Effects of a Tabata-style functional high-intensity interval training intervention on cardiometabolic risk factors and physical activity in female university students

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Publications

1. Lu, Y., Wiltshire, H.D., Baker, J.S., and Wang, Q. (2021). Effects of High Intensity Exercise on Oxidative Stress and Antioxidant Status in Untrained Humans: A Systematic Review. Biology (Basel) 10(12). doi: 10.3390/biology10121272.
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Abstract:

The increasing prevalence of metabolic syndrome, obesity, and physical inactivity among young adults has accelerated the aggregation of cardiometabolic risk factors, which results in the increased risk of cardiovascular diseases (CVD). Although physical activity (PA) is a major modifiable risk factor for CVD, data from epidemiological studies showed that university students are experiencing a decrease in PA, especially in females. These emerging adults are facing critical changes in their lifestyle. University is an important stage in the establishment of long-term healthy lifestyles, and it provides an opportunity for interventions to improve cardiometabolic health and PA. High-intensity interval training (HIIT) delivered with low-volume has been popular among young people due to its time efficiency. However, there is limited data on the effects of a Tabata-style HIIT using functional exercises as the exercise modality. Moreover, the association between objectively measured PA and women's cardiometabolic health is uncertain. Therefore, the primary aim of this program was to examine the effects of a novel Tabata-style functional HIIT on cardiometabolic health and PA in female university students. The second aim was to determine the influence of PA changes on intervention effects. Study 1 was a meta-analysis review to explore the association between objectively measured PA with adiposity and cardiometabolic health in adult women. This data informs public health on the association between PA and health in women. Moreover, these relationships provided the theoretical basis for further research on the role of PA in intervention effects. Study 2 and study 3 were pilot studies and data from these studies was used to evaluate the effectiveness and feasibility of the Tabata-style functional HIIT. In study 2, the novel HIIT protocol was designed, involving 8 different functional movements. Its effectiveness, heart rate (HR) and perceived exertion responses, and exercise enjoyment were compared with the conventional running based HIIT. The results showed that, after a 12-week intervention, the Tabata-style functional HIIT was equally effective in improving cardiorespiratory fitness and body composition compared to the running based HIIT. Additionally, this novel HIIT was able to induce a required high-intensity exercise response (≥80% of maximal HR) and provide a more enjoyable training experience for the participants. These findings provided support for functional exercises as the training modality, and this data, together with findings from the post-intervention focus group, were used to improve the design of the novel HIIT intervention. In study 3, the novel HIIT protocol was refined by reducing 8 different movements to 4 and participants' HR and perceived exertion responses to short-term intervention were examined. Meanwhile, the compensatory movement behaviors following short-term novel HIIT were evaluated. The results indicated that untrained female university students were able to achieve the target high intensity responses. Moreover, the novel HIIT resulted in simultaneous increases in sedentary time, moderate-to-vigorous intensity PA and total PA in the short term. These findings confirmed the compensatory effect of short-term HIIT on PA, as well as the feasibility of this novel HIIT. These results provided the basis to implement a 12-week HIIT intervention in untrained female university students and to examine its effect on their habitual PA. During the main intervention, we conducted a cross-sectional study, which was study 4, to assess the association between blood pressure with dairy intake and PA based on pre-intervention data. The results showed that dairy intake, moderate-to-vigorous intensity PA and total PA were all independently associated with systolic blood pressure, indicating that dietary intake was a contributor to cardiometabolic health independent of exercise. This provided evidence for its inclusion as a covariate in the intervention effects. Study 5 evaluated the effects of a 12-week Tabata-style functional HIIT program (Project: Just Four Minutes) on multiple cardiometabolic biomarkers and habitual PA in female university students. A mixed linear model was used to assess the intervention effects. After the intervention, compared to the control, there were large intervention effects on maximal oxygen uptake, resting HR, systolic blood pressure, moderate-to-vigorous intensity PA, total PA; moderate effects on percentage body fat, fat mass, high-density lipoprotein (HDL), total cholesterol; small effects on body mass index, waist circumference, low-density lipoprotein, HOMA-IR and fasting insulin. Regression analysis showed that only the percentage change of HDL was associated with the change of moderate-to-vigorous intensity PA and total PA. Conclusively, this project appeared to be a feasible and effective way to improving cardiometabolic health and PA in female university students. Only the improvement on HDL was associated with the increase on PA. Overall, Project Just Four Minutes was an effective strategy to improve cardiometabolic health and PA in female university students.

Chapter 1: Introduction

Cardiovascular disease (CVD) remains the leading cause of mortality worldwide and managing cardiovascular risk factors can effectively reduce the incidence of CVD. Metabolic syndrome (MetS) refers to a combination of several known cardiometabolic risk factors, mainly including abdominal obesity, hypertension, impaired glucose metabolism, increased triglycerides, and decreased high-density lipoprotein [Ford et al., 2002]. Previous studies have suggested that adults with MetS have a substantially increased risk of developing CVD and all-cause mortality [Ford, 2005; Mottillo et al., 2010]. Furthermore, the American Heart Association has proposed a more comprehensive cardiovascular health metric expanding the focus on CVD prevention in addition to treatment [Benjamin et al., 2017]. These cardiovascular health metrics comprise of both healthy behaviors (healthy diet pattern, sufficient physical activity (PA), healthy weight, nonsmoking) and optimal biomarker levels (blood cholesterol, blood pressure (BP) and blood glucose). Although most CVDs emerge in the middle-aged and elderly population because aging is a major independent risk factor for CVD [North and Sinclair, 2012], epidemiological evidence has shown that young adults are increasingly exposed to cardiovascular risk factors and there is an increasing prevalence of CVDs among this population [Andersson and Vasan, 2018]. This is not surprising as atherosclerosis, one of the most common causes of CVD, has been found to start in childhood and develops throughout the lifespan [Oliveira et al., 2010]. Although the clinical manifestation of CVD is rare in young adults, early and excessive exposure to established risk factors may accelerate the atherosclerosis progress and increase the risk of premature death [Buchan et al., 2011]. Moreover, the delayed manifestation may provide an illusion to young adults that CVD and its risk factors are not something they need to worry about or pay attention to [Bibbins-Domingo and Burroughs Peña, 2010].

In recent years, university students have attracted increasing attention from both the public and scientific communities because they are at the crucial transition period of life when adolescence ends, and adulthood begins. These emerging adults experience major life changes and enjoy considerable autonomy in their lifestyle habits during university years. Therefore, developing healthy lifestyles during this transition period will greatly benefit their future health [Jang and Kim, 2019].

The most reported behavioral risk factors among university students are unhealthy weight gain, adiposity, inappropriate diet, and insufficient PA [Fedewa et al., 2014; Vadeboncoeur et al., 2016; Peltzer and Pengpid, 2018; Whatnall et al., 2020]. Several studies have investigated weight gain during university years, and generally report a rapid and unhealthy weight profile, especially during the first year of university, which is referred to as "Freshman 15" [Brown, 2008; Vella-Zarb and Elgar, 2009; Vadeboncoeur et al., 2016]. The "Freshman 15" is a popular perception that gaining 15 lbs (6.8kg) is common among freshmen. However, data from both cross-sectional and longitudinal studies reveal that the actual weight gain is between 1.6 [Butler et al., 2004] and 8.8 lbs [Hovell et al., 1985] with a previous meta-analysis showing an average weight gain of 3.86 lbs based on a pooled sample of 3401 students [Vella-Zarb and Elgar, 2009]. Although the "Freshman 15" appears to be an exaggeration, findings from scientific research reinforce the fact that most young adults are at risk for unhealthy weight gain during university years, which results in an increase in the prevalence of overweight and obesity among university students. Results from the American College Health Association - National College Health Assessment III Fall 2021 survey show that, among a sample of 33,204 students, 22.2% were overweight and 14.3% were obese [American College Health Association, 2022]. Similar prevalence of unhealthy weight was reported in a study of 3,077 Australian students in 2017 with 23.8% being overweight and 15.8% classified as obese [Whatnall et al., 2020]. Despite that data from Asian countries demonstrate a lower incidence of overweight and obesity of 10% among university students according to the traditional classification of obesity based on body mass index (BMI) [Kim et al., 2013; Jiang et al., 2018; Yamamoto et la., 2021], the prevalence of normal weight obesity (NWO) was high. NWO is a relatively new concept that is defined as having a normal BMI but an excessive percentage of body fat (%BF) [De Lorenzo et al., 2006]. NWO is an emerging concern as individuals with NWO are easily underdiagnosed and associated with higher risk of cardiometabolic morbidity and mortality [Wijayatunga and Dhurandhar, 2021]. It is estimated that the worldwide prevalence of NWO varies between 4.5% and 22% across countries [Wijayatunga and Dhurandhar, 2021], with most studies suggesting a higher incidence of NWO among women [Marques-Vidal et al, 2010; Ohlsson and Manjer, 2020]. Likewise, female university students are more likely to be NWO in China, with the prevalence ranging from 27.5% [Zhang et al., 2018] to 40.1% [Maitiniyazi et al., 2021].

Furthermore, there are concerns about dietary practice and PA in university students. This population tend to have higher consumption of fast foods, convenience foods and snack foods while having an insufficient intake of fruits and vegetables [Racette et al., 2005; Moreno-Gómez et al., 2012; Thorpe et al., 2014; El Ansari et al., 2011, 2012; Scarapicchia et al., 2015]. The most recent report from American College Health Assessment shows that 30.1% of American university students are eating 3 or more servings of vegetables per day, while only 16.5% are eating 3 or more servings of fruits [American College Health Association, 2022]. In a study conducted in Canada, only 10.2% of the 2,812 university students surveyed consumed 5 or more servings of vegetables and fruits per day [Scarapicchia et al., 2015]. In addition, 31.6% of British university students develop risky dietary behaviors characterized by excessive intake of convenience and fast foods and insufficient fruits and vegetables [Tanton et al., 2015] and more than 80% of Spanish university students have an unhealthy diet [Ramón-Arbués et al., 2021]. With regard to Chinese university students, they were reported to have more egg, fish and meat and less fast foods and carbonated drinks compared to international students. However, milk consumption was lower in Chinese students [UI Haq et al., 2018]. It is worth noting that gender has been shown to be a predictive factor of diet quality and being female is generally associated with a higher consumption of fruits and vegetables [El Ansari et al., 2011; McCartney et al., 2021] as well as a better diet quality [Ramón-Arbués et al., 2021].

As for PA, a mediocre level of PA is reported by a recent systematic review, in which the authors quantitatively synthesize 21 scientific studies with a total of 7306 students [Kljajevic et al., 2021]. However, there are still associated concerns about satisfactory levels of PA. On the one hand, regardless of the bias and methodological errors in assessing PA, the transition to university is often accompanied by an overall decline in PA [Bray and Born, 2004; Han et al., 2008; Kwan et al., 2012]. On the other hand, along with high levels of PA, substantial sedentary behavior (SB) is observed among university students and has been rising over the past decade [Peterson et al., 2018; Vainshelboim et al., 2019; Castro et al., 2020]. SB, especially the prolonged one, has been evidenced to be associated with several CVD risk factors independent of PA in both cross-sectional and longitudinal studies [Helmerhorst et al., 2009; Barone Gibbs et al., 2015, 2017; Golubic et al., 2015]. University students accumulate more than 7 hours per day being sedentary from self-reported data, while the total sedentary time is significantly increased to 9.82 hours when measured by accelerometers [Castro et al., 2020]. Attending classes, studying, and computing contribute most of the sedentary time, leaving limited hours for PA in university students [Cotten and Prapavessis, 2016; Carballo-Fazanes et al, 2020].

Health promotion strategies aimed at increasing PA [Sharp and Caperchione, 2016; Chiang et al., 2019; Heeren et al., 2018], improving eating habits [Lhakhang et al., 2014; Castillo et al., 2019; Whatnall et al., 2019; Hernández-Jaña et al., 2020], managing weight [Hivert et al., 2007], or a combination of these [Brown et al., 2014; Shin et al., 2017; Duan et al., 2017] have been widely used in the university or college setting. However, these interventions vary substantially in their implementation forms, contents and effectiveness and there remain controversy over the best way to intervene [Plotnikoff et al., 2015]. Some studies report that an integrated strategy combined with a dietary and PA intervention tends to have a more favorable effect on reducing the prevalence of obesity and improving health outcomes [Kass et al., 2017; Lv et al., 2017], while another systematic review suggests that diet-only interventions are more effective than interventions that targeted PA, obesity, or multiple behaviors [Plotnikoff et al., 2015]. Such discrepancy may be because most PA interventions are only theoretical-based and in absence of practical PA sessions, which play a vital role in the effectiveness of an PA intervention [Maselli et al., 2018]. However, the experimental-based PA program has several limitations that, on the one hand, it only focuses on a small number of students at one time; on the other hand, it may bring additional burdens to students as they already have too many classes [Sweeney, 2011; Kim et al., 2018]. Accordingly, a novel exercise intervention is needed to effectively improve PA and cardiometabolic portfolio in university students. For this purpose, a gender-specified strategy is needed, as male and female students differ in their response to health promotion interventions. The females show greater interest and motivation in these interventions [von Bothmer and Firdlund, 2005], but the effect of exercise intervention is more difficult to be observed than males [Brownell et al., 1982; Ponjee et al., 1995]. Furthermore, gender differences are suggested in the CVD risk factors since females have specific anatomical, hormonal, and cardiovascular features. For example, physically inactive women are more likely to be obese

[Vainshelboim et al., 2019], nevertheless, the magnitude of the association between PA and cardiometabolic health appears stronger in women [Shiroma and Lee, 2010]. More importantly, women carry particular risks that pre-pregnancy obesity increases the risk of preterm delivery [Cnattingius et al., 2013], as well as the impaired cognitive development of their infants [Casas et al., 2013]. Given that female students are less physically active than the males [Haase et al., 2004; Grasdalsmoen et al., 2019; American College Health Association, 2022] and moreover, there are few studies using objectively derived PA in this population [Keating et al., 2005], we determined to include female university students only and use accelerometer-determined PA in the current study.

High intensity interval training (HIIT), identified as an efficient and effective mode of exercise, is gaining popularity among young people. In American College of Sports Medicine's worldwide survey of fitness trends, HIIT has remained in the top 5 from 2014 to 2020 after first making the top 20 in 2014 [Thompson, 2019]. Broadly, HIIT comprises repeated exercise bouts performed at high intensity, interspersed with a brief recovery period of low-intensity activities or inactivity between each bout [Laursen and Jenkins, 2002]. In contrast to traditional continues training, which is characterized by long duration and moderate intensity, HIIT appears to have a shorter duration and is often completed at higher intensity. A single exercise bout of HIIT lasts from a few seconds (i.e., 10 seconds) to a few minutes (i.e., 5 minutes) and the high intensity is generally defined as above the anaerobic threshold. Even though HIIT has been long used to improve the performance of athletes, its unique efficiency has attracted many young people since one of the most cited barriers to exercise is lack of time [Lovell et al., 2010; Awadalla et al., 2014; Blake et al., 2017]. Over the past decade, there has been a surge in scientific studies on the health-promoting effects of HIIT in young adults. Compared to traditional continuous training, HIIT has been reported to equal or be more effective in improving cardiorespiratory fitness [Gist et al., 2014; Sun et al., 2019; Hu et al., 2021], body composition [Trapp et al., 2008; Sijie et al., 2012; Hu et al., 2021], and reduce some risk factors associated with CVD, including elevated BP [Ciolac et al., 2010], waist circumference [Batacan et al., 2017], insulin resistance [Trapp et al., 2008; Sun et al., 2019], and fasting glucose [Kong et al., 2016]. In addition, short-term HIIT can elevate antioxidant capacity and attenuate exercise-induced oxidative stress [Fisher et al., 2011; Bogdanis et al., 2013; Gillen et al., 2013]. However, it is worth noting that despite the consistent potent effect on cardiorespiratory fitness, effects of HIIT remain controversial on both traditional and novel markers of CVD risk factors such as body composition, BP, lipid profile, insulin, glucose, and inflammation [Sawyer et al., 2016; Batacan et al., 2017]. A previous systematic review and meta-analysis reveals that the timescale of HIIT protocol plays a role on health promotion, with long-term HIIT (≥ 12 weeks) showing better gains than short-term HIIT (< 12 weeks) [Batacan et al., 2017]. Moreover, the improvement on body composition is limited following the low-volume HIIT protocol which was defined as less than 500 METs-min per week [Sultana et al., 2019]. Apart from the timescale and exercise volume, participants' characteristics have an impact on the beneficial effect of HIIT. For example, overweight or obese individuals are more likely to benefit from HIIT than normal weight individuals regarding cardiometabolic health outcomes [Batacan et al., 2017; Campbell et al., 2019]. Participants with poorer baseline health status are more responsive to HIIT-induced health benefits [Milanović et al., 2015; Astorino et al., 2022]. It is noteworthy that the majority of HIIT interventions are without PA and dietary assessments, resulting in an absence of control for participants' non-exercise PA and dietary intake. Since both PA and diet have been shown to be associated with cardiometabolic health, from this point of view, another potential explanation for varies outcomes across studies is the compensatory behaviors following exercises, which may attenuate the intervention effect. For the most part, exercise-induced energy expenditure is compensated by decreasing non-exercise PA [Skovgaard et al., 2019] and increasing energy intake [King et al., 2008]. These compensatory behaviors are mainly to balance the energy deficit caused by exercise and thus influenced by the exercise intensity and duration. In a previous crossover study, behavioral changes were examined after a single bout of moderate or vigorous exercise in overweight boys. The results show that vigorous intensity exercise is associated with a higher increase in subsequent SB than the moderate intensity one, and the daily vigorous intensity physical activity decreased sharply in the following 4 days [Paravidino et al., 2017]. While another study reports contrasting findings that sedentary time is significantly reduced during the 2-week period of HIIT in overweight or obese adults [Nugent et al., 2018]. Some studies support an increase in food intake following a single bout of high intensity exercise in healthy adult women [Finlayson et al., 2009; King et al., 2008]. However, in a study of children, the authors indicate that performing HIIT before lunch time does not affect their subsequent food intake and appetite [Morris et al., 2018]. In this regard, it seems that the appearance and magnitude of compensatory behavior during exercise intervention is unpredictable. Previous research suggests that there are considerable individual variabilities in exercise-induced compensatory movement behaviors [Schubert et al., 2017], as well as in energy intake [Hopkins et al., 2013]. In a systematic review investigating the contributors to energy compensation, age, baseline fat mass and timescale of intervention are found to explain 48% of the variance and surprisingly, sex, exercise frequency, intensity and exercise exergy expenditure are not significantly related to the following energy compensation [Riou et al., 2015]. Therefore, understanding changes of compensatory behaviors can broaden our current knowledge regarding to the effectiveness of HIIT.

Generally, cycling, running, and rowing are the conventional HIIT modalities utilized in adults [Buckley et al., 2015]. In fact, such repetitive and intense exercises provide lack of enjoyment for individuals who exercise for the purpose of health maintenance and promotion [Menz et al., 2019]. Moreover, the Wingate test, the most common HIIT protocol, which involves repeated 30 seconds maximal workout interspersed with 4 minutes of recovery, may produce negative affective responses in untrained individuals due to its severe intensity [Parfitt et al., 2006; Ekkekakis et al., 2008]. These negative responses include exercise exertion, unpleasant, maladaptive, or even noxious experience, resulting in the attenuated exercise fidelity and maintenance [Ekkekakis et al., 2008]. It is supposed that exercises at self-selected intensity [Parfitt et al., 2006] or with shorter work-out duration [Martinez et al., 2015] can produce more pleasure and enjoyment for inactive individuals.

To this end, a Tabata-style functional HIIT appears to be an alternative. In contrast to the traditional HIIT which uses a unimodal exercise modality (i.e., running, cycling, and rowing), the functional HIIT comprises multimodal functional exercises. Functional HIIT refers to the exercise that involves a variety of universal motor-recruitment patterns in multiple movement planes executed with participant's own body weight and are completed at the highest self-selected intensity [Feito et al., 2018a]. It has been suggested that functional movements when conducted in an interval training method at relatively high intensities are sufficient stimulation for improving target fitness domains including muscle strength and endurance [Dransmann et al., 2021; Hollerbach et al., 2021; Kapsis et al., 2022], cardiorespiratory fitness [Posnakidis et al., 2022; Brisebois et al., 2022], body composition [Feito et al., 2018b; Hollerbach et al., 2021; Kapsis et al., 2022] in healthy adults, as well as cardiometabolic risk factors in at-risk individuals [Nieuwoudt et al., 2017; Fealy et al., 2018]. Furthermore, participants are more likely to maintain exercise enjoyment and show less perceived exercise exertion and more willingness to continue when participating the functional HIIT [Menz et al., 2019; Heinrich et al., 2014; Mayr Ojeda et al., 2022]. In addition, HIIT protocols using functional exercises facilitates its implementation in real-life settings since it does not require expensive exercise equipment such as treadmills and cycle ergometers.

Tabata training, referred as one of the most effective HIIT methods, is featured by its unique training procedure and intensity. Conventionally, a Tabata protocol comprises of 8 exercise bouts, each involving a 20-second work-out followed with a 10-second rest, for a total of 4 minutes [Tabata, 2019]. The intensity required for original Tabata training is constant with intensities of 170% of maximal oxygen uptake (VO_{2max}) throughout, suggesting that participants should be exhausted after 7-8 bouts of exercise [Tabata, 2019]. However, for untrained individuals, it seems unfeasible in prescribing the original intensity proposed by Tabata et al. (1996). This makes most of existing "Tabata Protocols" in the real-world setting relax the control on intensity and only keep the same procedure used in the original Tabata training. A previous study demonstrates that Tabata training with an average of around 80% of maximal heart rate during exercises is effective in improving body composition, aerobic capacity [Domaradzki et al., 2020], and BP [Popowczak et al., 2022] in adolescents. Other research in adults also indicated health benefits following a Tabata-style HIIT whereas exercise intensities are not emphasized [Gurd et al., 2018; Engel et al., 2019; Murawska-Cialowicz et al., 2020; Pearson et al., 2020].

Although the Tabata protocol has gained popularity among young people in recent years, its effective intensity and health promotion effects remains unclear in non-athlete populations. Furthermore, there is limited research on the effect of this novel HIIT on PA and diet among university students. Such knowledge is important to aid in health promotion strategies in the university setting. Accordingly, the first aim of this program is to develop a Tabata-style functional HIIT protocol that was feasible and appealing to female university students, and to examine its effectiveness on improving cardiometabolic health and PA in this population. In addition, since PA and health are correlated, the second aim is to explore whether changes of PA have an impact on intervention effects.

