having surgery: A systematic review." PLoS One **12**(12): e0190071.
McLeod, A. I. (1985). " A remark on algorithm AS 183. An efficient and portable pseudo-random number generator." Applied Statistics **34**: 198-200.
Mendoza-Nunez, V. M., T. L. Arista-Ugalde, J. Rosado-Perez, M. Ruiz-Ramos and E. Santiago-Osorio (2018). "Hypoglycemic and antioxidant effect of Tai chi exercise training in older adults with metabolic syndrome." Clin Interv Aging **13**: 523-531.
Mendoza-Nunez, V. M., B. Hernandez-Monjaraz, E. Santiago-Osorio, J. M. Betancourt-Rule and M. Ruiz-Ramos (2014). "Tai Chi exercise increases SOD activity and total antioxidant status in saliva and is linked to an improvement of periodontal disease in the elderly." Oxid Med Cell Longev **2014**: 603853.
Miche, E., G. Herrmann, M. Nowak, U. Wirtz, M. Tietz, M. Hurst, B. Zoller and A. Radzewitz (2006). "Effect of an exercise training program on endothelial dysfunction in diabetic and non-diabetic patients with severe chronic heart failure." Clin Res Cardiol **95 Suppl 1**: i117-124.
Mochcovitch, M. D., A. C. Deslandes, R. C. Freire, R. F. Garcia and A. E. Nardi (2016). "The effects of regular physical activity on anxiety symptoms in healthy older adults: a systematic review." Braz J Psychiatry **38**(3): 255-261.
Muller, A. M. and S. Khoo (2014). "Non-face-to-face physical activity interventions in older adults: a systematic review." Int J Behav Nutr Phys Act **11**(1): 35.
Ntoumanis, N., C. Thogersen-Ntoumani, E. Quested and J. Hancox (2017). "The effects of training group exercise class instructors to adopt a motivationally adaptive communication style." Scand J Med Sci Sports **27**(9): 1026-1034.
Palasuwan, A., D. Suksom, I. Margaritis, S. Soogarun and A. S. Rousseau (2011). "Effects of tai chi training on antioxidant capacity in pre- and postmenopausal women." J Aging Res **2011**: 234696.
Piercy, K. L., R. P. Troiano, R. M. Ballard, S. A. Carlson, J. E. Fulton, D. A. Galuska, S. M. George and R. D. Olson (2018). "The Physical Activity Guidelines for Americans." JAMA **320**(19): 2020-2028.
Rhyner, K. T. and A. Watts (2016). "Exercise and Depressive Symptoms in Older Adults: A Systematic Meta-Analytic Review." J Aging Phys Act **24**(2): 234-246.
Rikli, R. E. and C. J. Jones (2013). "Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years." Gerontologist **53**(2): 255-267.
Rogers, C. E., L. K. Larkey and C. Keller (2009). "A review of clinical trials of tai chi and qigong in older adults." West J Nurs Res **31**(2): 245-279.
Rosado-Perez, J., R. Ortiz, E. Santiago-Osorio and V. M. Mendoza-Nunez (2013). "Effect of Tai Chi versus walking on oxidative stress in Mexican older adults." Oxid Med Cell Longev **2013**: 298590.