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Chapter 2: Literature review

Cardiometabolic risk factors

Metabolic syndrome

Metabolic syndrome (MetS) is characterized by the aggregation of multiple cardiometabolic risk factors in a single individual. The exact combination of MetS as well as the cut-point of individual components remains controversial because its components exhibit complex diversity across individuals and populations. Since Kylin first defined hypertension (HTN), hyperglycemia, and hyperuricemia as a syndrome in 1923, the concept of MetS had been constantly developing [Cameron et al., 2004]. In 1988, Reaven provided further support for the role of insulin resistance and HTN on cardiovascular diseases (CVD) and the co-existence of multiple metabolic disorders, including hyperinsulinemia, glucose intolerance, HTN, low high-density lipoprotein cholesterol (HDL), and elevated triglyceride (TG) [Reaven, 1988]. This cluster of disorders was proposed as "Syndrome X" by Reaven, although obesity was omitted in the original description. In 1989, Kaplan renamed it "The Deadly Quartet" [Kaplan, 1989] and some researcher also called it "insulin resistance syndrome" later [DeFronzo and Ferrannini, 1991]. Until 1998, the World Health Organization (WHO) recommended to use the term "Metabolic Syndrome" and described its main components as impaired glucose regulation (diabetes, impaired glucose tolerance), insulin resistance, lipid metabolism disorders, raised arterial pressure, central obesity, and microalbuminuria [Alberti and Zimmet, 1998]. In the following years, several definitions have been put forward by organizations including WHO [Alberti and Zimmet, 1998], European Group for the Study of Insulin Resistance (EGIR) [Balkau and Charles, 1999]; National Cholesterol Education Programme Adult Treatment Panel III (NCEP-ATP III) 2001 [The Expert Panel, 2001], which was revised in 2004 in accordance to the modification by American Diabetes Association to lower the threshold value of impaired fasting glucose (FPG) (rNCEP-ATP III) [Grundy et al., 2004]; American Association of Clinical Endocrinologists (AACE) [Einhorn et al., 2003], International Diabetes Federation (IDF) [Alberti et al., 2005], American Heart Association and the National Heart, Lung, and Blood Institute (AHA-NHLBI) [Grundy et al., 2005], as well as the Chinese Diabetes Society (CDS) [Chinese Diabetes Society, 2004]. These definitions, although similar in the core components, differ as they are applied in the clinical or research setting. Inevitably, inconsistencies in its definitions led to considerable confusion and lack of comparability between studies. The main debate had centered on whether MetS should be defined primarily as insulin resistance, obesity, risk of CVD, or simply a sum of statistically related risk factors [Cameron et al., 2004]. For example, the WHO definition emphasized that the necessary condition for diagnosis is abnormal glucose metabolism or insulin resistance, accompanied by at least two other risk factors, whereas the IDF listed central obesity as a must for diagnosis. In contrast, the NCEP identified each component equally and defined the MetS as having any three or more of the cardiometabolic risk factors. Another controversy is the diagnosis of central obesity, is where definitions produce varied applicability in different ethnic groups. For example, the waist-to-hip ratio or body mass index (BMI) is used to diagnose central obesity in the WHO definition, while waist circumference (WC) is used in the NCEP. The adoption of the NCEP definition had resulted in a significant underestimation of the prevalence of MetS in Asians [Tan et al., 2004]. More importantly, the value of MetS in identifying individuals at high risk of type 2 diabetes or CVD has been questioned. Epidemiological studies have shown that MetS, as a cluster of risk factors, is associated with increased risk of cardiovascular events or diseases [Gami et al., 2007] and this association is more potent than that of individual components [Kaplan, 1989]. Nevertheless, several studies demonstrate that the presence of MetS is not a better predictor of cardiovascular morbidity and mortality than its individual components [Wannamethee et al., 2005; Koskinen et al., 2009]. Therefore, IDF and AHA/NHLBI initiated a meeting, joint by the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity, to harmonize the criteria of MetS. In the joint statement published in 2009, the obligatory component was removed as an important step towards consensus, agreeing that 3 risk factors out of 5 would qualify an individual for MetS [Alberti et al., 2009]. Additionally, in this harmonized definition, cut-off points of each component were unified except WC and population specific cut points for WC were recommended.

In the present study, the MetS was defined as having 3 or more of the following 5 abnormalities: 1) central obesity (WC: women ≥ 80 cm); 2) elevated TG (≥ 150 mg/dL; 1.7 mmol/L) or drug treatment ; 3) low HDL (women < 50 mg/dL; 1.3 mmol/L) or drug treatment; 4) HTN (systolic blood pressure (BP) ≥ 130 and/or diastolic ≥ 85 mm Hg) or drug treatment; 5) elevated fasting glucose (FPG) (> 100 mg/dL; 5.6 mmol/L) or drug treatment.

The prevalence of metabolic syndrome

There is no doubt that the lack of a unified definition made it difficult to measure the global prevalence of MetS. A previous study suggested that the incidence of MetS was always associated with the incidence of obesity and type 2 diabetes. Furthermore, MetS affected three times as many people as diabetes and was estimated to affect one in four people globally [Saklayen, 2018]. A recent systematic review and meta-analysis estimated the global prevalence of MetS based on 1,129 prevalence date with a total of more than 28 million participants. The global prevalence of MetS ranged from 12.5% (NCEP-ATP III) to 31.4% (Harmonized definition 2009). Moreover, the global prevalence was positively associated with age and was significantly higher among women compared to men. The authors also analyzed individual components and reported that central obesity measured by ethnic-specified criteria was the most prevalent (45.1%), followed by elevated BP (42.6%), low HDL (40.2%), elevated TG (28.9%) and elevated FPG (24.5%) [Noubiap et al., 2022].

Regardless of multiple criteria used for defining MetS, epidemiologic studies demonstrate a high prevalence of MetS in adults globally. It is not surprising that the prevalence of MetS is positively associated with age because age is a strong predictor of CVD, and the MetS components progress in frequency with age.

North America

In an analysis of data from the Third National Health and Nutrition Examination Survey (NHANES) (1988-1994) in the United States, Ford et al. (2002) reported that the prevalence of MetS increased with age, with the lowest prevalence of 6.7% at the age of 20-29 and the highest prevalence of 43.5% at the age of 60-69. There was no difference in the age-adjusted prevalence between males (24.0%) and females (23.4%). [Ford et al., 2002]. In a separate analysis using the same data set, odds ratios (ORs) for MetS were increased significantly with age group. For women, the middle-aged group (35-64 years) and the old group (≥ 65 years) had an ORs of 2.4 and 4.9 for MetS compared with the young group (20-34 years) [Park et al., 2003]. In a longitudinal study, Kraja et al. (2006) followed 2,458 subjects for 7.4 years (1994-1996 to 2002-2003) and reported that MetS percentages increased from 17.1% to 28.8% using NCEP-ATP III criteria. The authors also indicated that MetS prevalence was approximately two to three times higher in subjects aged 50 years and older than in younger ages [Kraja et al., 2006]. Using 2003-2012 NHANES data, Aguilar et al. (2015) reported that the overall MetS prevalence in the US increased from 32.9% in 2003-2004 to 34.7% in 2011-2012. In the age-specific analysis, the prevalence was 18.3% and 46.7% among subjects aged 20-39 years and those aged 60 years or older, respectively. It was worth noting that, women had a significantly higher prevalence of MetS compared with men in this updated study (35.6% vs. 30.3%) [Aguilar et al., 2015]. Shin et al. (2018) analyzed the 2007-2014 NHANES data and indicated that the MetS prevalence was 19.3%, 37.7% and 54.9% among adults aged 20-39 years, 40-59 years, and ≥ 60 years, respectively. Regarding MetS components, the prevalence of high TG and FPG decreased, whereas the prevalence of central obesity (WC: ≥ 102 com for men and ≥ 88 cm for women) increased, especially among women [Shin et al., 2018].

In Canada, Riediger and Clara (2011) analyzed data from the Canadian Health Measures Survey (2007-2009), which comprised a total of 1,800 subjects aged 18 years and older. The incidence of MetS was 17.0% among participants aged 18-39 years and 39.0% among those aged 70-79 years. Central obesity, as measured by WC (men: > 102 cm; women: > 88 cm), was more prevalent among women than men across each age group. Specifically, among young women aged 18-39 years, 26.6% had excess WC and 39.4% had low HDL [Riediger and Clara, 2011].

Europe

The prevalence of the MetS in Europeans was reported based on data from the Monica, Risk, Genetics, Archiving and Monograph (MORGAM) Project, which comprised 36 cohorts in 10 European countries (Denmark, Finland, Sweden, Ireland, Scotland, France, Italy, Spain, Poland, and Russia). In this study, a total of 69,094 healthy subjects aged 19-78 years at baseline between 1982-1997 were included. Findings from the age-specific prevalence for men and women demonstrated that, regardless of the criteria used, age played a more important role on the prevalence of MetS among women. The prevalence increased fivefold in women aged 19-39 to 60-78 years (7.4%/7.6% - 35.4%/37.6% for IDF/rNCEP-ATPIII) and twofold in men (5.3%/10.5% - 11.5%/21.8%). Furthermore, using the IDF definition, women showed a higher prevalence of MetS compared to men in each age group. For young women (aged 19-39 years), the frequency of obesity (BMI ≥ 25 kg/m^2) was about 30% and was the most prevalent component. However, using WC (≥ 88 cm) instead of BMI, a sharp decrease was observed from around 30% to 10% [Vishram et al. 2014]. For other European countries, Gundogan et al. (2013) investigated the MetS prevalence in Turkey with a total of 4,309 samples aged 20-83 years. Using the IDF definition, the frequency based on the age group was as follows: 7.5% in 20-25 years, 23.1% in 26-30 years, 34.2% in 31-35 years, 37.2% in 36-40 years, 40.7% in 41-45 years, 46.8% in 46-50 years, 60.8% in 51-55 years, 60.7% in 56-60 years, 58.9% in 61-65 years, 59.3% in 66-70 years, and 51.9% over 70 years. Results from the gender-specified analysis showed that women had a 1.62 times higher risk of developing MetS than men. Additionally, BMI were found to be an independent risk factor for MetS, with overweight individuals having a 2.75-fold increased risk for MetS and obese individuals having a 7.8-fold compared with those with normal BMI. [Gundogan et al., 2013]. In an analysis based on the data from the Portuguese Metabolic Syndrome study, the prevalence was only 5% in young adults aged 18-30 years, rose to 16.0% in those aged 31-40 years, and reached the highest of 60.0% in those aged over 70 years. Moreover, MetS was more prevalent in women in Portugal [Raposo et al., 2017].

Other countries

In a recent systematic review and meta-analysis, which included a total sample of 226,653 Chinese adults aged 15 years and older, the pooled prevalence was 24.5% using the 2005 IDF criteria [Li et al., 2016]. Results from subgroup analysis revealed that the pooled prevalence of MetS increased with age, with 13.9% in adults aged 15-39 years, 26.4% in adults aged 40-59 years, and 32.4% in adults aged ≥ 60 years. Chinese women had a higher prevalence of MetS compared to men (27.0% vs. 19.2%) and the most prevalent component for women was central obesity (46.1%) [Li et al., 2016]. The overall prevalence was higher than the prevalence of 16.5% reported in 2000 using a nationally representative sample of 15,838 Chinese aged 35-74 years [Yang et al., 2007], indicating an increase in the prevalence of MetS in China in recent years. Yang et al. (2007) also compared the IDF and rNCEP-ATP III definitions in identifying the prevalence of MetS in Chinese population. The age-adjusted prevalence using rNECP-ATP III definition was higher of 23.3%. Specifically, using the same data set, Gu et al. (2005) reported that Chinese women suffered a higher prevalence of MetS than men for each age group, with 9.4% for age 35-44 years, 17.7% for age 45-55 years, 28.8% for age 55-64 years, and 28.6% for age 65-74 years [Gu et al., 2005]. In the study by Rampal et al. (2012), the overall prevalence of MetS in Malaysia aged 15 years and older was 27.5%. The subgroup analyses showed that 50% of women aged 40 years and older had MetS, which was significantly higher than 16.6% of women aged 15-40 years [Rampal et al., 2012]. Kalan Farmanfarma et al. (2019) conducted a meta-analysis to investigate the prevalence of MetS in Iran. With a total of 146,644 subjects included in the pooled analysis, the overall estimate of prevalence was 30.4%. The frequency significantly increased from 12.1% in in 20-29 years old to 51.7% in 60 years old and above. By sex, the prevalence was significantly higher in women compared to men (34.8% vs. 25.7%) [Kalan Farmanfarma et al., 2019]. Ajlouni et al. (2020) analyzed data from the 2017 Cardiovascular Disease Risk Factors Survey, which included a sample of 4,056 subjects aged 18-90 years old in Jordan. Using the IDF definition, women had higher MetS risk compared to men (OR: 1.42) and the age-specific frequency for women rose from 11.7% in the 18-29 age group to 85.2% in the 60-69 age group. For women, the most prevalent component was central obesity using either the IDF definition or the NCEP-ATP III definition (75.6% for IDF and 60.7% for NCEP-ATPIII) [Ajlouni et al., 2020]. Vietnamese people showed a relatively lower prevalence of 16.1%, with a slightly higher prevalence to be found in women (17.3%) [Dang et al., 2022]. In Korea, the overall prevalence was 28.2% while women had a lower prevalence of MetS compared to men (13.2% vs. 43.7%) [Park et al., 2015]. The MetS was also reported to be less prevalent in women in Japan and Macau. The frequency was 28.9% and 43.6% in Japanese women and men aged 65 years and older, respectively [Ishii et al., 2014]. In Macau's adults aged 18-44 years, the MetS prevalence was over two times higher in men than in women (10.5% vs. 3.7%), while for individual components, the prevalence of central obesity was more prevalent in women [Sobko et al., 2014].

The prevalence of metabolic syndrome in young adults

Although the prevalence of MetS is positively associated with age, its prevalence is increasing in young adults, especially in young women [Regitz-Zagrosek et al., 2007]. In the study by Ford et al. (2004), a total of 1430 women aged 20-39 years from the NHANES III (1988-1994) and 250 women with the same age range from NHANES 1999-2000 were included in the analyses. Using the rNCEP-ATP III definition, the MetS prevalence in women aged 20-39 years increased significantly from 10.8% in the NHANES III to 19.1% in the NHANES 1999-2000 [Ford et al., 2004]. Likewise, the increasing trend was reported in another study, as the prevalence in young women (20-39 years) increasing from 10% in NHANES III (1984-1994) to 20% in NHANES 1999-2006 [Mozumdar and Liguori, 2011]. Despite the absence of gender-specific data, the increasing trend in the MetS prevalence among young adults had also been reported in another study. Hirode and Wong (2020) analyzed 2011-2016 NHANES data to depict trends in the prevalence of MetS in US adults. The authors observed a significant increase in the MetS prevalence among subjects aged 20-39 years from 16.2% in 2011-2012 to 21.3% in 2015-2016 [Hirode et al., 2020]. Similarly, there had been an increase in prevalence among young Polish females aged 20-39 years, with a significant increase from 7.6% in WOBASZ (2003-2005) to 9.1% in WOBASZ II (2013-1024) [Rajca et al., 2021]. In a recent systematic review and meta-analysis investigating the prevalence of MetS in Brazilian adults in the last 10 years, no difference in the pooled frequency was observed between adults less than 45 years (43%) and those older than 45 years (42%) [de Siqueira Valadares et al., 2022]. Data from the Korean National Health Insurance Service Database (2009-2013) revealed that the prevalence of central obesity (WC ≥ 80 cm) increased among young Korean females aged 30-39 (Odds ratio: 1.21) [Lee et al., 2018].

The prevalence of metabolic syndrome in women

The majority of studies had reported a higher prevalence of MetS in women than in men [Riediger and Clara, 2011; Rampal et al., 2012; Gundogan et al., 2013; Aguilar et al., 2015; Chowdhury et al., 2018; Mokhayeri et al., 2018; Kalan Farmanfarma et al., 2019; Du et al., 2020; Ajlouni et al., 2020; Dang et al., 2022], whereas some studies suggested a higher prevalence in males among young people [Friend et al., 2013; Miller et al., 2014; Ye et al., 2015; Kuschnir et al., 2016]. Based on the data from NHANES (2001-2010), males had a higher prevalence than females in adolescents aged 12-19 years (13.0% vs. 6.4%) [Miller et al., 2014]. Likewise, a previous systematic review showed that sex and age were both associated with the incidence of MetS in children, and boys and older children were more likely to develop MetS [Friend et al., 2013]. It was consistent with findings from the study by Kuschnir et al. (2016), in which male adolescents and those aged 15-17 years were reported to have higher prevalence of MetS [Kuschnir et al., 2016]. Likewise, the prevalence of MetS was higher in boys than girls in China (2.9% vs. 1.8%) [Ye et al., 2015].

It was noteworthy that females had a lower MetS prevalence than males in children and adolescents, while with increasing age, females became more likely to develop MetS in adults. One of potential explanations was the specific anatomical, hormonal, and cardiovascular features shown in women. For example, the hearts and arteries were stiffer in women compared to men. This effect seemed to be protected by female hormones during young age. However, this protective effect was attenuated with age, which resulted a dramatic increase in the development of HTN in post-menopausal women. Data from the NHANES 1999–2004 revealed that 82.8% women with diagnosed HTN were post- menopausal and furthermore, women had a more potent relationship between HTN and other MetS components including low HDL and central obesity [Ong et al., 2008]. Because of the decrease of estrogens, post-menopausal women were also at an increased risk of visceral obesity, which had been found to be associated with CVD risk [Meyer et al., 2011]. On the other hand, women’s physical activity (PA) patterns might play an important role in the more rapid increase in MetS prevalence with age. It was well known that there was a sharp decline in PA among female adolescences, and the decline continued into adulthood [Sallis, 1993; Nelson et al., 2006; Pate et al., 2009; Corder et al., 2010; Dumith et al., 2011a]. Furthermore, although some studies reported a steeper decrease in boys compared to girls, girls had lower PA at all ages [Corder et al., 2015].

The metabolic syndrome and cardiovascular risk

Previous studies suggested that the incidence of CVD was positively associated with the presence of MetS and more components, especially for women. For studies without sex-specified analysis, Ascaso et al. (2011) investigated the relationship between the prevalence of MetS and CVD among subjects with hypertriglyceridemia. The results showed that subjects with MetS had a significantly higher incidence of CVD events compared to those without MetS (95.9% vs. 4.1%) [Ascaso et al., 2011]. According to the Family Heart Study, which comprised 2,458 participants from 480 families, individuals with MetS were 2.5 times more likely to develop CVD than those without MetS [Kraja et al., 2006]. In a previous study including a total of 4,483 subjects from Finland and Sweden, after adjusting for age and sex, MetS remained associated with an increased risk of CVD (RR: 2.96), and this association was stronger compared to any of the individual components [Isomaa et al., 2001]. In addition to these, Malik et al. (2004) indicated that having 1 to 2 MetS risk factors were also associated with the increased risk for CVD mortality but not for all-cause mortality according to a prospective cohort study including 5,255 subjects from the NHANES II [Malik et al., 2004].

Multiple studies provided sex-specified data. Wilson et al. (1999) examined the impact of a cluster of six metabolic risk factors (HDL, BMI, systolic blood pressure (SBP), TG, FPG and total-cholesterol (TC)) on coronary risks and found that clustering 3 or more risk factors were associated with a higher risk of developing coronary heart disease, with a 5.9-fold increase in risk among women and a 2.39-fold increase among men [Wilson et al., 1999]. Likewise, in an analysis based on the San Antonio Heart Study (2,815 subjects aged 25-64 years at baseline between 1984-1988), the hazard ratio for cardiovascular mortality with MetS was 4.65 for women MetS compared with 1.82 for men [Hunt et al., 2004]. In a longitudinal study with 11 years of follow-up, the incidence of coronary heart disease was 2 times higher in women with MetS compared to those without MetS, as 1.5 times higher among men [McNeill et al., 2005]. In a previous systematic review and meta-analysis, involving a total of 951,083 participants were included, MetS was associated with an increased risk of CVD, regardless of the definition used (NCEP-ATP III or rNCEP ATP III). Findings from the meta-analysis showed that MetS was associated with an increased risk of CVD, CVD mortality, and all-cause mortality with a relative risk of 2.35, 2.40, and 1.58, respectively. Furthermore, compared with men, women had a consistently higher cardiovascular risk in terms of CVD (women vs. men: RR: 2.87 vs. 2.14), CVD mortality (RR: 2.55 vs. 1.94), and all-cause mortality (RR: 1.86 vs. 1.42) [Mottillo et al., 2010].

Furthermore, whether individuals with more components of MetS were at higher risk of developing CVD was assessed in several studies. In a study with a follow-up of 13.6 years, based on data from 30,365 men, the authors reported that both the risk of all-cause mortality and cardiovascular mortality increased with the number of MetS risk factors presented. More specifically, after controlling for confounders including age and other MetS risk factors, elevated BP, central obesity, and elevated TG were independently associated with mortality risks [Ho et al., 2008]. Although not statistically significant, the positive relationship between the number of MetS components and all-cause mortality was also reported in the study by Kadota et al. (2007). Additionally, the authors pointed out that non-obese individuals with more MetS risk factors had higher HRs of CVD mortality, suggesting that MetS components were associated with CVD mortality regardless of obesity.

Indeed, substantial evidence demonstrated that obesity was associated with the development of CVD and CVD mortality independently of other cardiovascular risk factors [Powell-Wiley et al., 2021]. Compared to overall obesity, recent studies highlighted that abdominal obesity appeared to be a more potent predictor of cardiovascular risks [Piché et al., 2018; Sahakyan et al., 2015]. Recently, individuals with metabolically healthy obesity (MHO) were receiving increased attention in both research and clinical settings. MHO was defined as the condition that having obesity but not having MetS. Despite having comparable levels of excessive body fat, people with MHO had a relatively favorable metabolic profile compared to those who already developed MetS, which was referred to as metabolic unhealthy obesity (MUO) [Karelis et al., 2005; Primeau et al., 2011]. Based on a prospective cohort study (North West Adelaide Health Study) with 4,056 randomly selected participants who were without CVD or stroke at baseline, people with MHO were more likely to have metabolic risks with a median follow-up of 4.0 years. These increased risks were not observed in MHO people maintaining the healthy metabolic profile [Appleton et al., 2013]. In the study by Caleyachetty et al. (2017), the authors analyzed data from the Health Improvement Network, which were representative of the U.K. population from 1995 to 2015. Findings highlighted that, compared to non-obese people with none of MetS components, people with MHO had a higher risk of multiple cardiovascular consequences (coronary heart disease, cerebrovascular disease, heart failure, and peripheral vascular disease). Furthermore, the authors found a positive relationship between cardiovascular risk and the number of metabolic abnormalities, and this association was observed among individuals with normal-weight, overweight, and obese [Caleyachetty et al., 2017]. Recently, a systematic review and meta-analysis examined whether individuals with MHO were at an increased risk of cardiovascular events. Results from the pooled analysis showed that people with MHO had a higher risk of cardiovascular events than healthy non-obese people (RR: 1.45) but lower risks than metabolic unhealthy non-obese people (RR: 2.07) and MUO people (RR: 2.31) [Eckel et al., 2016]. Similarly, findings from the study by Kim et al. (2016) showed a slight increase in the risk of CVD (HR: 1.4) in MHO adults, whereas a significant increase in those with metabolically unhealthy normal weight (HR: 3.0) and MUO (HR: 4.0). Subgroup analysis revealed that young adults (aged < 45 years) with MHO were more likely to develop diabetes (HR: 1.9 vs. 1.1) [Kim et al., 2016]. Conversely, the study by Kaur et al. (2016) indicated that the risk of cardiovascular mortality was similar between metabolically healthy overweight or obese people and their normal weight counterparts. Despite the similar CVD mortality, people with MHO had higher insulin resistance, greater sub-clinical inflammation, and more instable metabolically healthy status [Kaur et al., 2016].

The characteristics of the instable and transient of MHO phenotype had been reported in other studies [Appleton et al., 2013; Hwang et al., 2015; Kim et al., 2016]. The transition from the MHO to the MUO phenotype was found to be associated with age [Appleton et al., 2013], gender [Hwang et al., 2015]; WC [Appleton et al., 2013; Hamer et al., 2015; Schröder et al., 2014], visceral abdominal tissue (VAT) [Hwang et al., 2015], obesity severity [Mørkedal et al., 2014; Hamer et al., 2015; Mongraw-Chaffin et al., 2016], obesity duration [Mørkedal et al., 2014; Bell et al., 2015a; Mongraw-Chaffin et al., 2016], and PA [Bell et al., 2015b]. Females were more likely to convert to MUO in the future [Hwang et al., 2015]. The younger age (18-39) and lower WC helped maintain metabolic health especially for women [Appleton et al., 2013].

Inflammation markers

Treatment of major traditional risk factors, such as MetS, is fundamental to reducing the risk of CVDs. However, despite optimal risk factors management, there is still a significant residual risk of CVD events [Dhindsa et al., 2020]. Basically, lipid metabolism disorder, endothelial cells injury, and hemodynamic damage are recognized as the basis of atherosclerosis and the atherogenic process is found to be initial with the accumulation of apolipoprotein B lipoproteins in the sub endothelium [Tabas et al., 2007] and the progress is often accompanied by oxidized lipoproteins and inflammatory processes in endothelial cells [Tabas et al., 2015]. As knowledge of the pathophysiology of atherosclerosis formation continues to improve, we hope to assess the biological process of atherosclerosis through a range of biomarkers reflecting inflammation and oxidative stress, and ultimately improve risk prediction. Recently, emerging evidence have highlighted the association between inflammation and CVDs, suggesting that lower inflammation level is associated with lower risk of CVD events in the future [Ridker et al., 2017; Zhu et al., 2018; Arnold et al., 2021].

Substantial evidence from epidemiological and clinical research suggest that C-reactive protein (CRP) is an inflammation marker that strongly predicts the risk of future CVD events [Ridker, 2003]. Furthermore, the association between the baseline level of CRP and the risk of CVDs in the future is independent of demographics and several traditional risk factors including cholesterol levels, BP, and type 2 diabetes [Ridker, 2003]. More importantly, there are few correlations between the CRP level and the lipid levels, making it difficult to predict inflammation levels using traditional metrics. Based on the Women's Health Study, Ridker et al. (2003) investigated the relationship between CRP and MetS among 14,719 American women with an 8-year follow-up. The authors found that women with more characteristics of MetS were associated with higher CRP lever at baseline, and CRP levels greater than 3.0 mg/L had additive effects on subsequent CVD events in all MetS process regardless of the definition used. Furthermore, CRP levels were equally effective in predicting cardiovascular event-free survival rates to MetS [Ridker et al., 2003]. Ebong et al. (2016) investigated the association between the CRP level and HTN in women based on data from the Coronary Artery Risk Development in Young Adults Study (CARDIA). Results showed that among premenopausal women, the CRP level was associated with HTN independent of BMI [Ebong et al., 2016]. Particularly, CRP levels are sufficiently stable to provide long-term predictive value [Ridker, 2003; Danesh et al., 2004]. Accordingly, the CRP levels are suggested to be measured alongside traditional biomarkers when predicting the future CVD events. It is suggested that CRP levels of less than 1.0 mg/L are interpreted as low risk, 1.0 – 3.0 mg/L as moderate risk, and more than 3.0 mg/L as high risk [Ridker et al., 2003].

Evidence from clinical studies indicated that CRP levels are associated with a range of lifestyle risk factors, such as adiposity, physical inactivity, and unhealthy diet. A previous systematic review and meta-analysis synthesized data from 51 cross-sectional studies to investigate the association between CRP and obesity. The results showed that CRP was moderately associated with BMI in adults, with a stronger association observed in women compared to men [Choi et al., 2013]. This gender difference was supported by other studies. Clark et al. (2016) found higher CRP levels in women with similar level of obesity as men [Clark et al., 2016] and in the study by Bi et al. (2019), obesity was only found to be associated with the high CRP level in women [Bi et al., 2019]. This might be explained by the body composition and sex hormones. Additionally, in the review by Plaisance and Grandjean (2006), evidence from both longitudinal and cross-sectional studies showed a 6%-35% lower CRP level associated with higher level of PA and cardiorespiratory fitness (CRF). A previous study showed that after a 6-months training program, CRP was decreased by 35% among participants who were at risk of CVDs [Smith et al., 1999]. The decreased CRP was also reported by Milani et al. (2004) after 3-months exercise training among rehabilitation patients [Milani et al., 2004]. Other longitudinal studies examined the effect of exercise on CRP in obese individuals. After 2 years lifestyle intervention that consisted of dietary and PA recommendations, obese postmenopausal women showed a 34% reduction in CRP [Esposito et al., 2003]. Kasapis and Thompson (2005) examined the acute inflammatory responses to exercise, and, based on data from 19 studies included, exercise was shown to induce a short-term, transient increase in CRP levels [Kasapis and Thompson, 2005]. This short-term response was expected to stimulate and benefit the long-term anti-inflammatory effect and regular exercise training can attenuate this acute response. In contrast, occupation-related PA (OPA) was found to potentially increase the risk of inflammation, suggesting that the domain of PA might have an impact on CRP levels. Lee et al. (2021) reported that OPA was associated with increased CRP levels, whereas leisure-time PA (LTPA) was beneficial to CRP levels. Similar findings were reported by Feinberg et al. (2022), who examined the association between OPA and LTPA with systemic inflammation. The authors specified that higher OPA level increased CRP by 6% and lower LTPA level increased CRP by 12% [Feinberg et al., 2022].

Cardiorespiratory fitness

Evidence from epidemiological studies have shown that CRF was negatively associated with CVDs and all-cause mortality in healthy people. A previous systematic review and meta-analysis attempted to quantitate the relationship between CRF, and cardiovascular events based on observational cohort studies. After synthesizing data from 33 studies, the pooled results showed that for 1 - MET higher of maximal aerobic capacity, the RR for all-cause mortality and CVD events were 0.87 and 0.85, respectively. Using individuals with high CRF as the reference, the RR for all-cause mortality and CVD events in those with low CRF was 1.70 and 1.56, respectively [Kodama et al., 2009]. Findings from the study by Wedell-Neergaard et al. (2018) demonstrated that an increase in CRF of 5 mL/min/kg resulted in an improvement in MetS (-11.2%), as well as its components including TG (-8.95%), SBP (-1.10%), diastolic blood pressure (DBP) (-1.75%), and HDL (3.05%). The authors further indicated that inflammatory biomarkers might partly explain the association between CRF and MetS. Consistent findings were reported by Adams-Campbell et al. (2016), who investigated the association between CRF and MetS in postmenopausal women, that women with very low CRF were more like to have MetS, obesity, high TG and low HDL compared to those with moderate CRF [Adams-Campbell et al., 2016]. In addition to reducing all-cause and cardiovascular mortality and the prevalence of MetS, better CRF had been shown to play an important role on improving BP [Holmlund et al., 2021; Cheng et al., 2022], reducing the incidence of diabetes [Juraschek et al., 2015; Holtermann et al., 2017; Tarp et al., 2019] and lowering inflammation [Wedell-Neergaard et al., 2018]. In a recent study by Cheng et al. (2022), the relationship between CRF and the risk of HTN was estimated based on data from 9 cohort studies. Results from meta-analysis showed that the RR for HTN was 0.92 for 1 - MET increase in CRF and participants with increased CRF had a RR for HTN of 0.71 compared to those with decreased CRF [Cheng et al., 2022]. Holmlund et al. (2021) found that an annual CRF increase of 3% contributed to a 11% lower risk of HTN and a small decrease less than 3% resulted in 21% higher risk, indicating the importance of maintaining a better CRF level [Holmlund et al., 2021]. Tarp et al. (2019) found a liner relationship between CRF and the type 2 diabetes risk that for 1 - MET increase in CRF, the RR for type 2 diabetes was reduced by 8% [Tarp et al., 2019]. The protective effect of CRF on diabetes was also reported by Juraschek et al. (2015) and Holtermann et al. (2017), and compared to normal weight individuals, obese individuals benefited more from increasing CRF [Holtermann et al., 2017]. Additionally, CRF was found to be inversely associated with inflammatory biomarkers such as CRP and interleukin-6 (IL-6) and higher CRF was important to maintaining lower inflammation level, particularly for individuals with high level of adiposity [Park et al., 2017; Wedell-Neergaard et al., 2018].

Several studies investigated the joint association of CRF and obesity with MetS. There was the consistent finding that individuals with low adiposity and high CRF had the lowest risk of developing MetS [Kim et al., 2014; Bopp and Wilson, 2022]. Although several studies suggested that obesity was more strongly associated with the risk of MetS than CRF [Kuk and Lee, 2010; Bopp and Wilson, 2022], CRF was evidenced to be associated with MetS independent of obesity and a high level of CRF could modify the negative effect of obesity on cardiometabolic health [Rankinen et al., 2007; Kim et al., 2014; Lätt et al., 2018]. Findings from the study by Katzmarzyk et al. (2005) supported the modifying effect of CRF because the association between obesity and MetS became insignificant when CRF was included [Katzmarzyk et al., 2005]. The association between BMI and the risk of HTN was also largely attenuated after controlling for CRF [Rankinen et al., 2007].

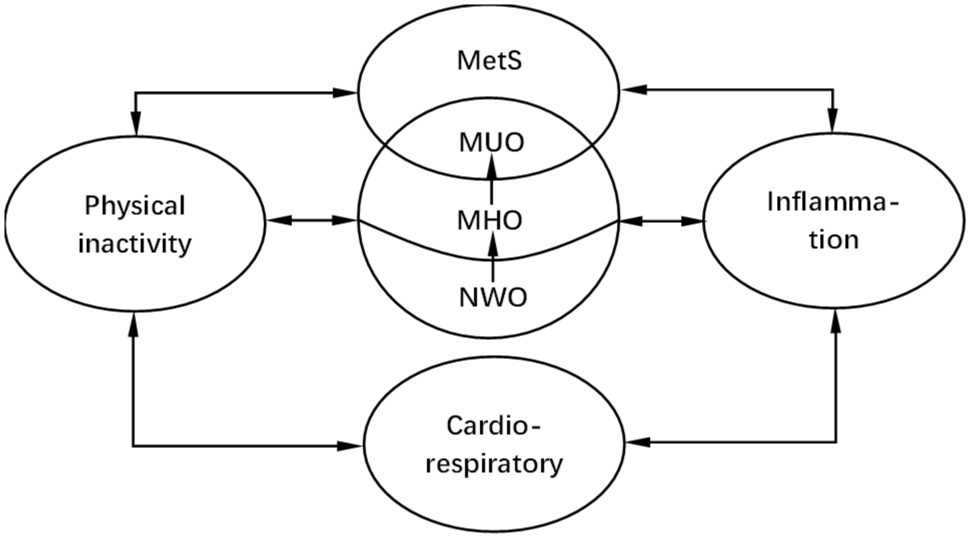
Additionally, CRF plays a role in the association between PA and cardiometabolic health. Findings from a systematic review reveal that compared to individuals with high CRF, those with low CRF had stronger associations between PA and cardiometabolic health [Husøy et al., 2021].

There is evidence that better CRF at a young age is strongly associated with lower MetS risk, lower inflammation, and health maintenance in later life [Sun et al., 2014; García-Hermoso et al., 2020; Mäestu et al., 2020]. Carnethon et al. (2003) conducted a population-based longitudinal cohort study based on the CARDIA study with a total of 2478 young adults. With a follow-up of 15 years, participants with low CRF were 3 to 6 times more likely to develop diabetes, HTN, and MetS than those with high CRF. While after controlling for BMI, these associations were largely attenuated, suggesting that obesity might play a role in these associations [Carnethon et al., 2003]. It should be noted that individuals with high, but later reduced CRF had a similar risk of developing MetS compared with those with persistently low CRF, indicating the importance of maintaining a better CRF across the lifespan [Mäestu et al., 2020].

Summary

Cardiometabolic health in young people has become a global concern over the last decades, fueled largely by the increasing prevalence of obesity and MetS in young adults. The metabolic pathway is presented in **Figure 1.**

Figure 1: Metabolic pathway



Note: MetS, metabolic syndrome; MHO, metabolic healthy obesity; MUO, metabolic unhealthy obesity; NWO, normal weight obesity.

Due to the absence of a standard definition of MetS, the high heterogeneity made the between-study comparison meaningless. Nevertheless, we can still find some results that tend to be consistent. The prevalence of MetS is increasing among young adults. Compared with adult men, adult women are more likely to develop MetS. However, in studies based on children or adolescents, females have a lower prevalence of MetS than males, suggesting that women suffer an enormous risk of MetS from childhood to adulthood. It is well documented that individuals with MetS have a significantly higher incidence of CVD events, CVD, and all-cause mortality, particular in women. Even having 1 or 2 components have been shown to be associated with the higher risk of CVD events and this risk increased with the number of MetS risk factors. Furthermore, the association between MetS and CVD consequents are independent of obesity since normal weight individuals with MetS also have the increased CVD risks. Meanwhile, obesity is evidenced to be an independent risk factor of the development of CVD and CVD mortality. Individuals with MHO are at lower risk for CVDs than those with MUO, but at higher risk than metabolically healthy non-obese individuals. Moreover, MHO is thought to be an instable and transient phenotype, and a lower risk of CVDs is found only in those who maintain the metabolically health, whereas most individuals with MHO will transfer to MUO. Individuals with young age (18-39) and lower WC are more likely to maintain metabolic health especially for women. Additionally, recent evidence show that inflammation and CRF have the mediating effect on the association between MetS and CVD events. CRP, a stable marker of inflammation, is found to provide an additive effect on predicting future CVDs and is proposed to be measured alongside conventional cardiometabolic biomarkers. For CRF, a negative association was found with risks of diabetes, MetS, CVD events and all-cause mortality. Higher CRF levels are also beneficial to improve BP and lowering inflammation. In addition, CRF plays a modifying role on the relationship between obesity and MetS, as well as PA and cardiometabolic health. More importantly, maintain a high CRF level throughout the life cycle is essential to maintain long-term health, and engaging in moderate-to-vigorous physical activity (MVPA) and high-intensity interval training (HIIT) are thought to be effective ways to maintain and improve CRF. Most studies have reported a higher prevalence of MetS in women than in men while the turning point in this trend is the rapid increase of MetS in young women. The emerging adulthood may be a window of opportunity to establish long-term healthy lifestyle and improve cardiometabolic health.

Physical activity

PA refers to any bodily movement caused by the contraction of skeletal muscles, which is accompanied by energy expenditure [Caspersen et al., 1985]. It includes all types, intensities, and categories of activities.

There are multiple ways to categorize PA. According to specific intensity ranges, PA is classified into sedentary behavior (SB), low- intensity physical activity (LPA), moderate-intensity physical activity (MPA), vigorous-intensity physical activity (VPA), MVPA, and very vigorous intensity physical activity (VVPA). SB is defined as any awake behavior with an energy expenditure of 1.5 METs or less, including passive sitting, reclining, or lying [Tremblay et al., 2017]. According to different purposes, PA can be categorized into exercise and non-exercise PA. Exercise is planned, structured, and repetitive PA performed to improve or maintain physical fitness or health. Non-exercise refers to all PAs other than exercise and it often done in a labor-saving manner [Caspersen et al., 1985]. Based on the portions of daily life when the activity take place, PA can be categorized into OPA, transportation PA, household PA and LTPA.

PA intensity can be expressed as either absolute or relative intensity. Absolute intensity is the amount of energy required to complete any PA, regardless of individual characteristics, and it is commonly described as light, moderate, vigorous, or moderate-to-vigorous intensity. Absolute rates of energy expenditure can be measured in terms of MET, calorie (cal), joule (J) or oxygen consumption. Among these, MET is the most used, with 1 - MET equal to the rate of energy expenditure when sitting at rest. Intensities of other activities are expressed by multiples of the MET. For adults, for example, reading while sitting is about 1.3 METs, strolling is 2.0 METs, walking at 4.8 kilometers per hour is 3.3 METs, and running at 5 kilometers per hour is about 8.3 METs. The study by Ainsworth et al. (2000) have reported the average intensity (defined as METs) of different types of PA for adults [Ainsworth et al., 2000]. Based on absolute intensity, the Physical Activity Guidelines for Americans 2nd edition defines VPA as 6.0 or more METs, MPA as 3.0 to less than

6.0 METs, LPA as 1.6 to less than 3.0 METs. Unlike absolute intensity, relative intensity focuses on the exertion that an individual presents in performing an activity. Relative intensity can be measured in terms of the percentage of an individual's maximal oxygen uptake (VO_{2max}), the percentage of maximal heart rate (HR_{max}), the percentage of heart rate reserve (HRR), or the rating of perceived exertion (RPE) [Siddique et al., 2020].

Basically, the volume of PA refers to the total amount of PA accumulated in a specific period is usually expressed as MET × minute or MET × h per day or week. It can be calculated as frequency × duration × intensity (METs). With the development of wearable monitors for measuring PA (e.g., accelerometer, pedometer, and heart rate monitors), the volume of PA is also expressed as activity counts or steps over a time period.

Physical activity assessment

The basic construct of PA assessment is the quantification of energy expenditure. The double labelled water method is recognized as the gold standard for the assessment of energy expenditure. When the double labelled water is applied for the PA measurement, total energy expenditure should be divided by resting energy expenditure to control for body size and composition. Generally, larger individuals had higher resting energy expenditure than smaller ones and further had higher total energy expenditure. Because body size and composition affect resting energy expenditure, controlling for these make the PA comparable between individuals with varied body characteristics. According to the definition from FAO/WHO/UNU expert consultation, individuals' PA level (total energy expenditure/resting energy expenditure) can be categorized as sedentary or light activity lifestyles (1.40 - 1.69), moderately active or active lifestyles (1.70 - 1.99), and vigorously active lifestyles (2.00 - 2.40). However, the double labelled water method has several limitations. First, it is too expensive to be used in large-scale studies. Furthermore, it is time-consuming (at least 3 days). More importantly, only total energy expenditure can be obtained and daily or hourly data are not available [Sirard and Pate, 2001]. In addition to the energy expenditure, other parameters associated with PA (duration, intensity, and frequency) are of equal interest. The study by Pettee Gabriel et al. (2012) proposed a framework to classify components of human movement to provide a fundamental basis for standardizing definitions, guiding the design and development of subjective measures, and providing consistency during the selection of tool [Pettee Gabriel et al., 2012]. Generally, subjective methods such as questionnaires and activity logs are widely used in large-scale research. The main concern of the subjective tool is associated with the reporting bias and the precision of recall. Quinlan et al. (2021) indicated that using the self-reported questionnaires, PA performed at low-to-moderate intensity had the largest margins of error and PA performed at high intensity was overreported [Quinlan et al., 2021]. The authors further indicated that women showed a weaker association between self-reported and objective measured PA. Likewise, a previous study reported a lower accuracy of PA questionnaire measurement in women [Ferrari et al., 2007]. Although self-reported PA show weak or modest correlation with objectively measured PA among adults [Lee et al., 2011; Colley et al., 2018], it has been evidenced to benefit health [Warburton et al., 2006]. Moreover, current PA guidelines have mostly relied on subjectively measured evidence. In recent years, the development of wearable monitor for assessing an individual's PA has made it possible to measure the various components of PA objectively and directly. Unfortunately, there remains no standard of practice for monitor calibration and validation. The selection of wearable monitors depends on characteristics of studies, participants, instruments, activities [Butte et al., 2012; Ainsworth et al., 2015]. It is to be regretted that there is no single wearable monitor to be recognized as the gold standard for measuring PA among free-living individuals [Freedson et al., 2012].

Self-reported measurements focus on PA domains and generally record PA lasting at least 10 minutes, while objective measurement tools can record PA accumulated in shorter periods, which is contributed to measuring adherence to PA recommendations and establishing dose-responses relationships to guide the optimal PA for health outcomes. Additionally, objectively measured PA can provide information on PA intensity, volume, duration as well as posture in some new devices. This information is vital to investigating the relationship between PA and cardiometabolic risk factors, morbidity, and mortality. However, objective measurement tools are not without limitations. On the one hand, objectively derived data rely on algorithms to quantify PA. On the other hand, objective tools are less effective in measuring non-ambulatory activities and energy expenditure and unable to identify the PA domain. Furthermore, objective PA data are mostly derived from small-scale research and high-income countries. Therefore, there is no single best PA assessment tool, and the combination of both objective and subjective methods can facilitate our knowledge of PA among free-living individuals.

Physical activity in adults

The health benefits of PA have been well documented, and, in fact, health benefits can be achieved by simply becoming more physically active [Warburton et al., 2017]. Accordingly, the national and international PA guidelines based on scientific evidence offer an PA recommendation to guide PA promotion. For adults, at least 150-300 minutes of MPA or 75-150 minutes of VPA, or an equivalent combination of MVPA per week are recommended for health benefits [Piercy et al., 2018; Bull et al., 2020]. Nonetheless, physical inactivity has become a global concern.

The prevalence of physical inactivity varies greatly between countries and populations, as well as the measuring tool used.

A recent study by Whiting et al. (2021) analyzed national population-based surveys from nine European and Asian countries (Armenia, Azerbaijan, Belarus, Georgia, Kyrgyzstan, Republic of Moldova, Tajikistan, Turkey, and Uzbekistan) and demonstrated that, for adults, the weighted prevalence of physical inactivity ranged from 10.1% (Republic of Moldova) to 43.6% (Turkey). Women had a higher prevalence than men in most of countries included, with the prevalence ranged from 9.4% (Republic of Moldova) to 53.9% (Turkey). Based on data from the Global Physical Activity Questionnaire (GPAQ), work or transport-related PA was the biggest component of total physical activity (TPA) [Whiting et al., 2021]. The validated GPAQ were also used in a previous study for assessing PA in 22 African countries from 57,038 participants [Guthold et al., 2011]. The results showed that the percentage of women who met the PA recommendation was 75.7%, lower than 83.8% of man. Consistent with findings from some European and Asian countries, most of the TPA consisted of work and transport-related PA in African countries, resulting in rare LTPA [Guthold et al., 2011]. The study by Guthold et al. (2018) estimated the global prevalence of physical inactivity in adults aged 18 years and older from 168 countries based on questionnaire derived PA data. In this study, physical inactivity was defined as not meeting the WHO recommendation for adults. The results showed that global age-adjusted prevalence of physical inactivity was 27.5% in 2016, with an 8% higher among women (30.7%) than men (23.4%). Women in Latin America and the Caribbean, south Asia, and high-income Western countries had the highest prevalence of more than 40%. Furthermore, the authors indicated that although the global prevalence was stable from 2001 to 2016, physical inactivity increased in high-income countries, where the prevalence was twice as high as in low-income countries in 2016 (36.8% vs. 16.2%) [Guthold et al., 2018]. Another study investigated the prevalence of physical inactivity in 76 countries based on the International Physical Activity Questionnaire (IPAQ) [Dumith et al., 2011b]. This questionnaire was able to identify MVPA lasting at least 10 minutes in four domains including occupation, transportation, household, and leisure-time. The overall prevalence of physical inactivity was 21.4% and women had a higher prevalence than men (23.7% vs. 18.9%). A substantial difference in the prevalence of physical inactivity was noted between countries included, with the lowest of 2.6% in Comoros and the highest of 62.3% in Mauritania. In line with the study by Guthold et al. (2018), developed countries showed a higher prevalence of physical inactivity than less developed countries (27.8% vs. 18.7%) [Dumith et al., 2011b]. Despite using a different definition of physical inactivity, the prevalence of physical inactivity was stable in the Brazilian adults from 2009-2017, that was in line with the stable prevalence worldwide reported previously. However, most cities showed an increased prevalence in women [Silva et al., 2021].

The gender differences were also reported in a recent study, in which PA was assessed using the IPAQ across 28 European countries in 2017 [Nikitara et al., 2021]. Women were observed to be less active compared to men (OR: 0.86) and, overall, more than 30% European adults were physical inactive [Nikitara et al., 2021]. Similarly, in a previous study by Bauman et al. (2009), the prevalence was estimated in 20 countries based on data from the IPAQ. The authors indicated a gender difference, especially for young adults, with women less physically active than men [Bauman et al., 2009]. Furthermore, the study by Hallal et al. (2012) described PA in adults aged 15 years or older based on data from 122 countries. Based on self-reported PA data, 31.1% of adults worldwide were identified as physically inactive and women were more inactive compared to men (33.9% vs. 27.9%) [Hallal et al., 2012]. In the university setting, Irwin (2004) also reported that females university students were less active than men in accordance with the PA guideline proposed by the American College of Sports Medicine (ACSM).

Tcymbal et al. (2020) collected data from a nationally representative sample of 2,380 American adults aged 18-69 years. Using the GPAQ, 21.6% of participants failed to meet the minimum levels of PA recommended by WHO. Results from the age-specified analysis indicated that the level of PA was low among young adults (18-29 years). Even though most of young people meet the WHO recommendation for PA, their total PA was as low and their sedentary time and was as long as that of older people [Tcymbal et al., 2020]. Physical inactivity in young adults was also reported by other studies. In a previous study focused on Nigerian young adults aged 16-39 years, using the IPAQ, the prevalence of physical inactivity was 41% and physical inactivity was more prevalent among young females [Adegoke and Oyeyemi, 2011]. Based on data collected from 17,928 university students in 23 countries, the study by Pengpid et al. (2015) showed that the prevalence of physical inactivity was 41.4%, ranging from 21.9% (Kyrgyzstan) to 80.6% (Pakistan) [Pengpid et al., 2015]. It was in line with several previous studies demonstrating that insufficient PA was also prevalent in individuals with higher education level. For example, more than 50% of university students from a total of 27 countries (Australia, Canada, China, Germany, Nigeria, the US, and 21 European countries) failed to meet the minimum recommendation proposed by the ACSM [Irwin, 2004]. In a meta-analysis by Keating et al. (2005), 40% - 50% of university students were founded to be physically inactive. Unfortunately, interventions aimed at improving students' PA were less effective [Keating et al., 2005]. University students in East Asia showed a lower prevalence of physical inactivity, with 7.2% in Singapore, 8.0% in Malaysia, 13.5% in Taiwan, 16.8% in Hong Kong, and 28.5% in South Korea [Seo et al., 2012]. A recent study in Mexican adults also reported that young adults were less likely to adhere to the PA guideline [Medina et al., 2021]. Regarding LTPA, 23% of university students in North-Western Europe and the US were inactive and the prevalence was 30% in Central and Eastern European, 39% in Mediterranean, 42% in Pacific Asian, and 44% in developing countries [Haase et al., 2004].