Rosado-Perez, J., E. Santiago-Osorio, R. Ortiz and V. M. Mendoza-Nunez (2012). "Tai chi diminishes oxidative stress in Mexican older adults." J Nutr Health Aging **16**(7): 642-646.
Ryan, R. M. and C. Frederick (1997). "On energy, personality, and health: subjective vitality as a dynamic reflection of well-being." J Pers **65**(3): 529-565.
Santos, D. A., A. M. Silva, F. Baptista, R. Santos, S. Vale, J. Mota and L. B. Sardinha (2012). "Sedentary behavior and physical activity are independently related to functional fitness in older adults." Exp Gerontol **47**(12): 908-912.
Sardinha, L. B., U. Ekelund, L. dos Santos, E. S. Cyrino, A. M. Silva and D. A. Santos (2015). "Breaking-up sedentary time is associated with impairment in activities of daily living." Exp Gerontol **72**: 278.
Sardinha, L. B., D. A. Santos, A. M. Silva, F. Baptista and N. Owen (2015). "Breaking-up sedentary time is associated with physical function in older adults." J Gerontol A Biol Sci Med Sci **70**(1): 119-124.
Shin, J. H., Y. Lee, S. G. Kim, B. Y. Choi, H. S. Lee and S. Y. Bang (2015). "The beneficial effects of Tai Chi exercise on endothelial function and arterial stiffness in elderly women with rheumatoid arthritis." Arthritis Res Ther **17**: 380.
Smets, E. M., B. Garssen, B. Bonke and J. C. De Haes (1995). "The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue." J Psychosom Res **39**(3): 315-325.
Smith, P. K., R. I. Krohn, G. T. Hermanson, A. K. Malia, F. H. Gartner, M. D. Provenzano, E. K. Fujimoto, N. M. Goeke, B. J. Olson and D. C. Klenk (1985). "Measurement of protein using Bicinchoninic acid." Analytical Biochemistry **150**: 76-85.
Song, Q. H., R. M. Xu, G. Q. Shen, Q. H. Zhang, M. Ma, X. P. Zhao, Y. H. Guo and Y. Wang (2014). "Influence of Tai Chi exercise cycle on the senile respiratory and cardiovascular circulatory function." Int J Clin Exp Med **7**(3): 770-774.
Song, Q. H., Q. H. Zhang, R. M. Xu, M. Ma, X. P. Zhao, G. Q. Shen, Y. H. Guo and Y. Wang (2014). "Effect of Tai-chi exercise on lower limb muscle strength, bone mineral density and balance function of elderly women." Int J Clin Exp Med **7**(6): 1569-1576.
Stathi, A., J. Withall, C. J. Greaves, J. L. Thompson, G. Taylor, A. Medina-Lara, C. Green, J. Bilzon, S. Gray, H. Johansen-Berg, C. E. Sexton, M. J. Western, J. L. de Koning, J. C. Bollen, S. J. Moorlock, N. Demnitz, P. Seager, J. M. Guralnik, W. Jack Rejeski and K. R. Fox (2018). "A community-based physical activity intervention to prevent mobility-related disability for retired older people (REtirement in ACTion (REACT)): study protocol for a randomised controlled trial." Trials **19**(1): 228.
Suksom, D., A. Siripatt, P. Lapo and S. Patumraj (2011). "Effects of two modes of exercise on physical fitness and endothelial function in the elderly: exercise with a flexible stick versus Tai Chi." J Med Assoc Thai **94**(1): 123-132.
Swift, D. L., J. Y. Weltman, J. T. Patrie, S. A. Saliba, G. A. Gaesser, E. J. Barrett and A. Weltman (2014). "Predictors of improvement in endothelial function after exercise training in a diverse sample of postmenopausal women." J Womens Health (Larchmt) **23**(3): 260-266.
Tanaka, H., K. D. Monahan and D. R. Seals (2001). "Age-predicted maximal heart rate revisited." J.Am.Coll.Cardiol. **37**(1): 153-156.
Tonet, E., E. Maietti, G. Chiaranda, F. Vitali, M. Serenelli, G. Bugani, G. Mazzoni, R. Ruggiero, J. Myers, G. Q. Villani, U. Corvi, G. Pasanisi, S. Biscaglia, R. Pavasini, G. R. Lucchi, G. Sella, R. Ferrari, S. Volpato, G. Campo and G. Grazzi (2018). "Physical activity intervention for elderly patients with reduced physical performance after acute coronary syndrome (HULK study): rationale and design of a randomized clinical trial." BMC Cardiovasc Disord **18**(1): 98.
Wadley, A. J., J. J. Veldhuijzen van Zanten and S. Aldred (2012). "The interactions of oxidative stress and inflammation with vascular dysfunction in ageing: the vascular health triad." Age.