Several studies objectively assessed PA using accelerometers and pedometers. In a study based on the 2003-2004 NHANES, 7176 participants with eligible accelerometer data were included [Troiano et al., 2008]. In this study, the intensity-threshold were 2020 counts for MPA and 5999 counts for VPA. The results showed that less than 5% of American adults met the recommendation of accumulating 30 minutes of MVPA. The adherence estimated based on accelerometer data was much lower than the one based on self-reported questionnaires, which was about 25% to 30% [Troiano et al., 2008]. Hallal et al. (2012) also synthesized evidence from accelerometry data. Using the same definition of MVPA as 2020 counts per minute or more, adult men spent 35.5 minutes of MVPA per day and adult women spent 32.0 minutes per day. Among women, there was a large variation in the time spent in MVPA, with the lowest of 19 minutes per day in the US and 44.6 minutes per day in Portugal [Hallal et al., 2012].

Trends in physical activity

PA is affected by several behaviors and environmental factors. The rapid megatrends result in changes in people's behaviors. For example, the increased use of motorized transport reduces the active transportation such as walking and cycling [Morency and Demers, 2010]. Furthermore, being obese [Kolovos et al., 2021; Guimarães et al., 2021], excessive working hours [Sung et al., 2021], longer screen time [Mineshita et al., 2021] were associated with the reduction of PA.

Evidence from a recent systematic review and meta-analysis showed that, using subjectively measured PA, there were significant decreases among both men and women between 1995 and 2017 [Conger et al., 2022]. Likewise, Pelclová et al. (2016) reported a decline in pedometer derived PA in Czech adults from 2008 to 2013. Women had a larger decrease in daily steps than men (1491 vs. 852 step/d) [Pelclová et al., 2016]. Decrease in steps determined PA seemed to be consistent and was supported by studies in Denmark [Matthiessen et al., 2015], Japan [Inoue et al., 2011; Takamiya and Inoue, 2019], However, the direction of change in accelerometer measured PA was less clear than the pedometer measured PA. There was no significant change in MVPA between 2002 and 2008 in Swedish adults. While a significant increase of MVPA was observed in women, their SB increased simultaneously [Hagströmer et al., 2015]. Time spent in MVPA was also reported to be stable in Canadian adults from 2007 to 2017, and the same result was shown in the gender-specified analysis [Clarke et al., 2019]. A study based on the CARDIA study reported that the accelerometry-based PA, including LPA and MVPA, reduced between 2005/2006 – 2015/2016, whereas SB increased [Pettee Gabriel et al., 2018]. A decrease of 12% in accelerometer measured PA was reported in participants from the Wisconsin Registry for Alzheimer's Prevention study with a 5-year follow-up [Dougherty et al., 2022].

Most studies investigated the trend of PA based on questionnaire measured PA. A pooled analysis based on data from population-based survey with 1.9 million participants showed that, from 2001 to 2016, there was an increase in people who met the PA recommendation worldwide [Guthold et al., 2018]. The increased trend in adherence level was also reported by studies from the US [Whitfield et al., 2021], Australia [Gugusheff et al., 2020], Poland [Biernat and Piątkowska, 2019], Korea [Lee and Vitiello, 2022] and Netherlands [Duijvestijn et al., 2020]. Whitfield et al. (2021) investigated the trend in the prevalence of meeting the PA guideline among the US adults between 2007/2008 and 2018/2018. The overall prevalence was 64.1% in 2007/2008 and 68.1% in 2017/2018, with a significant increase observed among women (56.9% in 2007/2008 and 61.8% in 2017/2018) [Whitfield et al., 2021]. The study in Australia reported that the frequency meeting PA guidelines was increased from 2002 (54%) to 2015 (61%) [Gugusheff et al., 2020]. As for Polish women, the prevalence of meeting the PA guideline was 38.5% in 2014 and 49.4 in 2018 [Biernat and Piątkowska, 2019]. In Korea, the adherence rate in adults aged 19 to 65 years increased from 37.26% in 2016 to 40.84% in 2019 [Lee and Vitiello, 2022]. In the Netherlands, the adherence level was increased from 39.9% in 2001 to 46.0% in 2018. More specifically, LTPA and strenuous work contributed most to the increase. Indeed, a previous study described trends in leisure-time, transportation-related, and occupational PA based on nationally representative data in Canada. The results showed that both men and women increased leisure-time and transportation-related PA between 1994 and 2005, whereas their PA at work were decreased [Juneau and Potvin, 2010]. The increasing trends in LTPA was in line with a previous study from England [Stamatakis and Chaudhury, 2008]. In this study, the authors further pointed out that the increase was only observed among middle-aged and older adults. Likewise, results from recent studies revealed similar trends. Biernat and Piątkowska, (2019) observed a constant increase in LTPA from 2014 to 2018 among Polish adults aged 15-69 years [Biernat and Piątkowska, 2019]. Morseth and Hopstock (2020) found an increase in leisure-time PA in a Norwegian general population between 1994-5 and 2001. However, the prevalence of SB during work time increased simultaneously [Morseth and Hopstock, 2020]. The study by López-Bueno et al. (2021) reported that, between 1987 to 2017, there was an increase in LTPA among Spanish adults across age groups [López-Bueno et al., 2021].

In contrast, several studies observed an increase in the prevalence of physical inactivity. In an analysis based on data from Iranian adults from 2006 to 2016, the prevalence of physical inactivity doubled from 23.1% in 2001 to 55.4% in 2016. Results from the gender-specified analysis revealed that, from 2001 to 2016, the percentage of physical inactivity increased in women and decreased in men. Young adults aged 25-34 years had the highest increase in the prevalence, with 19.54% in 2006 rising to 23.87% in 2016 [Kamalian et al., 2021]. Based on data from population-based surveys in 2003 and 2010, the study in Brazil found that the proportion of adults who participated at least 150 minutes per week was decreased from 39.9% in 2003 to 29.7% in 2010 (29.7%) [da Silva et al., 2014].

Physical activity and health benefits

PA guidelines synthesize scientific evidence and inform the public of the types and volumes of PA that provide a variety of health benefits. It is well known that adults should engage in at least 150 - 300 minutes of MPA a week, or 75 – 150 minutes of VPA a week, or an equivalent combination of MVPA. In addition, they should do muscle-strengthening activities of moderate or greater intensity on 2 or more days a week. Adhering to these PA recommendations has been evidenced to have significant health benefits. Recently, Zhao et al. (2020) investigated the association between the 2018 PA guideline for Americans and all-cause mortality through a population-based cohort study with a total of 479,856 participants aged 18 years or older. Based on self-reported PA, participants who met the recommended aerobic activity (hazard ratio (HR): 0.71) or muscle strengthening activity (HR: 0.89) were at reduced risk of all-cause mortality compared with those who did not meet the PA guideline, and among those who met both activities, a larger reduced risk was observed (HR: 0.60). Even for young adults aged 18-39 years, the survival benefits were observed among those who met the recommendation of aerobic (HR: 0.79) or strengthening activities (HR: 0.95), or both (HR: 0.71) [Zhao et al., 2020]. Zhao et al. (2014) also examined the 2008 PA guideline based on data from NHANES (1999-2004) and mortality data collected in 2006. Results showed that compared with adults who did not do any MVPA, those who engaged in ≥ 150 minutes of MVPA a week had a lower HR for both all-cause (HR: 0.64) and CVD mortality (HR:

0.57), and those who engaged in 0 - 150 minutes of MVPA a week also showed a reduced risk for all-cause (HR: 0.72) and CVD mortality (HR: 0.69) [Zhao et al., 2014]. Likewise, Schoenborn and Stommel (2011) suggested that significant survival benefits were found among adults who met the 2008 aerobic activity recommendation, especially among those having chronic diseases. However, survival benefits from strengthening activities were not observed in this study [Schoenborn and Stommel, 2011].

Additionally, complying with PA guidelines was found to be associated with multiple health benefits, such as the reduced risk of CVD [Dickie et al., 2014], type 2 diabetes [Dickie et al., 2014], MetS [Wu et al., 2016; Lim et al., 2021] and obesity [Bennie et al., 2020; Tittlbach et al., 2022], and favorable metabolic biomarkers [Bird and Hawley, 2016; Bennie et al., 2020; Gallo et al., 2021], and body composition [Gallo et al., 2021].

Intensity

It is well documented that MVPA brings health benefits and nearly all the current PA recommendations emphasize thresholds for MVPA. The increasing use of wearable monitors contributes to the identification of PA in real-life settings and there is a growing number of studies have reported health benefits from LPA and sporadic PA in adolescents [Carson et al., 2013] and adults [Healy et al., 2007; Gando et al., 2014; Marschollek, 2015; Loprinzi, 2017]. Previous studies reported that accelerometer measured LPA (100 – 1951 counts or ≥ 3.0 METs) was associated with 2-h postprandial glucose (PPG) [Healy et al., 2007] and insulin resistance [Gando et al., 2014]. Marschollek (2015) analyzed accelerometer data from the NHANES (2005-2006) and found that PA with light intensity and short duration (< 10 minutes) was favorably associated with health outcome [Marschollek, 2015]. In an analysis based on the NHANES (2003-2006), every 60-minute increase in accelerometer-measured LPA was found to be associated with a 16% reduction of HR for all-cause mortality [Loprinzi, 2017]. In a recent systematic review and meta-analysis, Chastin et al. (2019) synthesized evidence from experimental, cross-sectional, and prospective studies. With the definition of LPA as activities performed at the intensity of 1.5 - 3 METs, the pooled results from experimental studies revealed that, compared to prolonged SB, LPA were effective on reducing postprandial glucose and insulin. In the pooled analysis of interventional studies that consisted of > 150 minutes of LPA per week for at least 12 weeks, the improved BP and lipid profiles were observed and in prospective studies, a favorable association between daily LPA and risk of all-cause mortality were reported [Chastin et al., 2019]. It was supported by recent studies with all-cause mortality as the outcome. Results from a pooled analysis showed that, compared with participants engaged in less than 3 hours of LPA per day, the HRs of mortality were 0.71, 0.68 and 0.56 for those engaged in 3 - 5 hours per day, 5 - 7 hours, and > 7 hours, respectively [Ku et al., 2020]. Del Pozo Cruz. (2021) reported that, among young adults, life expectancy was significantly benefited from modest (2.89 years) and high (3.07 years) levels of LPA [Del Pozo Cruz., 2021]. Based on data from the NHANES dataset, Füzéki et al. (2017) conducted a systematic review to investigate whether LPA was associated with health outcomes in adults. Results showed that LPA was beneficially associated with obesity, lipid profiles, glucose regulation, and overall mortality [Füzéki et al., 2017]. However, several studies did not find any association between LPA and health outcomes, including mortality [Lee and Paffenbarger, 2000], MetS [Laaksonen et al., 2002], insulin resistance [Ekelund et al., 2009].

Duration

Previous PA recommendations emphasized MVPA that lasting at least 10 minutes whereas emerging evidence revealed that, regardless of the duration of each MVPA bout, health benefits associated with the total amount of PA could be achieved. A recent systematic review challenged the current threshold-based PA guideline and indicated the fact that everyone can benefit from simply becoming more physically active [Warburton et al 2017]. Evidence from cross-sectional and prospective studies demonstrated that, PA accumulated with bouts lasting less than 10 minutes was beneficially associated with body composition [Loprinzi and Cardinal, 2013; Wolff-Hughes et al., 2015], BP [Loprinzi and Cardinal, 2013; White et al., 2015; Wolff-Hughes et al., 2015], lipid profiles [Wolff-Hughes et al., 2015], glucose regulation [Loprinzi and Cardinal, 2013; Wolff-Hughes et al., 2015], MetS [Ayabe et al., 2012; Clarke and Janssen, 2014; Jefferis et al., 2016], and inflammation markers [Loprinzi and Cardinal, 2013; Wolff-Hughes et al., 2015].

Some studies have compared health outcomes of PA accumulated from PA bouts that less than 10 minutes with those that at least 10 minutes. The study by Fan et al. (2013) suggested that, when performing at higher intensity (≥ 2020 counts per minute), PA accumulated with short bouts or long bouts were both associated with lower BMI and risk of obesity [Fan et al., 2013]. Similar findings in relation to obesity also were reported by Ayabe et al. (2013), Glazer et al. (2013), Jefferis et al., (2016), and Carmeron et al. (2017). Loprinzi and Cardinal, (2013) and Glazer et al. (2013) reported similar association with blood lipid profiles, including HDL and TG. Similar association with FPG and fasting insulin was reported by Loprinzi and Cardinal, (2013), Ayabe et al. (2012) and Jefferis et al., (2016). Moreover, a more potent association was found between favorable lipid profiles and glucose metabolism with short bouts of PA than long bouts of PA [Wolff-Hughes et al., 2015]. Few studies examined very short bouts and provided positive outcomes. MVPA lasting more than 32 seconds had significantly association with MetS components [Ayabe et al., 2012]. MVPA lasting more than 1 minutes played an important role on controlling abdominal fat [[Ayabe et al., 2013] and predicting the MetS [Clarke and Janssen, 2014].

Domain

Current PA recommendation focused on the total amount of PA regardless of domains in which PA was accumulated. Contrast to LTPA, which confer health benefits, OPA was suggested to be associated with elevated risk [Holtermann et al., 2012]. According to the Copenhagen Male Study, the amount of OPA was positively associated with the risk of ischemic heart disease among adult men with low and medium physical fitness [Holtermann et al., 2010]. Holtermann et al. (2016) also analyzed data from the Copenhagen City Heart Study, which included 4724 adults aged 20-67 years without CVDs at baseline and found that high levels of self-reported OPA was found to be associated with an increased risk for CVD mortality compared to the low level [Holtermann et al., 2016]. The association between OPA with the risk of CVDs and mortality was supported by other studies. In an analysis based on the Cardiovascular Occupational Risk Factor Determination in Israel Study, adult men with moderate-to-vigorous self-reported OPA and no LTPA were found to have the greatest risk for all-cause and CVD mortality [Harari et al., 2015]. Similarly, Krause et al. (2015) assessed the relative workload which took participants' fitness into account and reported that men with high level of OPA (measured by relative workload) had higher risk for acute myocardial infarction [Krause et al., 2015]. Findings were consistent from studies based on adult women. Korshøj et al. (2013) found that higher steps at work was associated with lower CRF among female hospital cleaners [Korshøj et al., 2013]. Likewise, with a total of 12,093 female nurses aged 45-64 years, findings from the Danish Nurse Cohort Study demonstrated that women, especially those with HTN, were at high risk of CVDs when exposure to high level of OPA [Allesøe et al., 2016]. One of potential explanations for the PA health paradox might be the contrasting effects on nocturnal heart rate, with LTPA reduced the heart rate during sleep whereas OPA increased the heart rate, and the prolonged elevated heart rate was evidenced to be a strong predictor for CVDs [Johansen et al., 2013; Korshøj et al., 2015]. Recently, 6 hypotheses for underlying mechanisms for the PA health paradox were proposed by Holtermann et al. (2018) as follows: (1) OPA was of a combination of low intensity and long duration which deteriorated CRF and cardiovascular health; (2) OPA increased 24-hour heart rate; (3) OPA might cause sustained high BP when it involved heavy lifting and prolonged static postures; (4) OPA might induce fatigue and exhaustion when it performed without sufficient rest; (5) OPA was often performed under conditions that lacked worker control and this condition was more likely to induce over exhaustion; (6) OPA might result in elevated levels of inflammation markers, which was recognized as new risk factors for CVDs [Kasapis and Thompson, 2005; Silveira Rossi et al., 2022].

However, a prospective cohort study from 17 countries suggested the health could be benefited from both LTPA and OPA [Lear et al., 2017], supporting the notion that health benefits could be obtained by simple becoming more active.

Summary

PA is a well-known modifiable lifestyle factor in primary and secondary prevention of CVDs. PA assessment is critical in evaluating its association with health. Basically, the double labelled water method is regarded as the gold standard for the assessment of energy expenditure, which is the basic construct of PA assessment. However, as our understanding of PA has developed, in addition to energy expenditure, other components of PA such as domain, duration, intensity, and frequency are also gaining increasing attention. This information could be obtained through questionnaires, activity logs, accelerometers, pedometers, or others. However, both subjective and objective tools have limitations, and the selection of PA assessment tools depends on the study design, participants, instruments, and activities.

Although the health benefits have been widely reported, the prevalence of physical inactivity in adults is high worldwide, especially in low-income countries. Women are found to be less physically active than men in most studies. Fortunately, with multiple strategies aimed at improving PA, the global prevalence of physical inactivity has remained stable in recent years, however the frequency of physical inactivity among women continues to increase. Physical inactivity is also prevalent among young people and those with higher education level. In the case of young adults, the satisfied rate of meeting PA recommendations is accompanied by low levels of TPA and high levels of SB. Particularly, PA interventions appear to be less effective in young adults with higher education level. Furthermore, the PA measured is lower if objective tools are used instead of subjective ones and women are more likely to have reporting bias.

There is substantial evidence that, for adults, adhering to PA recommendations that engage in at least 150 - 300 minutes of MPA, or 75 - 150 minutes of VPA, or an equivalent combination of MVPA per week reduces risk of CVD and all-cause mortality, as well as brings multiply health benefits, including lowering risk of CVDs, type 2 diabetes, MetS and obesity, and improving metabolic biomarkers and body composition. Generally, PA performed at moderate-to-vigorous intensity and lasts at least 10 minutes are recommended to maintain and improve the cardiometabolic health. However, emerging evidence showed that LPA and sporadic PA also have health promoting effects. In fact, individuals can obtain health benefits by simply becoming more physically active than before. Additionally, the domain in which PA accumulated is found to influence the association between PA and health outcomes. In contrast to LTPA, which has been evidenced to benefit health by substantial evidence, OPA is found to be associated with the increased risk of CVDs and mortality. The reason why high intensity OPA is harmful to health is not clear. The reason for the negative association between OPA and health is also not clear but may be due to the fatigue and increased heart rate caused by prolonged low-intensity OPA. Despite extensive evidence that the increase in PA can positively affect health outcomes, there is still no optimal intervention to promote PA. In recent years, HIIT has been recognized as an efficient way to improving health and fitness outcomes, but its effects on PA have not been fully investigated. Since PA is strongly associated with a variety of health outcomes, exploring the effect of HIIT on PA may explain the effectiveness of HIIT programs.

High-intensity interval training

Even though the current PA guidelines have emphasized aerobic exercise, HIIT has gained increasing attention in the last 20 years. However, there are various definitions in relation to HIIT in the literature. Basically, HIIT is one form of interval training, which refers to intermittent exercise that comprise of short or long bouts of high-intensity exercise interspersed by the sufficient or insufficient recovery period between each bout [Fox et al., 1973]. Although there is not a unified definition for HIIT, the associated intensity was shown to be high that is equal to or above the anaerobic threshold/maximal lactate steady state. The work and rest duration are normally ranged from a few seconds to a few minutes. In 1959, Reindell and Roskamm first described interval training in the academic journey while interval training was popularized as a training method in 1952 by the Helsinki Olympics [Billat, 2001]. Interval training improve the performance of endurance athletes by keeping their oxygen uptake at or near the maximal level for a longer time [Billat, 2001]. Regarding to the training protocol, the velocity at which VO_{2max} is achieved and fractions (50 - 75%) of the time to exhaustion were originally used as the work intensity and interval duration respectively, and this protocol had successfully improved the performance among endurance athletes [Laursen and Jenkins, 2002]. In addition to the improvement of aerobic capacity, Laursen and Jenkins (2002) indicated that HIIT is also beneficial to anerobic capacity. These findings from athletes have led to increased interests in HIIT among people who expect to promote health or rehabilitation through activities [Wisløff et al., 2007; Keating et al., 2014].

Tabata training

Tabata training, as one of the HIIT protocols, is gaining popularity among young adults worldwide in recent years. Tabata training involved a conventional protocol that consists of a total of 8 bouts of exercise with each bout comprising of 20 seconds of workout followed by 10 seconds of rest [Tabata, 2019]. Tabata training was originally designed to improve athletic performance in speed skating athletes, the original exercise modality was cycling, and the original intensity was a constant of 170% VO_{2max} from the first to the last bout. However, for untrained individuals who exercise for health, this supramaximal intensity is unfeasible, especially for clinical individuals.

Therefore, in practice, the relative intensity that exhausts participants during the last bout are recommended. Generally, studies with modified Tabata protocol require participants to exercise with their best effort to complete maximal repetitions [Fortner et al., 2014; Harnish and Sabo, 2016; Menz et al., 2019; Murawska-Cialowicz et al., 2020; Islam et al., 2020]. Meanwhile, HR_{max} and the RPE will be measured to verify the high intensity during Tabata training [Logan et al., 2016; Domaradzki et al., 2020; Popowczak et al., 2022]. Intervention studies showed that participants could benefit from Tabata training that was less intense of 70 - 80% HR_{max} [Menz et al., 2019; Popowczak et al., 2022]. Characterized by the simple format of 20/10-second work/rest and the shorter total duration of 4 minutes, the Tabata training removes obstacles for individuals who lack time to exercise. Although cycling is originally used in Tabata training, it is equipment-dependent and inconvenient for the general population. Functional training may be an alternative to cycling since it can be done everywhere. For example, in the study by Talisa Emberts et al. (2013), multiple functional movements were grouped into a Tabata-style protocol, including high knee run, plank punch, jumping jacks, side skaters, jump rope, in/out boat, line jumps and push-ups. Each movement was instructed to perform as many repetitions as possible for 20 seconds, followed by 10 seconds rest, and then repeat it. Talisa Emberts' workout consisted of multiple 4-minut bouts, intermitted by 1-minute rest and the average heart rate during exercise was 86% of HR_{max}. In another Tabata-style HIIT, participants were instructed to complete the squat jumps for each 20-second workout at the average intensity of 95% VO_{2max} for a total of 4 minutes, with 10 seconds rest between each workout [Olson, 2014]. The Tabata-style functional HIIT offered a variety of intensities, durations and functional movements that could be selected and organized according to individual exercise goals.

High intensity interval training and health outcomes

For general people, health outcomes in relation to HIIT include cardiometabolic health, CRF, body composition, musculoskeletal health as well as mortality.

Findings regarding to the association between HIIT, and CRF seemed consistent. Evidence from systematic review and meta-analysis based on intervention studies showed that HIIT was effective in improving VO_{2max} in adults with varies BMI and health conditions [Kessler et al., 2012; Jelleyman et al., 2015; Batacan et al., 2017]. In the study by Batacan et al. (2017), HIIT performed at maximal effort, ≥ 85% VO_{2max}, ≥ 85% heart rate or ≥ 90% HR_{max} were included. The modality of HIIT included treadmill running, cycling, and swimming. The authors analyzed 65 intervention studies according to the duration of protocol and participants' BMI and reported differences in the effects of HIIT between participants with normal weight and overweight or obesity. Among normal weight participants (BMI: 18.5 – 24.9 kg/m^2), HIIT protocol with both short (< 12 weeks) or long duration (≥ 12 weeks) were effective in increasing VO_{2max}, but not cardiometabolic risk factors such as SBP, DBP, TC, HDL, low-density lipoprotein (LDL), TG, FPG and fasting insulin. While among overweight (BMI: 25.0 – 29.9 kg/m^2) or obese (BMI: ≥ 30 kg/m^2) participants, both short-term and long-term HIIT could significantly increase VO_{2max}, decrease SBP and WC, especially with long-term HIIT also lowering resting heart rate, DBP, and percentage of body fat (%BF).