Wadley, A. J., J. J. Veldhuijzen van Zanten and S. Aldred (2013). "The interactions of oxidative stress and inflammation with vascular dysfunction in ageing: the vascular health triad." Age (Dordr) **35**(3): 705-718.
Wang, J. S., C. Lan, S. Y. Chen and M. K. Wong (2002). "Tai Chi Chuan training is associated with enhanced endothelium-dependent dilation in skin vasculature of healthy older men." J Am Geriatr Soc **50**(6): 1024-1030.
Wang, X. Q., Y. L. Pi, P. J. Chen, Y. Liu, R. Wang, X. Li, B. L. Chen, Y. Zhu, Y. J. Yang and Z. B. Niu (2016). "Traditional Chinese Exercise for Cardiovascular Diseases: Systematic Review and Meta-Analysis of Randomized Controlled Trials." J Am Heart Assoc **5**(3): e002562.
Ware, J., Jr., M. Kosinski and S. D. Keller (1996). "A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity." Med Care **34**(3): 220-233.
Westhoff, T. H., N. Franke, S. Schmidt, K. Vallbracht-Israng, R. Meissner, H. Yildirim, P. Schlattmann, W. Zidek, F. Dimeo and M. van der Giet (2007). "Too old to benefit from sports? The cardiovascular effects of exercise training in elderly subjects treated for isolated systolic hypertension." Kidney Blood Press Res **30**(4): 240-247.
Wichmann, B. A., Hill, I.D (1982). " An efficient and portable pseudo-random number generator." Applied Statistics **31**: 188-190.
Wilson, M. G., G. M. Ellison and N. T. Cable (2015). "Basic science behind the cardiovascular benefits of exercise." Heart **101**(10): 758-765.
Wu, G., W. Liu, J. Hitt and D. Millon (2004). "Spatial, temporal and muscle action patterns of Tai Chi gait." J Electromyogr Kinesiol **14**(3): 343-354.
Wu, I. C., S. C. Shiesh, P. H. Kuo and X. Z. Lin (2009). "High oxidative stress is correlated with frailty in elderly chinese." J Am Geriatr Soc **57**(9): 1666-1671.
Xiang, Y., L. Lu, X. Chen and Z. Wen (2017). "Does Tai Chi relieve fatigue? A systematic review and meta-analysis of randomized controlled trials." PLoS One **12**(4): e0174872.
Yu, B. P. and H. Y. Chung (2006). "Adaptive mechanisms to oxidative stress during aging." Mech.Ageing Dev. **127**(5): 436-443.
Zeeuwe, P. E., A. P. Verhagen, S. M. Bierma-Zeinstra, E. van Rossum, M. J. Faber and B. W. Koes (2006). "The effect of Tai Chi Chuan in reducing falls among elderly people: design of a randomized clinical trial in the Netherlands [ISRCTN98840266]." BMC Geriatr **6**: 6.
Zheng, G., S. Li, M. Huang, F. Liu, J. Tao and L. Chen (2015). "The effect of Tai Chi training on cardiorespiratory fitness in healthy adults: a systematic review and meta-analysis." PLoS One **10**(2): e0117360.
Zhu, Y., Z. Liu, Y. Wang, Z. Wang, J. Shi, X. Xie, L. Jin, X. Chu and X. Wang (2016). "C-reactive protein, frailty and overnight hospital admission in elderly individuals: A population-based study." Arch Gerontol Geriatr **64**: 1-5.
Zigmond, A. S. and R. P. Snaith (1983). "The hospital anxiety and depression scale." Acta psychiatrica Scandinavica **67**(6): 361-370.

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Aldred: Conceptualization, Methodology, Supervision, Writing- Original draft preparation. **Fadila Kasim**: Investigation, data collection, ***Veldhuijzen van Zanten****:* Supervision. Conceptualization, Methodology, Writing- Reviewing and Editing.

Tai Chi is an effective form of exercise to reduce markers of frailty in older age.

Highlights:

- Exercise has the potential to prevent, delay or even reverse frailty, but not all exercise is perceived as suitable for an older age population.
- In this study twenty-one participants (65 to 75 years old) were recruited and randomized to a 12-week Tai Chi or Zumba Gold® exercise intervention.
- Tai Chi improved systolic blood pressure, vascular function, and functional fitness following the 12-week intervention.
- Antioxidant capacity was significantly increased and lipid oxidation significantly reduced after 12 weeks of Tai Chi compared to baseline.
- Anxiety, physical and mental fatigue decreased in the Tai Chi group after 12 weeks.
- These changes suggest that Tai Chi has the potential to reduce frailty in older age adults.