Jelleyman et al., (2015) conducted a meta-analysis to quantify the effects of HIIT on cardiometabolic risk factors compared with moderate intensity continuous training (MICT) or control groups (CON). A total of 50 intervention studies included in the meta-analysis. The HIIT protocol used varied widely between studies, with the bout duration ranging from 4 seconds to 5 minutes, the exercise intensity ranging from 65% VO_{2max} to all-out, the recovery duration ranging from 12 seconds to 5 minutes, and the recovery intensity ranging from rest to 70% HR_{max}. Findings from the pooled analysis showed that VO_{2max} increased by 0.30 L/min after HIIT and this increase was significantly higher than MICT and CON. Compared with CON, insulin resistance, HbA1c and body mass decreased with HIIT. Furthermore, more favored health outcomes were found among participants with MetS or type 2 diabetes, who were experienced reductions in postprandial glucose (PPG) and HbA1c following HIIT.

In a previous systematic review by Kessler et al. (2012), HIIT was classified as aerobic interval training (AIT) and sprint interval training (SIT). SIT was characterized by 4 – 6 bouts of 30-second all-out sprint separated by 4 -4.5 minutes of recovery. Because of its extremely high intensity, SIT was mostly used among healthy young adults. AIT was usually completed at a slightly lower intensity than SIT but had a longer workout duration. In this systematic review, the intensity of AIT studies was about 80 – 95% VO_{2max} and the workout duration was 4 minutes. Despite the limited number of SIT studies, there was an improvement on aerobic capacity following SIT programs.

Consistent findings were reported by AIT studies and in addition, improvements on FPG, HDL and BP were observed following AIT. Although health outcomes in relation to body mass, BMI, %BF, and WC were equivocal, those appeared to be more consistent among overweight/obese individuals.

HIIT was consistently reported to be effective in improving CRF among a variety of adults [Martin-Smith et al., 2020]. Nevertheless, the improvements in cardiometabolic health and body composition associated with HIIT were more common in overweight/obese individuals (with or without CVDs and diabetes), especially when these individuals involved in training for 12 weeks or more.

Furthermore, HIIT is gaining popularity among individuals who seek to lose weight [Thompson, 2014]. In the study by Talanian et al. (2007), 8 young female adults were involved in a two-week HIIT protocol with a total of 7 sessions. Each session included 10 cycles of 4-minute exercise at 90% of peak oxygen uptake (VO_{2peak}) with 2-minute recovery between intervals. The results demonstrated that there was a significant increase in fat oxidation during exercise after training [Talanian et al., 2007]. Similar findings were reported by Perry er al. (2008) and Whyte et al. (2010). Maillard et al. (2018) conducted a meta-analysis to examine the efficacy of HIIT in reducing fat mass in adults with various body mass. Findings from the pooled analysis showed that total, abdominal, and visceral fat mass were significantly reduced after HIIT. More specifically, HIIT performed at 90% peak heart rate or above was more effective in reducing total fat mass, while HIIT performed at lower intensity was effective in reducing abdominal and visceral fat mass. Consistent findings were found in gender-specified analysis, whereas the fat-reducing effects of HIIT were found to be only effective among overweight or obese individuals [Maillard et al., 2018]. Unfortunately, the absence of control groups in these studies made it impossible to determine whether this effect was induced by the training itself or by HIIT. The study by Trapp et al (2008) involved HIIT, MICT and CON group. In this study, 45 young women were randomly assigned to one of three groups and those in HIIT or MICT were instructed to participant in a 15-week exercise program. After the intervention, only those in HIIT group significantly reduced body mass, fat mass, trunk fat and fasting insulin, with the greater fat loss in legs compared to arms [Trapp et al., 2008]. It was in line with the study by Zhang er al. (2021) that interval training performed at high intensity induced greater fat loss than MICT after a 12 - week intervention [Zhang et al., 2021]. It was supported by a systematic review and meta-analysis that there was a 28.5% greater reduction of total absolute fat mass observed with interval training compared with MICT. The authors further suggested that supervised interval training, young age (< 30 years) and short duration (< 12 weeks) were favorably associated with the reduction of fat mass [Viana et al., 2019].

However, several studies reported that HIIT and MICT elicited similar reductions of fat mass. Tjønna et al. (2008) found that HIIT and MICT were equally effective at reducing body weight [Tjønna et al., 2008]. A systematic review and meta-analysis compared the effects of HIIT with MICT on body composition in overweight or obese adults. With the frequency of 3 sessions per week for 10 weeks, HIIT and MICT were equal and significantly reduced whole body fat mass and WC [Wewege et al., 2017]. Another systematic review and meta-analysis examined low-volume HIIT and found that there was no difference between low-volume HIIT and MICT on fat mass, %BF, and lean body mass [Sultana et al., 2019]. Consistent findings were also reported in obese young women [Kong et al., 2016; Zhang et al., 2017] and adults with MetS [Aristizabal et al.,2021].

Among women, a recent meta-analysis assessed the effect of HIIT on body composition. A total of 959 women with a range of body mass and menopausal status were included and the pooled analysis revealed that overall, HIIT was effective in reducing weight, total and abdominal fat mass in women. However, abdominal fat mass was improved only among women with excessive adiposity. The result from the stratified analysis of hormonal status suggested that the fat lowering effect was only observed among women before menopause [Dupuit et al., 2020]. In addition to the reduction of fat mass, another study found that HIIT was effective in improving exercise tolerance among overweight or obese women [Smith-Ryan et al., 2016]. Zhang et al., (2021) indicated that, for obese women, interval training performed at 90% of VO_{2max} or above was effective in reducing visceral fat [Zhang et al., 2021].

In contrast, the study by Nybo et al. (2010) found HIIT was less effective than MICT in treating obesity. It was supported by the studies from Keating et al. (2014), in which MICT was superior to HIIT in improving fat distribution among overweight adults, and Youssef et al. (2022), in which MICT was superior to HIIT in reducing relative gynoid fat mass in obese older adults [Youssef et al., 2022].

It was evidenced that HIIT interventions with longer duration were more likely to provide health promotion than those with shorter duration, while there was still no consensus on the optimal duration. The study by Kessler et al. (2012) suggested that AIT or SIT programs that lasted 4 to 8 weeks showed similar improvements on aerobic capacity compared with MICT, and those lasted 10 to 24 weeks resulted in a significantly greater increase in aerobic capacity [Kessler et al., 2012]. In particular, the authors indicated that HIIT could rapidly increase aerobic capacity and this improvement could be observed following 2-week SIT [Whyte et al., 2010] and 4-week AIT [Moholdt et al., 2009]. It was supported by another systematic review and meta-analysis that short-term HIIT that lasting 2 - 8 weeks was effective in improving VO_{2max} in healthy adults with a range of PA level [Sloth et al., 2013]. Indeed, a previous investigation by Gibala and McGee (2008) suggested that as short as 2 weeks of HIIT with a frequency of 3 times a week was able to show improvements in skeletal muscle oxidative capacity and endurance performance [Gibala and McGee, 2008]. It seemed that both short-term (< 12 weeks) and long-term (≥ 12 weeks) HIIT were able to improve VO_{2max} and the finding from a systematic review and meta-analysis demonstrated that the greater improvement in aerobic capacity was observed with longer intervention periods (≥ 12 weeks) [Batacan et al., 2017].

The effects of HIIT on CVD risk factors reduction appeared to take longer. Kessler et al. (2012) suggested that at least 12 weeks was necessary to demonstrate improvement in FPG, BP, body composition and glucose regulation and at least 8 weeks was required to show improvement in HDL [Kessler et al., 2012]. The study by Batacan et al. (2017) showed that, among overweight or obese adults, HIIT programs lasting less than 12 weeks only had a favorable effect on DBP whereas those that lasting 12 weeks or longer significantly reduced both SBP and DBP by 4.57mm Hg and 2.94 mm Hg, respectively. A reduction in SBP of more than 4mm Hg was associated with a substantial reduction (5-20%) of CVD mortality [Taylor et al., 2011]. Long-term HIIT was also beneficial to WC and %BF in overweight/obese adults [Batacan et al., 2017]. Despite the lack of direct comparisons, previous studies had provided some evidence that long-term HIIT conferred more health benefits. Some SIT studies of 2 - 4 weeks found no improvement on glucose metabolism outcomes in participants with normal FPG [Babraj et al., 2009; Richards et al., 2010; Whyte et al., 2010], whereas studies of 12 weeks or longer showed some improvements. Moreira et al. (2008) and Schjerve et al. (2008) suggested that 12 weeks of HIIT with the frequency of three times a week was beneficial to some cardiometabolic risk factors (weight, BMI, WC, DBP and glucose) in overweight adults [Moreira et al., 2008]. Similarly, HIIT for 12 weeks with a total of 40 minutes of training time per week was found to be effective in improving glucose tolerance [Nybo et al., 2010]. With the same frequency but longer duration of 16 weeks, results from the study by Tjønna et al., (2008) and Ciolac et al., (2010) showed improvement in MetS risk factors in adults with MetS [Tjønna et al., 2008; Ciolac et al., 2010].

On the other hand, there was growing evidence to support the efficacy of HIIT with shorter exercise duration in a single session. The study by Hazell et al. (2010) shortened the exercise duration of original Wingate protocol from 30 seconds to 10 seconds and observed a similar improvement in VO_{2max} in young adults after 2-week intervention, suggesting that shorter HIIT bouts were effective in improving aerobic and anerobic capacity [Hazell et al., 2010]. Likewise, Zelt et al. (2014) compared the original SIT protocol with 30-second bouts to the modified one with 15-second bouts and found no significant difference in the increase in VO_{2max} [Zelt et al., 2014]. Gillen et al. (2014) examined the impact of a 6-week HIIT protocol, which involved three 20-second Wingate sprints per session, 3 sessions per week, and found that SBP, mean arterial pressure and insulin sensitivity were improved after training [Gillen et al., 2014]. Additionally, exercise-induced fatigue and perceived exertion would be attenuated by reducing the bout duration, as well as by reducing the bout number [Vollaard et al., 2017]. Vollaard et al. (2017) conducted a meta-analysis to investigate whether the number of bouts in a SIT session had an impact on change in VO_{2max}. Findings from the pooled analysis showed that, taking 7 bouts as a reference, every two more bouts reduced the improvement in VO_{2max} by 1.2%, suggesting that the fewer bouts per session did not attenuate the gain in VO_{2max} but might enhanced it [Vollaard et al., 2017].

Safety and tolerance of high-intensity interval training

Participants' safety is vital to the utility of HIIT to reduce risk of CVDs and promote overall health, especially for those with overweight or obesity, MetS, diagnosed CVDs and type 2 diabetes, or other chronic diseases. Since HIIT was originally used in elite athletes, there had been concerns that HIIT might be unsafe and intolerant for individuals with lower fitness [MacDonald and Currie, 2009]. This concern had been challenged as there was growing evidence from studies in real-world or clinical settings. In the study by Jelleyman et al. (2015), exercise adherence, attrition and adverse events were synthesized and reported. An average adherence of 90% were reported, with the minimum adherence ranging from 66% to 90%. The average dropout was 10% and a total of 19 adverse events were reported in 17 out of 50 studies. Of the 18 adverse events related to musculoskeletal injuries, 14 occurred in the HIIT group. Fortunately, none of these injuries was severe and participants did not have to interrupt or withdraw from training, and furthermore, none of studies included reported serious adverse events [Jelleyman et al., 2015]. Even when used for cardiac rehabilitation, HIIT showed a low risk of adverse events (3%) [Taylor et al., 2020] and appeared to be safe and better tolerated than MICT [Guiraud et al., 2012]. The following paper is a study published from this thesis.

Effects of high intensity exercise on oxidative stress and antioxidant status in untrained humans: a systematic review

Abstract: Participation in exercise promotes health. High intensity exercise (HIE) has become increasingly popular among the general population, its effects on exercise induced oxidative stress and antioxidant status in untrained humans is not clear. The aim of this systematic review was to investigate the influence of HIE on oxidative stress and antioxidant status in untrained humans. Web of Science, PubMed, MEDLINE, and Scopus were searched until March 2021. A methodological quality assessment valuation/estimation was additionally carried out in the final sample of studies. Following the PRISMA selection process, 21 studies were finally included. There was strong evidence that acute oxidative stress following the cessation of HIE exists when compared to resting states. The HIE induced oxidative stress is transient and is most likely restored to normal levels within 24 hours due to the stimulated endogenous antioxidant system whose response was lagging and lasting. Physically active humans had better antioxidant systems and suffered less oxidative stress after HIE. A physically active lifestyle was considered to enhance antioxidant capacity. For untrained humans, HIE with intensities above 70% of VO_{2max} are proposed for initial exercise levels based on the findings.

1. Introduction

Free radicals are rogue molecules that damage cells. Denham Harman (1956) first discovered the active properties of free radicals and suggested the free radical theory of aging [Harman, 1956]. The theory proposed that the production of free radicals, such as reactive oxygen species (ROS), is inevitable during metabolism. ROS are active substances containing oxygen occurring in the human body or the natural environment. Normal metabolism in the body can produce ROS, which can initiate the formation of free radicals [Forsberg et al., 2001]. However, any uncontrolled production of ROS can lead to oxidative damage to proteins, DNA, and lipids [Gutteridge et al., 1996; Halliwell, 1996].

Antioxidants are substances that minimize the harmful effects of oxygen. These substances help trap and neutralize free radicals, thereby preventing the damage they inflict on the human body. The antioxidant system in the human body consists of antioxidant metabolites and enzymes that impede the production of ROS by removing these active substances before they can cause damage to the important components of cells [Cooper et al., 2002]. However, ROS are not always harmful, and physiologically, appropriate amount of ROS can promote immunity [Banerjee et al., 2003]. Therefore, the role of the body's antioxidant system is not to remove ROS completely, but to control them at appropriate levels.

Physiologically, antioxidants and oxidants are in equilibrium. The body's endogenous antioxidant defense system (non-enzymatic and enzymatic), under normal conditions, is effective against the potentially harmful effects of ROS [Koska et al., 2000; Banerjee et al., 2003]. When oxidizing substances increase, oxidative stress occurs. Increasing evidence shows that most health problems and diseases caused by aging are related to endogenous ROS production and oxidative stress [Cooke et al., 2003]. It is widely believed that most age-related health problems, ranging from wrinkles, and including cardiovascular disease, cancer, and Alzheimer's disease, are linked to excessive oxidative stress [Valko et al., 2006; Liguori et al., 2018; Kruk et al., 2019;].

Many studies have shown that with the increase in oxygen consumption during exercise, the production of ROS increases [Cooper et al., 2002; Djordjevic et al., 2016]. When the ability of the antioxidant system is insufficient to counterbalance the ROS produced during exercise, oxidative stress occurs. Davies et al. (1982) used Electron spin resonance (ESR) for the first time to directly confirm the significant increase of free radicals in muscles following exercise [Davies et al., 1982]. Over the past 40 years, various studies have emerged investigating the effects of oxidative stress induced by exercise.

Studies have also indicated that regular exercise can upregulate the body's antioxidant system and increase its resistance to oxidative stress [Alessio, 1993; Radák et al., 2000, 2002, 2008]. Regular exercise is beneficial to health, and it can reduce the risk of cancer, cardiovascular disease, diabetes, and other chronic diseases [Blair et al., 2001; Forsberg et al., 2001; Oguma et al., 2002; Crespo et al., 2002; Cooke et al., 2003].

Despite this, Davies et al. (1982) and Jackson et al. (1985) used ESR to provide direct evidence that exercise may induce oxidative stress [Davies et al., 1982; Jackson et al., 1985]. The elevation of biomarkers of oxidative damage in the blood and skeletal muscle also provides indirect evidence for oxidative stress induced by exercise. During exercise, skeletal muscle contractions produce free radicals, while increased oxygen consumption produces a large amount of ROS [Alessio et al., 1988; Duthie et al., 1990; Reid et al., 1992; Castrogiovanni and Imbesi, 2012]. If the body's antioxidant defense is insufficient, cells and tissues will suffer oxidative damage [Kanter, 1998].

Physical exercise is a complex biological activity that constantly challenges the oxidation-antioxidant balance of the body (cells, tissues, organs, etc.) while maintaining biological balance [Ji et al., 2008]. The adjustment of exercise on oxidative stress can be acute or long-term. Acute adjustment is an incomplete adaptation that can easily lead to oxidative damage, so it is important to give the body sufficient rest following exercise to restore balance. The process of balancing - breaking the balance - restoring the balance helps improve the body's ability to cope with oxidative stress. In fact, regular exercise can fundamentally upregulate the body's endogenous antioxidant system [Radak et al., 2001]. Moderate aerobic exercise is often used to improve the body's antioxidant capacity and reduce chronic diseases. At the same time, more and more studies suggest that high intensity exercise (HIE) may be more effective in promoting fitness and health than traditional continuous training [Gibala, 2007; Burgomaster et al., 2008; Hood et al., 2011].

Due to its high efficiency, HIE has been the subject of more and more attention in recent years among athletes, bodybuilders, and individuals with chronic diseases. However, along with the increasing interest in HIE, there are questions that need consideration. One such question relates to the influence of HIE on oxidative stress. This question may directly affect the arrangement of athletic training loads, the choice of fitness methods, and the safety of exercise for patients with chronic diseases.

To date, effects of HIE on oxidative stress in untrained humans are inconclusive. Therefore, this systematic review aims to systematically analyze effects of a single bout of HIE on oxidative stress markers and antioxidant status in untrained humans. A further aim is to investigate if long term HIE can influence exercised induced oxidative stress and upgrade the antioxidant system, and furthermore, to provide important information for physically inactive individuals to participant in HIE.

2. Methods

2.1 Data sources and searches

According to the Preferred Reporting Items for Systematic reviews and me-ta-analysis (PRISMA), a systematic literature search, limited to literature published in English and Chinese, was conducted in March 2021 using four electronic databases (PubMed, MEDLINE, Web of Science, SCOPUS). Following this process, the literature list obtained was then manually searched and the results were placed in Endnote (Endnote 20, Wintertree Software Inc., China).

Search terms were limited to titles and abstracts and based on all possible combinations of the following keywords: high-intensity, interval, high-intensity interval, exhaustive, acute, training, exercise, exercised-induced, physical activity, oxidative stress, damage, oxidative damage.

2.2 Inclusion Criteria

2.2.1 Type of study

Studies involving high intensity exercise protocols targeted at exploring the effects on oxidative stress markers and antioxidant status were included. Exercise protocols with a principal focus on high-intensity, high-intensity interval/intermittent, sprint, maximal, exhaustive, acute are considered as HIE in this review.

2.2.2 Type of participants

Studies conducted in healthy untrained humans were included. No gender constraints were applied to all participants without disability and obesity. Participants under 16 years old were not included. Studies that used HIE as a treatment for specific illnesses were excluded and so were animal studies. Participants were considered as untrained when participants were described as physically inactive, sedentary, non-athletes, recreationally active and physically active.

2.2.3 Type of protocols

The inclusion criteria for studies in the review was as follows: (a) at least one bout of training/exercise was carried out; (b) oxidative stress markers were measured at baseline and post-training.

High intensity can be broadly defined as an intensity that is greater than that of exercise performed at a level corresponding to the anaerobic threshold. In this review, protocols were defined as high intensity if: (a) the participant performed with an "all-out" effort [Gibala and McGee, 2008]; (b) protocols were described as "maximal" , "sprint" or "high"; (c) the intensity was ≥ 70% maximal oxygen uptake (VO_{2max}) ; (d) the participant's heart rate was ≥ 70% of their maximal heart rate (HR_{max}); (e) There were no restrictions applied regarding the mode and the duration of the protocol.

2.2.4 Type of outcomes

Outcomes included oxidative markers [directly detected by ESR and indirectly measured by malondialdehyde (MDA) and thiobarbituric acid reactive substances (TBARS)], antioxidant enzyme activities [superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase (CAT) and glutathione (GSH)] and total antioxidant capacity (TAC).

Articles that satisfied the above criteria were included in the review. Meanwhile, articles were excluded if; (a) they were published after March 2021; (b) full text of the articles were not found; (c) articles were not written in English or Chinese; and (d) studies that used a different intervention (e.g., drugs or diet) that may have impacted on oxidative stress were excluded. When the same data were presented in multiple publications, the first published study was used for the review and analysis.

2.3 Identification of eligible studies

Eligible studies were empirical studies conducted in untrained humans that measured oxidative markers and antioxidant enzyme activities after a single bout of HIE or a long term HIE protocol. Two authors were responsible for retrieving selected articles from four databases and applying inclusion and exclusion criteria to determine eligible studies. The articles were then carefully read and evaluated by a further two independent authors to determine whether they should be included.

2.4 Quality assessment

The results were analyzed using methodological quality assessment (MQA) according to the revised Downs and Black Quality Index (1998) (Table 1) [Downs and Black, 1998].

Table 1: Methodological quality assessment questions

Reporting	
1.Is the hypothesis/aim/objective of the study clearly described?	**Yes 1/No 0**
2.Are the interventions of interest clearly described? Treatments and placebo (where relevant) that are to be compared should be clearly described.	**Yes 1/No 0**
3.Are the characteristics of the subjects included in the study clearly described?	**Yes 1/No 0**
4.Are the main findings of the study clearly described? Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions.	**Yes 1/No 0**
5.Have all important adverse events that may be a consequence of the intervention been reported?	**Yes 1/No 0**
Internal validity-bias	
6.Was an attempt made to blind those measuring the main outcomes of the intervention?	**Yes 1/No 0/unable to determine 0**
7.Were the statistical tests used to assess the main outcomes appropriate?	**Yes 1/No 0/unable to determine 0**
Internal validity-confounding (selection bias)	
8.Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period?	**Yes 1/No 0/unable to determine 0**

9.Were study subjects randomized to intervention groups?	**Yes 1/No 0/unable to determine 0**
Power	
10.Did the study have sufficient power to detect an important effect where the probability value for a difference being due to chance is less than 5%?	**Yes 1/No 0/unable to determine 0**
Methodological quality assessment questions modified from Downs and Black (1998).	

The MQA was implemented by two authors and were proofread by the other authors. Finally, a consultation session was arranged to reconcile any differences. The revised edition contained a total of 10 questions; 5 of the questions assessed report quality, 4 assessed internal validity, and 1 assessed power. A "yes" or "no" for each question was recorded as a 1 or 0 respectively. The total score was 10. Studies were defined as high quality if they scored an overall score of 7 or higher. Studies were defined as low quality if they received a total score of 5 or 6, and studies were defined as very low quality when they obtained a score under 4 [Ruiz et al., 2009].

2.5 Level of evidence

The levels of evidence were divided into three levels. Evidence was strong when three or more high-quality studies indicated consistent findings. The evidence was considered moderate when two high-quality studies showed consistent results. The evidence was limited when it was based on low-quality studies or a single study [Ruiz et al., 2009].

2.6 Data extraction

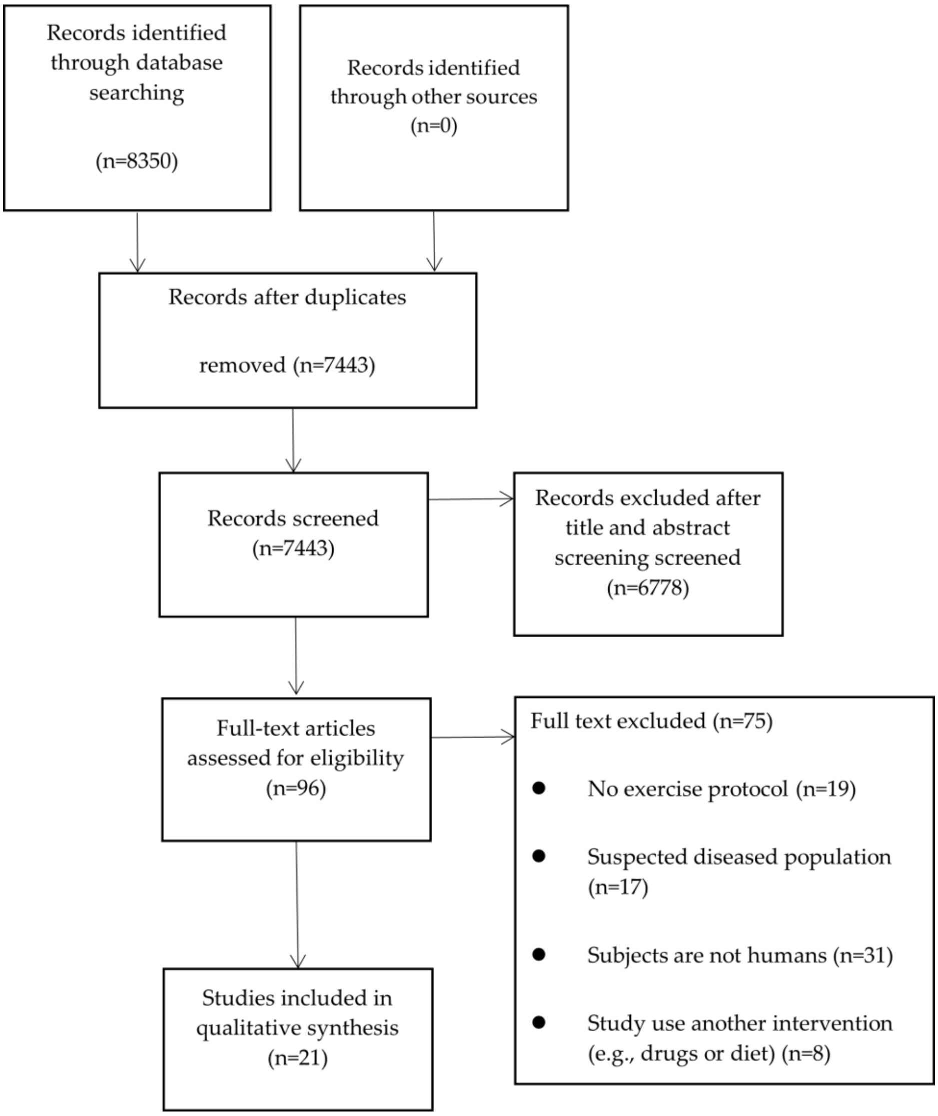
The data included in the study was extracted in several structured table formats covering the following topics: sociodemographic characteristics of participant (age, gender, weight, body mass index, maximal oxygen uptake, diet, lifestyle, socio-economic level, tobacco and alcohol), exercise protocol (specified as modality, type of protocol, No. of bouts , duration of bouts, duration of protocols, work/rest ratio, intensity), training protocols (specified as duration, frequency, No. of bouts, duration of bouts, intensity, duration of recovery), selected biomarkers, and findings. All studies measured the baseline status of the subjects. Some studies measured oxidative damage and antioxidant status at only one time-point (TP), mostly at the cessation of exercise, while others included multiple post-exercise measures following exercise completion.

3. Results

3.1 Search results

The selection process and the number of articles identified on each step are shown in Figure 2. 8350 records were retrieved in the initial database search. 907 duplicates were removed. After title and abstract screening, 96 records were reserved for eligibility assessment. 75 articles were excluded after full text examination (excluded reasons detailed in Figure 2). The most common reason for exclusion was that the participants were not human. Finally, 21 were included in the present review.

Figure 2: PRISMA flow diagram displaying the selection process



3.2 Methodological quality assessment

The MQA scoring results of the selected 21 manuscripts are shown in Table 2. The total quality score of the papers is shown as a percentage value in the last column. The quality of manuscripts ranged from 60% to 80%, and the average quality index was 69%. 12 studies were high quality (score ≥ 7), 9 studies were low quality (5 ≤ score ≤ 6), and no study was defined with a very low quality (score ≤ 4).

All manuscripts specified objectives (21/21), characteristics of the participants (21/21), findings (21/21), use of statistical tests (21/21), and significance levels of P < 0.05 (21/21). In addition, 11 of the 21studies explicitly mentioned the intervention, and 8 of the 21 studies were randomized. Finally, none of studies reported exercise-induced adverse events.

Table 2: Methodological quality assessment

Reference	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total
Ammar et al., 2020	1	1	1	1	0	0	1	1	1	1	80%
Baker et al., 2004	1	1	1	1	0	0	1	1	1	1	80%
Berzosa er al., 2011	1	1	1	1	0	0	1	1	1	1	80%
Bogdanis et al., 2013	1	1	1	1	0	0	1	0	0	1	60%
Bouzid et al., 2014	1	1	1	1	0	0	1	1	0	1	70%
Djordjevic et al., 2012	1	1	1	1	0	0	1	1	0	1	70%

Falone et al., 2010	1	1	1	1	0	0	1	1	0	1	70%
Finkler et al., 2016	1	1	1	1	0	0	1	0	0	1	60%
Fisher et al., 2011	1	1	1	1	0	0	1	0	0	1	60%
Groussard et al., 2003	1	1	1	1	0	0	1	0	0	1	60%
Hajizadeh et al., 2017	1	1	1	1	0	0	1	1	1	1	80%
Jammes et al., 2004	1	1	1	1	0	0	1	0	0	1	60%
Jamurtas et al., 2018	1	1	1	1	0	0	1	1	1	1	80%
Kyparos et al., 2007	1	1	1	1	0	0	1	0	1	1	70%
Miyazaki et al., 2001	1	1	1	1	0	0	1	1	0	1	70%
Parker et al., 2014	1	1	1	1	0	0	1	0	0	1	60%
Parker et al., 2018	1	1	1	1	0	0	1	1	1	1	80%
Seifi-Skishahr et al., 2008	1	1	1	1	0	0	1	0	0	1	60%
Steinberg et al., 2007	1	1	1	1	0	0	1	0	0	1	60%
Wadley et al., 2016	1	1	1	1	0	0	1	1	1	1	80%
Wiecek et al., 2018	1	1	1	1	0	0	1	0	0	1	60%
	Reporting				Internal validity-bias			Internal validity-confounding		Power	Average
TOTAL/21	21	21	21	21	0	0	21	11	8	21	69%

3.3 Type of studies

Details of exercise testing and training are outlined in Table 3. Exercise testing were exercise protocols used to analysis the acute changes in oxidative stress and antioxidant status, while training were protocols used to investigate the effect of long-term exercise on oxidative stress and antioxidant capacity. 15/21 studies investigated acute oxidative response following a single bout of HIE at TP0 (Table 4 details corresponding TPs and findings for each study); 13/21 studies included multiple post-exercise measures after exercise; 3/21 studies compared HIE induced oxidative stress and antioxidant status pre and post high intensity training; 2/21 studies measured oxidative damage between untrained participants and others with different physical activity characteristics; 8/21 studies compare oxidative stress following different types of HIE.

Table 3: Details of exercise testing and training of the included studies

Reference	Exercise testing							Training
	Modality	Type of protocol	No. of Bouts	Duration of bouts	Duration of protocol	W/R ratio	Intensity(W/R)	Duration, frequency, (No. of bouts) x (duration of bout/intensity) / duration of recovery
Ammar et al., 2020(Anerobic)	Cycling	Maximal	1	30s	30s		All-out	
Ammar et al., 2020 (Combined)	Cycling	Combined (maximal and moderate intensity continuous)	1	30s+30min	30s+30min		All-out+60% MAP	
Baker et al., 2004 (TBM)	Cycling	Maximal	1	30s	30s		All-out	
Baker et al., 2004 (FFM)	Cycling	Maximal	1	30s	30s		All-out	
Berzosa er al., 2011 (Incremental)	Cycling	Incremental	1				Incremental intensity to exhaustion	
Berzosa er al., 2011 (100%VO_{2max})	Cycling	Maximal	1				100%VO_{2max} to exhaustion	
Berzosa er al., 2011 (70%VO_{2max})	Cycling	High intensity continuous	1	30min	30min		70%VO_{2max}	
Bogdanis et al., 2013 (Pre-training)	Cycling	Sprint interval	4	30s	14min	1/8	All-out/Active recovery	3 weeks, 3 sessions/week, (4-6)*(30s/all-out)/4min
Bogdanis et al., 2013 (post-training)	Cycling	Sprint interval	4	30s	14min	1/8	All-out/Active recovery	
Bouzid et al., 2014 (Young)	Treadmill	Incremental	1				Incremental intensity to exhaustion	
Bouzid et al., 2014 (Old)	Treadmill	Incremental	1				Incremental intensity to exhaustion	

Djordjevic et al., 2012 (Athletes)	Cycling	Incremental	1				Incremental intensity to exhaustion	
Djordjevic et al., 2012 (Non-athletes)	Cycling	Incremental	1				Incremental intensity to exhaustion	
Falone et al., 2010 (Amateur runner)	Treadmill	Incremental	1				Incremental intensity to exhaustion	
Falone et al., 2010 (Untrained)	Treadmill	Incremental	1				Incremental intensity to exhaustion	
Finkler et al., 2016	Cycling	Incremental	1				Incremental intensity to exhaustion	
Fisher et al., 2011 (First)	Cycling	High intensity interval	4	30s	14min	1/8	90% Max-AP/15% Max-AP	
Fisher et al., 2011 (Second)	Cycling	High intensity interval	4	30s	14min	1/8	90% Max-AP/15% Max-AP	
Fisher et al., 2011 (Third)	Cycling	High intensity interval	4	30s	14min	1/8	90% Max-AP/15% Max-AP	
Groussard et al., 2003	Cycling	Maximal	1	30s	30s		All-out	
Hajizadeh et al., 2017 (HICE)	Treadmill	High intensity continuous	4	10min	49min	10/3	70-75%VO_{2max}/50-60%VO_{2max} for the first 12 weeks; 75-85%VO_{2max}/50-60%VO_{2max} for the final 12 weeks	24 weeks, 3 sessions/week, 4*[10min/(70-75%)-(75%-85%)VO_{2max}]/3min
Hajizadeh et al., 2017 (HIIE)	Treadmill	High intensity interval	10	1min	19min	1/1	75-85%VO_{2max}/45-50%VO_{2max} for the first 12 weeks; 85-95%VO_{2max}/45-50%VO_{2max} for the final 12 weeks	24 weeks, 3 sessions/week, 10*[1min/(75-85%)-(85%-95%)VO_{2max}]/1min
Jammes et al., 2004	Cycling	Incremental	1				Incremental intensity to VO_{2max}	
Jamurtas et al., 2018 (HIIE)	Cycling	Sprint interval	4	30s	14min	1/8	All-out	
Jamurtas et al., 2018 (HICE)	Cycling	High intensity continuous	1	30min	30min		70%VO_{2max}	
Kyparos et al., 2007	Shuttle run	Maximal	1				All-out	

Miyazaki et al., 2001 (Pre-training)	Cycling	Incremental	1				Incremental intensity to exhaustion	12 weeks, 5 sessions/week, 1*(60 min/80%VO_{2max})
Miyazaki et al., 2001 (post-training)	Cycling	Incremental	1				Incremental intensity to exhaustion	
Parker et al., 2014 (70% VO_{2max})	Cycling	High intensity interval	1	5min	5min	5/12	70%VO_{2max}/passive seated rest	
Parker et al., 2014 (85% VO_{2max})	Cycling	High intensity interval	1	5min	5min	5/12	85%VO_{2max}/passive seated rest	
Parker et al., 2014 (100% VO_{2max})	Cycling	High intensity interval	1	5min	5min	5/12	100%VO_{2max}/passive seated rest	
Parker et al., 2018 (HIIE)	Cycling	High intensity interval	5	4min	24min	4/1	75%Wmax	
Parker et al., 2018 (SIE)	Cycling	Sprint interval	4	30s	15.5min	1/9	All-out	
Seifi-Skishahr et al., 2008	Treadmill	High intensity continuous	1	30min	30min		75%VO_{2max}	
Steinberg et al., 2007	Cycling	Incremental	1				Incremental intensity to exhaustion	
Wadley et al., 2016 (LV-HIIE)	Cycling	High intensity interval	10	1min	19min	1/1	90%VO_{2max}	
Wadley et al., 2016 (HICE)	Cycling	High intensity continuous	1	20min	20min		80%VO_{2max}	
Wiecek et al., 2018	Cycling	Maximal	1	20s	20s		All-out	

Note: FFM, fat-free mass; HICE, high intensity continuous exercise; HIIE, high intensity interval exercise; LV-HIIE, low volume high intensity interval exercise; Max-AP, maximum an-aerobic power; min, minute; SIE, sprint interval exercise; TBM, total body mass; VO_{2max}, maximal oxygen uptake; All-out: encompasses intensities described by the authors as "sprints", "maximal", "maximal exercise", "exhaustion", "near the VO_{2max} ".

Table 4: Individual time-points (TP) of measures of oxidative stress and relevant findings for each study

Reference	TP0(0min)	TP1(5min)	TP2(10min)	TP3(20min)	TP4(30min)	TP5(1h)	TP6(2h)	TP7(3h)	TP8(24h)	TP9(48h)	TP10(72h)	Findings
Ammar et al., 2020	0min	5min	10min	20min								MDA↑ at TP0 in AnEx; MDA↑ at TP2 in CombEx. MDA continued to increase at TP3 in both Ex; GPX, SOD↑ at TP0 in both Ex; AnEx resulted in greater SOD and GPX at TP0 and TP1. SOD peaked at TP0 in the AnEx; GPX peaked was at TP3 in the CombEx; TAC did not change until TP3 in both Ex.
Baker et al., 2004	0min								24h			MDA↑ at TP0 in the TBM protocol; MDA returned to baseline values at TP8.
Berzosa er al., 2011	0min											GPX, CAT and TAC↑ at TP0 in all three Ex; SOD↑ at TP0 in all-out and high intensity continuous Ex.
Bogdanis et al., 2013					30min				24h	48h		TBARS↑ at TP4 and peaked at TP8 in both pre and post training; Post training resulted in lower TRARS at all TPs. GPX↑ and peaked at TP8 in both pre and post training; CAT↑ and peaked at TP4 in both pre and post training; TAC↑ at TP4 and peaked at TP8 only in pre training. Post training resulted in higher GPX, CAT and TAC in all TPs.
Bouzid et al., 2014		5min (MDA)		20min (SOD, GPX)								MDA↑ at TP1 in old group; GPX and SOD↑ at TP3 in young group.
Djordjevic et al., 2012	0min											TBARS↓ at TP0 only in non-athletes; CAT↓ at TP0 only in athletes. GSH did not change in both groups.
Falone et al., 2010	0min											MDA did not change at TP0 in both amateur runner and untrained group; TAC↓ at TP0 only in untrained group.
Finkler et al., 2016		5min				1h						TBARS↑ at TP1 and returned to baseline values at TP5; CAT↑ at TP1 and continued to increase at TP5. GPX did not change until TP5.
Fisher et al., 2011	0min							3h	24h			TBARS↑ at TP0 in the first and second test and at TP7 in the second test; CAT↑ at TP0 in the first and second test; SOD↑ at TP0 and TP7 in all three tests, and returned to baseline value at TP8; GPX↑ at TP0 in the first and third test, and returned

												to baseline value at TP7.
Groussard et al., 2003	0min	5min	10min	20min		40min						MDA and TBARS↓ at TP3 and TP5; SOD↓ at TP0; GPX did not change until TP5.
Hajizadeh et al., 2017									24h			SOD and CAT↑ at TP8 in both HICT and group after 24 weeks' training; MDA and TAC↑ at TP8 only in HIIE group after 24 weeks' training.
Jammes et al., 2004	0min	5min	10min	20min	30min							TBARS↑ at TP1 and remained increased until TP4; GSH↓ at TP1 and returned to baseline at TP2.
Jamurtas et al., 2018	0min								24h	48h	72h	TBARS and CAT did not change until TP10 in both HIIE and HICE; TAC↑ at TP0 in HICE, and↑ at TP0 and TP8 in HIIE.
Kyparos et al., 2007	0min											TBARS, CAT and TAC↑ at TP0; GSH↓ at TP0.
Miyazaki et al., 2001	0min											TBARS↑ at TP0 in both pre and post training; Post training resulted in lower TBARS at TP0; SOD, GPX and CAT did not change at TP0.
Parker et al., 2014	0min											OS did not change in all three test; TAC↑ at TP0 in all three test; 100%VO_{2max} test resulted in the highest TAC at TP0.
Parker et al., 2018	0min					1h	2h	3h				TBARS and SOD↓ at TP0, TP5 and TP6 in both HIIE and SIE; CAT did not change until TP7 in both HIIE and SIE.
Seifi-Skishahr et al., 2008	0min						2h		24h			MDA↑ at TP6.
Steinberg et al., 2007	0min	5min	10min	20min	30min							TBARS↑ at TP1 and TP2; GSH↓ at TP2 and TP3.
Wadley et al., 2016	0min				30min							TAC↑ at TP4 relative to TP0 in both LV-HIIE and HICE.
Wiecek et al., 2018		3min		15min	30min	1h			24h			SOD↓ at TP3 relative to TP1; SOD↑ at TP4 and returned to baseline value at TP8; CAT↓ at TP3 relative to TP1; CAT↓ at TP5 and returned to baseline value at TP8; GPX↓ at TP3 and ↑ at

									TP8.	

Note: AnEx, Anerobic exercise; CAT, catalase; CombEX, Combined exercise; Ex, exercise; GPX, glutathione peroxidase activity; GSH, glutathione; h, hour; MDA, malondialdehyde; min, minutes; SOD, superoxide dismutase; TAC, total antioxidant capacity; TBARS, thiobarbituric acid-reactive substance; TP, time-point; ↑, significantly increase; ↓, significantly decrease.

3.4 Participants of selected studies

Table 5 showed the sociodemographic characteristics of participants. Participants mean age in selected studies ranged from 17.3 to 65.1 years old. Participants body mass index ranged from 21.5 to 27.6. VO_{2max} of participants ranged from 31.7 to 49.7 ml/kg/min. 16 studies reported no medications and antioxidant dietary supplement prior and throughout the test. 8 studies described participants lifestyle as physically active, 1 study descried as physically inactive, 3 studies decried as no regular physical activity and 6 studies used sedentary participants. 2 studies included groups of trained participants with one used handball athletes with regular training and the other used amateur runners. 9 studies used non-smoking participants, and 2 studies reported participants refrained from to-bacco in the last 6 months. Finally, 8 studies reported participants with no alcohol at least 24 hours prior to the test.

3.5 Oxidative stress markers

7 oxidative stress markers were analyzed, these included: thiobarbituric acid reactive substances (TBARS) (9/21), malondialdehyde (MDA) (8/21), glutathione (GSH) (4/21), glutathione peroxidase (GPX) (8/21), superoxide dismutase (SOD) (8/21), cata-lase (CAT) (10/21), and total antioxidant capacity (TAC) (8/21) (Table 6).

Table 5: Sociodemographic characteristics of participants

Reference	Age	Gender	Weight	BMI	VO_{2max}	Diet	lifestyle	Socio-economic level	Tobacco	Alcohol
Ammar et al., 2020	19.5±1.7	male	71.8±2.1	-	-	no medications and antioxidant dietary supplement	physically inactivity	-	-	-
Baker et al., 2004	23±2	male	75.3±11	-	-	no medications and antioxidant dietary supplement	physically activity	university student	-	-
Berzosa er al., 2011	23±0.41	male	75.25±2.84	23.72±0.69	43.8±1.58	no medications and antioxidant dietary supplement	physically activity	-	-	-

Bogdanis et al., 2013	24.3±1.4	male	77.9±2.9	-	-	no medications and antioxidant dietary supplement	physically activity	-	-	-
Bouzid et al., 2014 (young)	20.3±2.8	9 males/ 6 females	66.1±11.7	-	44.2±5.2	-	Sedentary	-	-	-
Bouzid et al., 2014 (old)	65.1±3.57	7 males/ 8 females	71.8±7.6	23.2±4.4	-	-	Sedentary	-	-	-
Djordjevic et al., 2012 (Athletes)	17.3±0.2	male	80.9±1.4	23.9±0.3	44.6±0.9	no medications and antioxidant dietary supplement	regular training	-	non-smoking	no alcohol 48h before test
Djordjevic et al., 2012 (non-athletes)	17.3±0.3	male	81.6±6.1	23.6±1.3	39.7±1.3	no medications and antioxidant dietary supplement	no regular physical activity	-	non-smoking	no alcohol 48h before test
Falone et al., 2010 (amateur runner)	42±1	male	-	23.5±0.5	48.5±0.9	no medications and antioxidant dietary supplement	regular training	-	-	no alcohol
Falone et al., 2010 (untrained)	39±3	male	-	26.1±1.1	33.3±1.2	no medications and antioxidant dietary supplement	Sedentary	no manual labor	-	no alcohol
Finkler et al., 2016	26.8	male	77.9	23.4	48.9	no medications and antioxidant dietary supplement	physically activity	-	non-smoking	-
Fisher et al., 2011	22±2	male	83±13.6	-	44.6±8.2	no medications and antioxidant dietary supplement	no regular physical activity	-	-	-
Groussard et al., 2003	22.2±0.6	male	73.4±2.2	-	-	no medications and antioxidant dietary supplement	physically activity	university student	no tobacco in the last 6 months	no alcohol in the last 1 week
Hajizadeh et al., 2017 (HICE)	32.3±7.3	male	81.9±7.2	26.8±5.9	36±4.6	no medications and antioxidant dietary supplement	physically activity	-	no tobacco in the last 6 months	no alcohol in the last 6 months

Hajizadeh et al., 2017 (HIIE)	30.4±8.9	male	83.4±6.3	27.6±4.8	35.9±4.7	no medications and antioxidant dietary supplement	physically activity	-	no tobacco in the last 6 months	no alcohol in the last 6 months
Jammes et al., 2004	49±3	14 males/ 5 females	74±3	-	-	-	Sedentary	-	-	-
Jamurtas et al., 2018	22.4±0.5	male	75.3±8.9	-	45.3±8.4	no medications and antioxidant dietary supplement	-	-	non-smoking	no alcohol in the last 72h
Kyparos et al., 2007	21.9±0.9	male	73.9±6.1	-	-	-	-	college student	-	-
Miyazaki et al., 2001 (pre-training)	19.4±0.2	male	70.5±2.6	23.4±0.6	44.9±1.5	-	no regular physical activity	-	-	-
Miyazaki et al., 2001 (post-training)	19.4±0.2	male	70.4±2.7	23.3±0.7	49.7±1.6	-	no regular physical activity	-	-	-
Parker et al., 2014	22±1	male	81.4±2	25.4±0.7	42.6±2.1	no medications and antioxidant dietary supplement	Sedentary	-	non-smoking	no alcohol in the last 24h
Parker et al., 2018	25±2	6 male/ 2 female	79.4±2.1	25±1	48.4±4	no medications and antioxidant dietary supplement	physically activity	-	non-smoking	no alcohol in the last 24h
Seifi-Skishahr et al., 2008	24.1±3.1	-	71.9±9.8	-	34.1±2.7	no medications and antioxidant dietary supplement	Sedentary	-	non-smoking	-
Steinberg et al., 2007	42±4	9 males/ 6 females	70±3	22±2	31.7±2.5	-	Sedentary	-	non-smoking	-
Wadley et al., 2016	22±3	male	-	24±3.1	42.7±5	no medications and antioxidant dietary supplement	-	-	non-smoking	no alcohol in the last 48h
Wiecek et al., 2018 (female)	22±0.5	female	59.8±2.1	21.5±0.6	-	no medications and antioxidant dietary supplement	physically activity	-	non-smoking	-
Wiecek et al., 2018 (male)	21.6±0.4	male	77.1±2.7	23.7±0.5	-	no medications and antioxidant dietary supplement	physically activity	-	non-smoking	-

Table 6: Oxidative stress markers

Reference	Sample size	Acute response on oxidative stress and antioxidant status							
		MDA	TBARS	OS	TAC	CAT	SOD	GPX	GSH
Ammar et al., 2020 (Anerobic)	10	sig ↑	-	-	ns ↑	-	sig ↑*	sig ↑*	-
Ammar et al., 2020 (Combined)	10	ns ↑	-	-	ns ↑	-	sig ↑*	sig ↑*	-
Baker et al., 2004 (TBM)	18	sig ↑*	-	-	-	-	-	-	-
Baker et al., 2004 (FFM)	18	ns ↑*	-	-	-	-	-	-	-
Berzosa er al., 2011 (Incremental)	34	-	-	-	sig ↑	sig ↑	ns ↑	sig ↑	-
Berzosa er al., 2011 (All-out)	34	-	-	-	sig ↑	sig ↑	sig ↑	sig ↑	-
Berzosa er al., 2011 (70%VO_{2max})	34	-	-	-	sig ↑	sig ↑	sig ↑	sig ↑	-
Bogdanis et al., 2013 (pre-training)	8	-	sig ↑	-	sig ↑	sig ↑	-	ns ↑	-
Bogdanis et al., 2013 (post-training)	8	-	sig ↑	-	ns ↑	sig ↑	-	ns ↑	-
Bouzid et al., 2014 (Young)	15	ns ↑*	-	-	-	-	sig ↑*	sig ↑	-
Bouzid et al., 2014 (Old)	15	sig ↑*	-	-	-	-	ns ↑*	ns ↑	-
Djordjevic et al., 2012 (Athletes)	58	-	ns ↑	-	-	sig ↓	ns ↓	-	ns ↑
Djordjevic et al., 2012 (Non-athletes)	37	-	sig ↓	-	-	ns	ns ↑	-	ns ↑
Falone et al., 2010 (Amateur runner)	33	ns ↓*	-	-	ns*	-	-	-	-
Falone et al., 2010 (Untrained)	25	ns ↑*	-	-	sig ↓*	-	-	-	-
Finkler et al., 2016	32	-	sig ↑	-	-	sig ↑	-	ns ↑	-
Fisher et al., 2011 (First)	8	sig ↑	sig ↑	-	-	sig ↑	sig ↑	sig ↑	-
Fisher et al., 2011 (Second)	8	sig ↑	sig ↑	-	-	sig ↑	sig ↑	ns ↑	-
Fisher et al., 2011 (Third)	8	ns ↑	ns ↑	-	-	ns ↑	sig ↑	sig ↑	-
Groussard et al., 2003	8	ns ↓	ns ↓	-	-	-	sig ↓	ns	-
Hajizadeh et al., 2017 (HICE)	62	-	-	-	-	-	-	-	-
Hajizadeh et al., 2017 (HIIE)	65	-	-	-	-	-	-	-	-
Jammes et al., 2004	19	-	ns ↑	-	-	-	-	-	ns ↓
Jamurtas et al., 2018 (HIIE)	12	-	ns ↑	-	sig ↑*	ns ↑	-	-	-
Jamurtas et al., 2018 (HICE)	12	-	ns ↑	-	sig ↑*	ns ↑	-	-	-
Kyparos et al., 2007	11	-	sig ↑	-	sig ↑	sig ↑	-	-	sig ↓
Miyazaki et al., 2001 (pre-training)	9	-	sig ↑*	-	-	ns	ns ↑	ns ↑	-
Miyazaki et al., 2001 (post-training)	9	-	sig ↑*	-	-	ns	ns ↑	ns ↓	-
Parker et al., 2014 (70% VO_{2max})	14	-	-	ns ↑	sig ↑*	-	-	-	-

Parker et al., 2014 (85% VO_{2max})	14	-	-	ns ↑	sig ↑	-	-	-	-
Parker et al., 2014 (100% VO_{2max})	14	-	-	ns ↑	sig ↑*	-	-	-	-
Parker et al., 2018 (HIIE)	8	-	sig ↓	-	-	ns ↑	sig ↓	-	-
Parker et al., 2018 (SIE)	8	-	sig ↓	-	-	ns ↑	sig ↓	-	-
Seifi-Skishahr et al., 2008	10	ns ↑	-	-	-	-	-	-	-
Steinberg et al., 2007	15	ns ↑	-	-	-	-	-	-	ns ↓
Wadley et al., 2016 (LV-HIIE)	10	-	-	-	ns ↓	-	-	-	-
Wadley et al., 2016 (HICE)	10	-	-	-	ns ↓	-	-	-	-
Wiecek et al., 2018	20	-	-	-	-	ns ↑	ns ↑	ns ↓	-

Note: CAT, catalase; FFM, fat-free mass; GPX, glutathione peroxidase activity; GSH, glutathione; HICE, high intensity continuous exercise; HIIE, high intensity interval exercise; LV-HIIE, low volume high intensity interval exercise; MDA, malondialdehyde; ns, not significant; SIE, sprint interval exercise; sig, significant; SOD, superoxide dismutase; TAC, total antioxidant capacity; TBARS, thiobarbituric acid-reactive substance; TBM, total body mass; VO_{2max}, maximal oxygen uptake; *, significant difference between groups.

3.6 Exercise modality

In terms of exercise modality, cycling on ergometers were the most common HIE used, 3 used treadmills and 1 used a shuttle run. In terms of exercise intensity, there were 9 studies that included incremental exercise, 6 performed a single bout of exhaustive/maximal exercises, 6 implemented interval exercises, and 5 conducted continuous exercise. The duration of a single high intensity exercise bout ranged from 20 seconds to 5 minutes.

3.7 Levels of evidence

Conclusive strong evidence was obtained in the selected high-quality samples. In terms of acute oxidative stress assessed immediately following a bout of HIE, among these studies, oxidative stress was significantly increased in 5 high quality studies, and antioxidant status was significantly stimulated in 7 high quality studies. Moderate evidence on significantly decreased oxidative damage was found in 2 high quality studies. However, the evidence that antioxidant status was not affected immediately after HIE is also strong due to 3 high quality studies.

In relation to the effects of different protocols and measurement time on oxidative stress, we observed the following results:

3.7.1 Acute effect of oxidative stress and antioxidant status after HIE

17 studies assessed the acute response of oxidative stress immediately following HIE (TP0 and TP1). Among them, 9 studies reported significantly increased acute oxidative damage immediately post HIE. 4 studies reported significant acute oxidative damage following a maximal exercise. 3 studies used incremental protocols and another 2 used intermittent protocols. On the contrary, only 2 studies reported significantly decreased acute oxidative damage. The one used incremental exercise, and the other one adopted interval protocol. 6 studies did not observe significant changes. 3 of them used incremental protocols, one of them executed high intensity interval exercise, and one of them used high intensity continuous exercise. The remaining one compared interval exercise with continuous exercise performed at high intensity, indicating no between-group differences regarding to acute oxidative responses. It was worth noting that, one study also used ESR to directly test the production of lipid free radicals to study oxidative stress responses to a maximal exercise. The authors found that lipid free radicals increased significantly after exercise, while plasma TBARS concentrations did not increase.

For antioxidant status immediately after HIE, data were available from 18 studies. 12 studies reported the alterations of redox homeostasis. Most studies (9/18) indicated elevated antioxidant enzyme activities. There were 4 studies used interval exercise. 3 studies used incremental protocols and 3 used maximal exercises. 2 performed high intensity continuous exercises and only 1 applied combined protocol, consisting of maximal exercise followed by a moderate continuous exercise. Among them, 4 studies investigated antioxidative responses between different types of protocols. In contrast, 3 studies indicated decreased antioxidant activities. Incremental, interval and maximal protocols were used. Besides, 6 studies reported no changes on antioxidant activities immediately after HIE. 4 of them performed incremental protocols. One used maximal exercise and the remaining one compared antioxidant changes between high intensity interval and high intensity continuous exercises.

3.7.2 Time of measurement effects of oxidative stress and antioxidant status after HIE

11 studies used multiple post-exercise measures on oxidative markers after exercise. 8 studies observed increased oxidative damage following HIE. Among them, increased oxidative damage was observed from TP0 (0 minute) to TP9 (48 hours) following HIE, with peak value at various time points. Peak oxidative damage occurred at TP1 (5 minutes) in 2 studies. One study reported peak value at TP6 (2 hours) and the other study observed the highest oxidative damage at TP8 (24 hours). No conclusive peak value could be found in 4 studies. Generally, oxidative damage was returned to baseline within 24 hours after HIE in most studies (5/8). Only one study reported increased damage after 24 hours. No recovery data could be recorded in the other 2 studies due to the limited measurement time.

On the contrary, 2 studies reported decreased oxidative stress markers from TP0 (0 minute) to TP6 (2 hours). Only one study indicated no change on oxidative stress at any measurement time from TP0 (0 minute) to TP10 (72 hours).

For endogenous redox status, data was analyzed from 11 studies. All studies reported significant changes in antioxidant from TP0 (0 minute) to TP4 (30 minutes). 7 studies indicated early alterations within 5 minutes after HIE, while 2 studies did not observe significant changes until 30 minutes. Another 2 studies indicated altered antioxidant from 10 minutes to 15 minutes following HIE.

4. Discussion

This systematic review aimed to investigate the effects of HIE on oxidative stress and antioxidant capacity in untrained adults. The results suggest that HIE induces oxidative stress compared to a resting state. Regardless of whether HIE is performed on treadmills, cycle ergometers or other forms, if the duration is more than 30 seconds and VO_{2max} reaches 70% or more, the balance of oxidative and antioxidant systems in the body will be disrupted, leading to oxidative stress and cellular damage. The results also show that regular exercise, sufficient recovery, and a young age increased protection against exercise-induced oxidative damage; however, further studies are needed to confirm and explore this finding.

HIE can interfere with the balance between oxidation and anti-oxidation systems in the body. During HIE or during a short period following HIE, the production of ROS significantly increases, which is related to the sharp increase in oxygen consumption, activation of inflammatory cells, and contraction of muscle. However, the endogenous antioxidant capacity was simultaneous elevated.

HIE can be either aerobic or anaerobic exercise, or a combination of both. Incremental exercise, maximal exercise, intermittent exercise, and high intensity continuous exercise at 70% VO_{2max} or above were the common HIE methodologies used in untrained adults.

Studies that refer to different types of HIE report the almost conclusive finding that: 1) HIE induces oxidative stress, 2) HIE-induced oxidative stress is transient, 3) antioxidant capacity is also activated after HIE, 4) regular exercise enhanced the antioxidant defense mechanisms, 5) HIE-induced oxidative stress is related to individual characteristics.

4.1 HIE induces oxidative stress

HIE induces oxidative stress, regardless of exercise modality. In this review, cycling and running were the more common exercises used. A cycling exercise to exhaustion can induce oxidative stress [Bouzid et al., 2014; Falone et al., 2010; Seifi-Skishahr et al., 2008; Kyparos et al., 2007; Jammes et al., 2004; Miyazaki et al., 2001; Ammar et al., 2020; Baker et al., 2004; Wiecek et al., 2018; Bogdanis et al., 2013; Jamurtas et al., 2018; Parker et al., 2018; Wadley et al., 2016] and a running exercise to exhaustion has a similar effect [Berzosa et al., 2011; Finkler et al., 2016; Groussard et al., 2003; Hajizadeh Maleki et al., 2017]. This has been evidenced by a recent study [Kröpfl et al., 2021], in which oxidative stress was assessed using two different HIE modalities: running and cycling. The study concluded that both cycling and running induce oxidative stress, even though TAC recovers faster among runners.

Furthermore, the intensity of HIE can also influence oxidative stress. Using an incremental intensity, Parker et al. (2014) observed significant oxidative stress at intensities of 70% VO_{2max} or above with increasing oxidative stress accompanied by increased exercise intensity [Parker et al., 2014]. This has also been reported by Fogarty et al. (2011), who conducted 3 aerobic exercises at 40%, 70%, and 100% of VO_{2max} [Fogarty et al., 2011]. Oxidative damage to DNA was increased at 70% and 100% of VO_{2max} and the extent of damage was positively related to the intensity. Similarly, during a 30s maximal cycling test, the selection of resistive forces (total body mass or fat-free mass) may induce different metabolic responses for oxidative stress [Falone et al., 2010]. This study indicated that a fat-free mass protocol was metabolically more efficient compared to the total body mass protocol and produced less oxidative stress and muscle damage during exercise. It can be concluded that when the exercise intensity is higher than 70% of VO_{2max}, significant oxidative stress occurs, and the extent of oxidative damage is positively related to the intensity. This finding is consistent with the recent work of Tryfidou et al. (2020), who reported DNA oxidative stress damage increased after exercise with intensities higher than 75% [Tryfidou et al., 2020].

The duration of HIE can also be one of the most important factors for exercise-induced oxidative stress. Using data from this review, we observed that for a single high intensity exercise bout, oxidative stress occurs when the exercise duration is more than 30s. The most common HIE protocol consists of several 30s "all-out" bouts separated by recovery. As such, we believe that most HIE protocols will induce oxidative stress. However, a single bout duration shorter than 30s was proven to be associated with less oxidative stress [Cipryan, 2017]. With the same modality and intensity. Cipryan (2017) performed 3 HIE protocols with a total of 12-minute exercise. The durations were 15 seconds, 30 seconds, or 60 seconds, respectively and the work/rest ratio was 1. The auhors observed an immediate increase in oxidative stress markers in all three protocols. Among them, oxidative stress in 30s/30s protocol showed the smallest increases, while the TAC in 15 seconds/15 seconds protocol demonstrated the largest increase. However, further studies are needed to investigate oxidative damage following exercises performed at the same intensity but using different modalities (continuous or intermittent).

4.2 HIE-induced oxidative stress is transient

Using data from this review, we conclude that there is a significant increase in oxidative stress markers following exercise at TP0 (0 h) when compared to rest. To investigate oxidative damage after exercise at multiple TP, data were available from 13 studies (details in Table 3). This review demonstrates, the acute effect on oxidative stress following HIE often occurs within 5 minutes at the end of the exercise, remaining increased within 30 minutes following exercise. Moreover, several studies reported that oxidative stress peaked at 5 minutes post exercise. Most of the increased oxidative damage returned to basal level within 24 hours following exercise cessation [Falone et al., 2010; Jammes et al., 2004; Miyazaki et al., 2001; Hajizadeh Maleki et al., 2017; Jamurtas et al., 2018]. They found that the greatest oxidative stress occurred in healthy subjects 5 minutes post exercise and then recovered gradually, with different markers recovering at different rates [Ammar et al., 2020; Jamurtas et al., 2018].

Basically, responses of antioxidant enzymes to oxidative stress are lagging and lasting. Significant changes of SOD, CAT and TAC were observed at 15 minutes after exercise [Wadley et al., 2016]. SOD was increased continuously until 3 hours of the end of exercise [Miyazaki et al., 2001]. Finkler et al. (2016) also indicated that TBARS concentrations increased immediately, whereas the activation of CAT appears to be small and continues to increase during the recovery period [Finkler et al., 2016]. Similarly, TAC is significantly elevated from rest to post exercise and remained above pre-exercise levels for 24 hours [Cipryan, 2017, 2018; Turner et al., 2011]. This agrees with the previous study. Farney et al. (2012) reported an absence of oxidative stress in trained men following HIE [Farney et al., 2012]. One study reported significant changes in antioxidant activities were found 20 minutes post exercise [El Abed et al., 2011]. Therefore, stimulated antioxidant could be observed or not at the cessation of HIE.

4.3 The antioxidant capacity is also activated after HIE

The degree of oxidative stress depends on the balance between the generation of ROS and the effectiveness of the antioxidant defense system. Studies have shown that the antioxidant defense system in the body was rapidly activated after HIE [Seifi-Skishahr et al., 2008; Parker et al., 2014; Baker et al., 2004; Groussard et al., 2003; Bogdanis et al., 2013; Otocka-Kmiecik et al., 2010, 2014]. Fisher et al. (2011) also found that the absence of lymphocyte cell viability decreases after HIE and was due to the increased activity of antioxidant enzymes in lymphocytes [Fisher et al., 2011]. Many studies have also shown a significant increase in antioxidant activity after HIE compared to baseline values [Suzuki et al., 2003; Kyparos et al., 2007; Miyazaki et al., 2001; Ammar et al., 2020; Cipryan, 2017; Turner et al., 2011; Chaki et al., 2019; Sureda et al., 2005]. In contrast, several studies found that antioxidant enzyme activities did not increase but decreased after HIE. Others, Falone et al. (2010) and Kröpfl et al. (2021) also found that some endogenous antioxidants did not change after exercise [Falone et al., 2010 and Kröpfl et al., 2021]. It supported one of our strong types of evidence that antioxidative status did not change after HIE. Such results showed that oxidative stress caused by HIE had been rapidly neutralized by the antioxidant system, and that there was no significant change in antioxidant markers.

Whether moderate oxidative stress, which stimulates the antioxidative system temporarily and appropriately, contributes to the improvement of antioxidant levels in the body deserves further investigation.

4.4 Regular exercise enhanced the antioxidant defense mechanisms

Individuals who are physically active have better antioxidant systems and can respond to oxidative stress induced by HIE more quickly than sedentary individuals. In the resting state, physically active people have higher baseline values of TAC, and lower TBARS [Djordjevic et al., 2012; Finkler et al., 2016; Cipryan, 2018; Otocka-Kmiecik et al., 2014]. After exercise, TAC showed the largest changes, indicating that regular exercise can improve the activity of the antioxidant system and reduce exercise-induced oxidative damage. It also shows that under the same HIE protocol, the higher the fitness levels of individuals, the less obvious the oxidative stress increases should be after exercise. In addition, physically active individuals have stronger ability to counter oxidative stress, affecting the recovery time of oxidative indicators, such as TBARS, MDA and TAC, which did not change immediately after exercise [Alessio et al., 1988; Otocka-Kmiecik et al., 2010; Margaritis et al., 1997; Rokitzki et al., 1994; Leaf et al., 1997]. Even in the study of Groussard et al.

(2003), a sharp post-exercise decrease was observed in plasma TBARS and MDA levels in university physical education students [Groussard et al., 2003]. This is more likely to happen in individuals who are physically active.

Compared with a single bout of HIE, however, short-term HIE leads to different conclusions on the effects on oxidative stress. Faruk Ugras (2013) conducted a 10-day HIE protocol and concluded that HIE could increase the oxidative stress of participants [Faruk Ugras, 2013]. On the contrary, a HIE protocol lasting 3 weeks with training frequency of 3 times weekly and the total training time over 2 hours was proven to reduce oxidative stress and to upregulate the antioxidant system [Kyparos et al., 2007]. In the study of Fisher et al. (2011), 3 HIE protocols were completed with 2 days' recovery between each session [Fisher et al., 2011]. The author found that oxidative stress occurred on the first and second session but did not significantly increase in the third session. Similar findings were reported by Miyazaki et al. (2001). Furthermore, Falone et al. (2010) specified that long-term regular and moderate aerobic physical activity can increase antioxidant capacity [Falone et al., 2010]. Similar findings were provided by Hajizadeh et al. (2017). After a long period of moderate intensity continuous training, high intensity continuous training and high intensity interval training, the authors indicated 3 types of interventions attenuated oxidative stress with different kinetics and moderate intensity continuous training was superior in the promotion of antioxidant capacity.

Using the evidence from the studies reviewed, we can infer that a single session of HIE can induce oxidative stress; however, a HIE protocol lasting a longer period will attenuate oxidative stress. This statement agrees with the findings that regular HIE could keep oxidative DNA damage at a lower level for a long period [Asami et al., 1988] and consecutive days of HIE improved endogenous antioxidant capacity and reduced exercise-induced oxidative stress [Shing et al., 2007]. However, further studies are needed to explore the efficiency of long-term HIE and moderate intensity exercise on antioxidant capacity.

4.5 HIE-induced oxidative stress is related to individual characteristics

In terms of gender, oxidative stress in both male and female individuals changed following HIE [Faruk Ugras, 2013]. In the study of Jammes et al. (2004), the maximum increase in plasma TBARS after exercise was slightly higher in men than in women, while this difference was almost negligible [Jammes et al., 2004]. Furthermore, Wiecek et al. (2018) indicated no differences concerning changes in antioxidant activity post HIE between males and females, while males represented higher level of baseline antioxidant activity [Wiecek et al., 2018]. However, Steinberg et al. (2007) and Jammes et al. (2004) observed that maximal increase in TBARS was positively related to VO_{2max} [Steinberg et al., 2007 and Jammes et al., 2004]. From these studies, we can conclude that high-intensity exercise-induced oxidative stress is not related to gender. Since limited studies focused on women, more studies exploring oxidative stress using different gender participants are needed.

Generally, aging is related to a decline in antioxidant capacity and aged populations are more susceptible to oxidative stress. Bouzid et al. (2014) compared changes in oxidative stress with aging populations at rest and post HIE [Bouzid et al., 2014]. There was no difference in oxidative markers between young and elderly groups at rest and antioxidant activities only increased in the young group post exercise. Furthermore, Boisseau and Delamarche (2000) found that post-pubertal boys have higher muscle mass, higher mitochondrial respiration, and greater oxygen uptake during exercise [Boisseau and Delamarche, 2000]. This resulted in greater ROS production and subsequent oxidative stress because of puberty. At the same time, post-pubertal boys had higher antioxidant capacity. Higher baseline value of TBARS, CAT, and SOD were observed in post-pubertal populations, and more significant changes in these markers after exercise were found. Therefore, post-pubertal populations were considered to have a stronger ability to counter oxidative stress [Chaki et al., 2019].

The findings from cross-sectional studies are limited. However, longitudinal studies are needed to demonstrate the response of aging and fitness levels in relation to oxidative stress and antioxidant capacity.

5. Limitations and strengths

There are several limitations in the present review. Firstly, the heterogeneity among selected studies is considerable ($I^2 > 75\%$). It may be due to the exercise protocols with different characteristics, making us difficult to draw a more precise conclusions regarding exercise type, duration, and intensity. Second, although most studies reported no medications and antioxidant dietary supplement before and during the test, they did not analyze daily diet, which could have an impact on the results. Finally, this review chose to focus solely on studies that have reported oxidative stress assayed from blood TBARS (MDA) concentration as it represents the most frequently used indicator. We acknowledge that oxidative damage can also be detected directly by ESR or indirectly in urine and muscle indicators. Furthermore, this is the first systematic review investigating the influence of HIE with untrained humans and MQA was executed rigorously through all the selected studies.

6. Practical applications

- HIE induced oxidative stress is acute and recoverable, and in young healthy untrained humans, oxidative stress after a single bout of HIE will not elevate to a dangerous level.
- Higher physical fitness level is associated with shorter time to recovery from the exercises induced oxidative stress.
- Higher intensity is related to higher exercise induced oxidative stress, and 70%VO_{2max} with sufficient recovery is better for untrained human to initiate HIE.
- Establishing a standardized HIE protocols in order to specifically investigate the oxidative responses post exercise will help to provide us a better knowledge in this aera.

7. Conclusion

This systematic review demonstrates that an increase in oxidative damage occurs following a HIE bout. The data further demonstrates that oxidative stress was positively associated with increases in exercise intensity, while benefits were observed in studies using more than one HIE session. Although oxidative stress occurs after HIE, this is not a negative outcome per se. Such exercise-induced oxidative stress is transient and most likely recovers within 24 hours, or even sooner. Short-term oxidative stress can stimulate the body's antioxidant system, which in the long term will improve the body's antioxidant capacity and have a positive effect on health promotion.

The exercise modality during HIE is not related to oxidative stress, but the intensity and duration of HIE are closely related to increases in oxidative stress. It is generally believed that the greater the intensity and the longer the duration of HIE, the more intense the oxidative stress would be. At the same time, the degree of oxidative stress is also related to the individual's exercise habits, individual fitness levels and age. Individuals who are physically active appear to have greater antioxidant capacities. From this review, we can conclude that HIE can be an alternative for untrained humans to improve antioxidant capacity and promote health.

However, the combination of frequency, intensity, and duration of HIE protocols needs to consider individual characteristics comprehensively when prescribing individual training programs, since induced oxidative stress level responses are not identical between individuals.

Summary

HIIT, characterized by its high efficiency, is gaining popularity worldwide, especially in young adults. Findings regarding to the effect of HIIT on CRF seem to be consistent. HIIT can significantly improve VO_{2max} in adults with normal weight, overweight and obesity. However, the effects of HIIT on other cardiometabolic biomarkers have been mixed, with relatively consistent results observed in obese and impaired participants. HIIT has similar or greater effects on CRF than MICT, but the exercise time and energy expenditure of HIIT are much less than those of MICT. From a weight-loss prospective, the effect of HIIT on losing weight and fat remains uncertain. This is not surprising, given the lower energy expenditure associated with HIIT. Nevertheless, some studies have reported the weight-losing effect of HIIT, and these effects are more significant in adults with obesity. Generally, long-term HIIT program tend to provide more favorable health outcomes compared to short-term program. There is data to suggest that an increase in VO_{2max} can be detected after as short as 2 weeks of HIIT, whereas the improvement in other cardiometabolic indicators require longer duration. Basically, more cardiometabolic benefits can be observed in HIIT programs lasting 12 weeks or more. Furthermore, HIIT protocol with shorter bout duration and fewer bout number appears to be more effective and meanwhile induce less fatigue and perceived exertion. Tabata training is a HIIT protocol that characterized by 8 repetitions of 20 seconds workout with 10 second rest between each workout. The intensity of 170% VO_{2max} is required with the original Tabata protocol, which is designed for elite athletes, however it is unfeasible for untrained people. Data

from intervention studies show that Tabata protocol performed at a submaximal intensity also provide health benefits. Moreover, Tabata protocol can be used in various exercise modalities such as cycling, running, rowing, kettle bell, functional exercises, and resistance training. However, data on the health improvements of the Tabata protocol are limited. Not surprisingly, there are several concerns about the safety and tolerability of HIIT, as well as the exercise-induced oxidative stress, but the data suggest that only a few of studies have reported extremely low probability of adverse events, and none of them are serious. Furthermore, HIIT have an acute effect on increasing oxidative stress, but the HIIT-induced oxidative stress tends to be transient. This short stimulate may help enhance antioxidant capacity in the long term. As such, a Tabata-style functional HIIT may be a feasible and effective way to improve health, while its impact on PA remains unclear and deserve further investigation in the following chapters.

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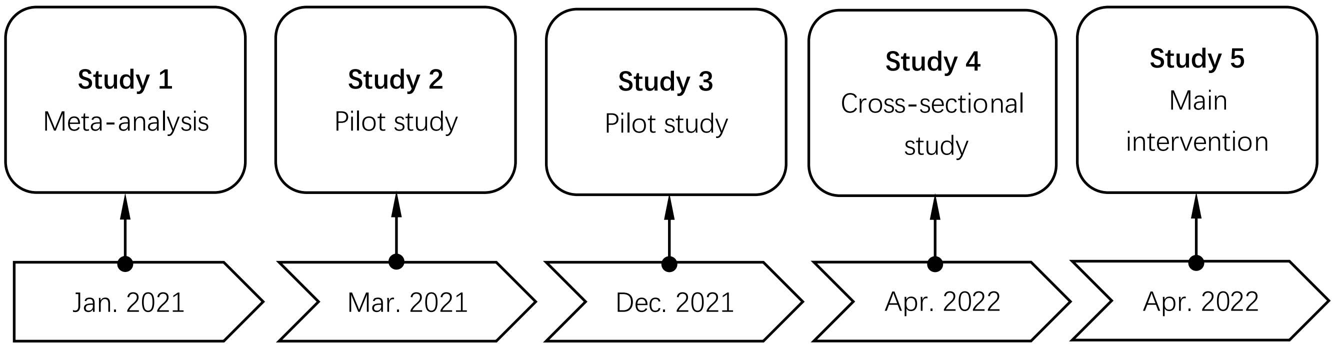
Chapter 3: Program framework

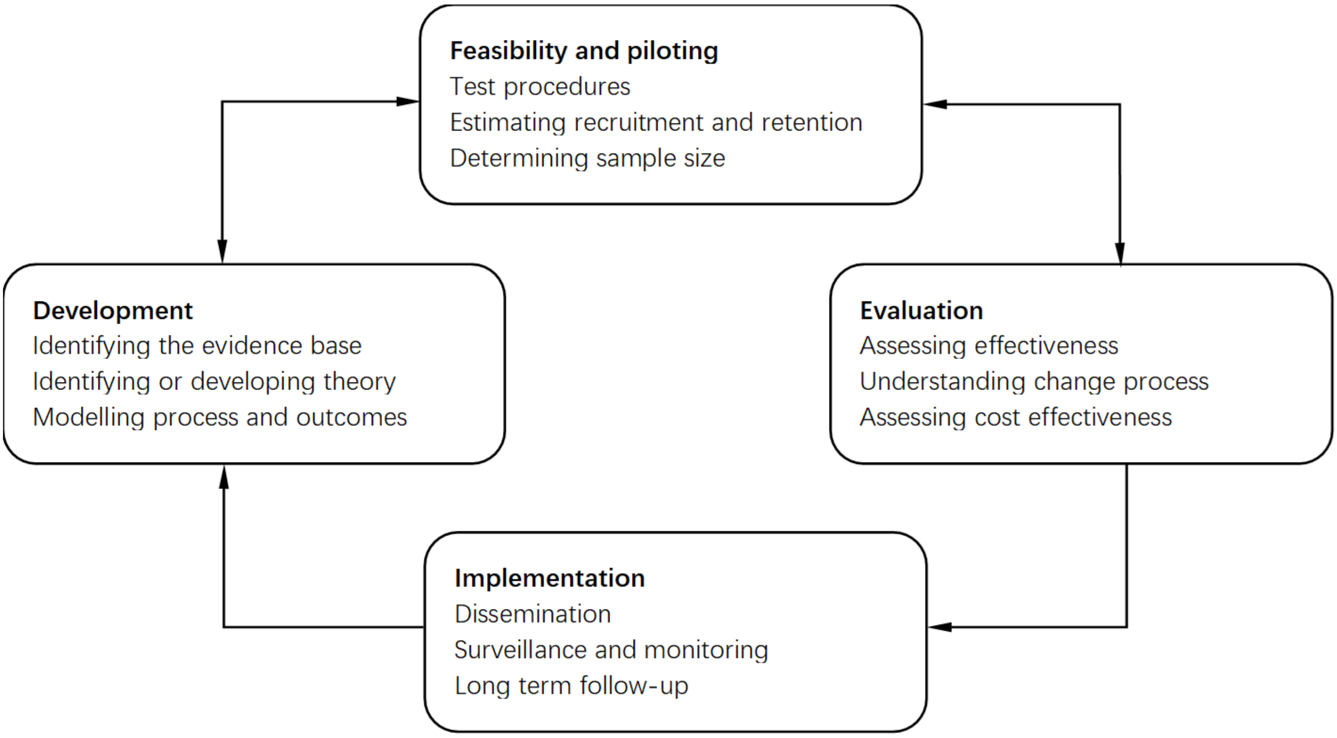
The Project JFM (Just Four Minutes) was conducted among female freshmen who were not sports majors at Ningbo University. Recently, the unhealthy lifestyle in university students has been widely concerned, including physical inactivity, sedentary behaviors, unhealthy dietary habits, and others. These risk factors have seriously affected the health of university students. Furthermore, university students have the poor awareness of cardiovascular health risks factors [Yahia et al., 2016; Hanna et al., 2017; Peltzer and Pengpid, 2018; Chew et al., 2019], and lack of time was the most reported barrier to physical activity (PA) [Awadalla et al., 2014]. When these findings are combined with the increased prevalence of both metabolic syndrome and physical inactivity in young adults, the implementation of effective cardiovascular health and PA promotion programs for university students is timely and reasonable. Figure 3 presented time course of Project JFM.

Figure 3: The time course of Project JFM



The Project JFM was developed based on the Medical Research Council's (MRC) guidance for developing and evaluating complex interventions [Craig et al., 2008]. The Project JFM could be identified as a complex intervention in following ways. Firstly, there were several interacting components within interventions, including health status at baseline, habitual PA, dietary intake, and other lifestyle-related components. Secondly, although in terms of the number of interventions, this appeared to be a single intervention, since there were four different functional movements included in a session, the completion and intensity of each movement was delivered differently to each participant. Finally, the duration of main trial was 12 weeks, and the collections of multiple outcome measurements took place in a flexible manner that provided only a test deadline and allowed participants to choose their own test time. The MRC framework indicated that before developing interventions systematically, best available evidence should be tested, and a series of pilot studies were recommended to assess the key uncertainties in the intervention design. The key elements of the development process were presented in Figure 4.

Figure 4: The key elements of the development and evaluation process of MRC framework



There were several uncertainties included in this project: first of all, the effect of the Tabata-style functional high-intensity interval training (HIIT) on cardiometabolic health was unclear, as well as its effect on habitual PA; secondly, the association between objectively measured PA and health in women was unclear; thirdly, the feasibility and fidelity of high-intensity exercise in untrained women was unclear; finally, there was uncertainty of the role of dietary intake in Chinese women's cardiometabolic health.

The JFM project began with a systematic review and meta-analysis of association between objectively determined PA with adiposity measures and cardiometabolic health in adult women, with young and middle-aged women analyzed separately (Study 1). Accumulating existent knowledge and research findings was an important thing in scientific research. The systematic review and meta-analysis were chosen because, on the one hand, the systematic review was capable of providing a comprehensive literature review with the pre-defined criteria, making the literature search replicable [Liberati et al., 2009]. Replicability was important for scientific research [Francis, 2013]. On the other hand, the meta-analysis aimed at statistically combining the effect sizes [Cheung and Vijayakumar, 2016]. In addition to the synthesized effect, the calculation of the heterogeneity provided the information on the consistency of the effect across studies. Study characteristics were further used to interpret the heterogeneity between studies. Previously, the association between PA and health outcomes had been largely overlooked in HIIT intervention studies. These findings established the evidence base for the association between objectively derived PA and cardiovascular risk factors in adult women, indicating a reliable scientific basis for examining the effect of PA changes on intervention effects.

Study 2 and Study 3 piloted the feasibility and appropriateness of the novel HIIT intervention. These pilot studies tested key steps and worked out uncertainties of the intervention. Without these pilot studies, the acceptability, the adherence, and the delivery of the intervention would be unknown [Craig et al., 2008]. Therefore, Study 2 evaluated female freshmen' responses to the Tabata-style HIIT using functional exercises and compared these responses to traditional running based HIIT. These responses included quantitatively assessed body composition, cardiorespiratory fitness, heart rate, perceived exertion, and exercise enjoyment responses. Participants' feedback was collected via focus group after the intervention. Focus groups were selected to generate data because it provided a permissive circumstance, in which participants were more like to exchange their experience and opinions [Krueger and Casey, 2000]. This was useful to explore not only what they thought but also why they thought that way. Furthermore, focus groups allowed researchers to collect more critical comments than individual interview [Kitzinger, 1995]. These types of comments were important if the aim of interviews was to making improvements. Therefore, focus groups seemed an appropriate way to subjectively generate data. Findings from study 2 reflected the appropriateness of the proposed novel HIIT in terms of training effectiveness, physiology, enjoyment, and adherence, underpinning the improvements to the protocol used in the main intervention.

Based on findings from Study 2, the novel HIIT protocol was refined through reorganizing functional exercises included. Accordingly, Study 3 assessed the heart rate and perceived exertion responses of female university students using the refined HIIT protocol. Moreover, the compensative movement behaviors after the proposed HIIT were examined in the short term. Previous studies suggested that exercise intervention increased the energy expenditure during exercises. In response to the exercise-induced energy deficit, participants might have several compensatory behaviors such as increasing the energy intake and decreasing the habitual PA [Herrmann et al., 2015]. It was surprising that compensatory behaviors after exercises were largely overlooked in previous intervention studies. Given that these compensatory behaviors were supposed to play a role on the intervention effects [Church et al., 2009], it was imperative to examine the compensatory behaviors following the proposed HIIT. Findings from study 3 underpinned the implementation of the novel HIIT from a physiological and behavioral perspective.

Study 4 was a cross-sectional study based on the data from the pre-test of main trial. In this cross-sectional study, the association between blood pressure with dairy intake and PA in this population were explored. Previous studies suggested a positive relationship between dairy intake and blood pressure in women [Celik and Inanc, 2016; Skowrońska-Jóźwiak et al., 2017]. However, these findings were based on the Western circumstance. Findings from Study 4 would provide insight to this relationship in the Chinese young women. Since the dietary intake was a contributor to intervention effects, gaining knowledge of this relationship enabled a more comprehensive screening of covariables, so that the outcomes could be more truly reflected by the intervention effects.

Study 5 incorporated the main exploratory trial, which examined the effect of a 12-week Tabata-style functional HIIT program on PA level and cardiometabolic health in female university students. The participants were recruited from female freshmen who enrolled in September 2021. The recruitment process started in March 2022 through the introduction of the project by PE teachers during weekly PE classes, during which project backgrounds, objectives, and requirements were described in detail. Participants were required to complete all pre-intervention measurements by the end of March 2022. The main intervention of Project JFM began on April 4th, 2022, and ended on June 26th, 2022, for a total of 12 weeks. The randomized control trial design was planned, and participants were randomly assigned to the intervention group and the control group. According to Armstrong et al. (2008), a clear intervention model is required to describe the intervention-process-outcome pathway and clarify how the intervention is intended to induce the outcomes expected [Armstrong et al., 2008]. As such, the Template for Intervention Description and Replication (TIDieR) checklist and guideline were used to improve the reporting of interventions [Hoffman et al., 2014]. Furthermore, the reliability and validity of study outcomes is affected by the intervention fidelity, which refers to the extent to which the intervention is implemented, accepted, and enacted as intended [Moncher and Prinz, 1991], and without sufficient attention to the fidelity assessment, the findings of the intervention will be useless [Bellg et al., 2004]. Implementation evaluated whether the intervention was delivered as intended to all participants throughout the intervention. Acceptance assessed participants' knowledge of the intervention, including whether they accepted new knowledge and were capable to performing it. Enactment examined the extent they apply this new knowledge to their daily life [Resnick et al., 2011]. In the context the Project JFM, the fidelity was objectively assessed throughout the main intervention period and reported by both between and within participants' heart rate responses during exercises. Furthermore, the fidelity was subjectively explored through post-intervention focus groups, during which all participants were invited to attend focus groups to share their intervention experiences.

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Chapter 4: Objectively Determined Physical Activity and Adiposity Measures in Adult Women: A Systematic Review and Meta-analysis (Study 1 Part 1)

1. Introduction

The prevalence of adiposity is one of the biggest concerns for global public health. Obesity has been significantly associated with the increased risk of type 2 diabetes, hypertension, cardiovascular diseases, certain cancers [Dwivedi et al., 2020; Julian et al., 2022; Wagner et al., 2012], and increased mortality [Whitlock et al., 2009]. Adiposity indicates a state of positive energy balance. To deal with adiposity, a negative energy balance is required. Since physical activity (PA) is an important component of energy expenditure, many studies have examined the effect of PA on body weight management, and furthermore the related health outcomes. The Advisory Committee for the 2008 Physical Activity Guidelines reported that a minimum of 150 minutes moderate-to-vigorous intensity physical activities (MVPA) per week could contribute to 1% to 3% weight loss [Jakicic et al., 2011]. Furthermore, an hour of moderate physical activity (MPA) is indicated to reduce the risk of adiposity by 19% among normal-weight and by 12% in overweight women [Rosenberg et al., 2013], and for substantial weight loss and adiposity improvement, a minimum of 300-420 minutes of MVPA weekly is needed [Johnson et al., 2021]. On the contrary, several studies report limited weight loss after engaging in exercises due to the compensatory effects of other components of energy balance and gender differences in activity energy expenditures [Donnelly et al., 2005; Foright et al., 2018]. Nonetheless, health benefits can be evoked with MVPA among both normal-weight and overweight or obese individuals irrespective of weight loss [Gaesser and Angadi, 2021; Johnson et al., 2021]. Of note, the prediction of adiposity related health risk varies with the indicator used [Kahn et al., 2012; Tselha et al., 2019]. Generally, overweight is defined as a body mass index (BMI) $\geq$ 25, and obesity as BMI $\geq$ 30. However, the measures of central adiposity such as waist circumference (WC) have been demonstrated as better indicators for detecting type 2 diabetes mellitus [Kapoor et al., 2020]. Likewise, better predictive utility has been reported when using percentage body fat (%BF) and visceral adipose tissue (VAT) for metabolic health [Baudrand et al., 2013; Oliverors et al., 2014]. Therefore, a wide range of adiposity indicators need to be taken into consideration when assessing its relationship with PA.

One the other hand, the majority of findings are based upon subjectively estimated PA (e.g., questionnaires and interviews) and focus on PA performed at least moderate intensity which preclude the ability to precisely determine the relationships between all patterns of PA and adiposity. Although there has been emerging evidence that light intensity physical activity (LPA) and non-bout PA are beneficial to health [Carson et al., 2013; Spittaels et al., 2012; Loprinzi, 2017; Marschollek, 2015], few studies have examined the association with adiposity using objective measured PA, which eliminates the measurement error regarding lower intensity and sporadic PA. Despite the health benefits, 30.7% of adult women fail to meet the PA recommendations [Guthold et al., 2018]. Furthermore, women suffer a consistently higher prevalence of adiposity than men, and have a greater increase of obesity prevalence, with 3.4% recorded in 1975 rising to 15% recorded in 2016 [Collaboration N.R.F., 2017; Kelly et al., 2008]. Furthermore, women possess special biological, behavioral and socioeconomic characteristics which contribute to differences in attitude to physical activity patterns, and ultimately in exposure to increased risk of overweight or obesity [Herman et al., 2011; Althoff et al., 2017; Cooper et al., 2021; Kim et al., 2022]. Moreover, age, race and menopausal status also influence the associations between PA and weight gain, %BF and fat distribution [Sims et al., 2012; Slater et al., 2021; Toth et al., 2000]. Therefore, a better understanding of the association between PA and adiposity among women is important for preventing and improving increasing prevalence.

Given the paucity of investigations focusing on the relationship between all patterns of PA and a wide range of adiposity indicators, rigorous scientific assessments of these associations in adult women are needed. Therefore, the main purpose of this systematic review and meta-analysis was to qualitatively synthesize and quantitatively assess any associations between objectively determined PA and adiposity markers among adult women to guide PA prescription.

2. Method

2.1 Protocol registration

The research protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO: registration number CRD42022307774). The systematic review and meta-analysis were conducted following guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [Moher et al., 2009].

2.2 Inclusion criteria and study selection

The Participants Interventions, Comparisons, and Outcomes (PICO) formatted research questions were used to clarify the inclusion criteria [Schardt et al., 2007].

Participants

Apparently healthy women with a mean age range of 18-64 years were included in the study. Participants aged 18-39 and 40-64 were further stratified as young and middle-aged adults respectively [Murray et al., 2021].

Women with any conditions that tended to be a barrier to physical activity were excluded, including the presence of cardiovascular disease risk factors (e.g., hypertension, elevated fasting glucose, and dyslipidemia), diagnosed cardiovascular diseases (e.g., heart failure, serious arrhythmias, and peripheral vascular disease), physical or psychological disorders, previous stroke or myocardial infarction, diabetes (type 1 or type 2), previous surgery / banding, and chronic pain. Women who were pregnant, postpartum, or lactating, or were elite athletes were also excluded.

Interventions (exposures)

PA assessed by accelerometers or pedometers were identified as exposures. For interventional studies, interventions were focused on physical activity exclusively with no other combined interventions, such as diet and supplements, which might affect health outcomes directly. Total energy expenditure obtained from double labelled water and calorimetry were not recognized as an included exposure because these were also affected by dietary intake and there were not daily or hourly data available for energy expenditure calculation [Sirard et al., 2001]. Additionally, activity energy expenditure was not included due to the invalid estimation by accelerometers [Kossi et al., 2021].

Comparisons

Studies reported the estimates in quantiles, and studies that treated PA variables as continuous measures were included. Various steps, volumes, frequencies, durations, and intensities of objectively measured PA were identified for comparisons.

Outcomes

Five adiposity outcomes were included: 1) BMI, 2) %BF, 3) WC, 4) fat mass (FM), 5) visceral adipose tissue (VAT).

Study design

Observational studies and intervention studies were included.

Other criteria

Only literatures published in English and in peer-reviewed journals were included. Abstracts, conference proceedings, unpublished studies and grey literatures were excluded. Studies included participants of both sexes and were considered eligible when data for women were available. When literatures were from the same study, the one with the largest sample size, the longest total intervention period, or with the most detailed data set were used.

2.3 Information sources and search strategy

The electronic search strategy was guided by two researchers with expertise in systematic reviews. Four electronic databases including PubMed, Web of Science, Scopus and the Cochrane Library were searched from 1 January 1990 to 31 January 2022. Search terms were applied to titles and abstracts and combined with the keywords such as “objectively”, “physical activity”, “pedometer”, “accelerometry”, “body composition”, “overweight”, “obesity”, “adiposity”, “BMI”, “fat”, “waist”, and “fat mass”. The detailed search strategy is available in Supplementary Table A. Additionally, the literature list obtained was then manually searched to identify eligible references from included studies. Finally, search results were all imported into Endnote (Endnote 20, Wintertree Software Inc., China).

2.4 Data extraction

For each included study, descriptive data, exposure, finding, as well as information regarding confounders were extracted independently by two reviewers (Yining Lu and Qiaojun Wang) and inputted into Excel (Microsoft Corp.). Disagreements at any stage were resolved through discussion and all results were checked by a third reviewer (Shanshan Ying). The extracted data were: 1) reference details (e.g., first author, publication year, country); 2) study design, follow-up period (if applicable); 3) participants (e.g., sample size, sociodemographic characteristics); 4) protocol for PA assessment (e.g. device details, location, setting, required wearing time, valid wearing time); 5) PA measures (e.g., PA categories, definitions/cut-off points; 6) adiposity measures; 7) statistical analysis; 8) main findings (e.g., risk ratios, associations and differences in means). Statistically significant findings were identified when $p < 0.05$.

2.5 Risk of bias and quality assessment

The Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias in nonrandomized studies (nonrandomized interventions and observational studies) [Wells et al., 2019]. The NOS consisted of three components: selection, comparability, and outcome. A star was awarded for each question within the selection and outcome domains and a maximum of two stars was awarded for the comparability domain. For the comparability domain, we considered age to be the most important confounder due to its association with both PA and health. The maximum number of stars that a cross-sectional design and a longitudinal design could be awarded was seven and nine respectively. For cross-sectional designs, a total number of stars greater than or equal to 4 was defined as high quality, and below 4 was defined as low quality. The cut-off for longitudinal designs was 5 [Ramsey et al., 2022; Ramakrishnan et al., 2021]. For RCTs, the Cochrane collaboration's tool was used [Higgins et al. 2011], which comprised 6 domains with 7 questions, including: selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting), and other sources of bias. The risk of bias for each question was judged as "low", "unclear" or "high", and finally, the overall quality was defined as high if all domains were low risk of bias.

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was used to evaluate the quality of evidence for each PA measure [Guyatt et al., 2011]. The quality of evidence was classified as high, moderate, low, and very low, with the evidence from randomized studies starting as high quality and the evidence from non-randomized or observational studies starting as low. Any discrepancy in rating was resolved by discussion and the results were verified by a third reviewer. Details of the risk of bias and quality assessment are presented in Supplementary Table B.

2.6 Statistical Analysis

When there were more than 2 studies with comparable PA measures and adiposity indicators, a meta-analysis was planned. Regardless of the different cut-off points and definitions, LPA, MPA, vigorous intensity physical activity (VPA), MVPA and TPA were defined as reported in the studies. If studies measured physical activities in metabolic equivalents (METs), we used the cut-points proposed Ainsworth et al. (2011) (e.g., 1.6–2.9 METs was defined as LPA, 3-5.9 METs as MPA, and ≥6 METs as VPA).

When more than one statistical analysis was used, the following hierarchy was applied: 1) regression, 2) correlation, 3) ANOVA, 4) t-test/U-test/K-S test [Ramsey et al., 2022]. When more than one adjusted model was used, the most adjusted model was applied [Aune et al., 2015].

Fisher's z transformation was applied as recommended for correlational meta-analysis [Peterson et al., 2005]. The standardized mean differences (SMD) were calculated using Hedges' g. With regards to the effect size, according to Cohen's recommendations, we classified the effect size as low (r=0.1/ SMD=0.2), moderate (r=0.3/ SMD=0.5), and high (r=0.5/ SMD=0.8) [Cohen, 1988].

The random-effects model was used because of the high degree of heterogeneity among populations (age, BMI, ethics, and baseline PA). I^2 statistics were used to measure heterogeneity among included studies, with I^2 values of 25%, 50% and 75% being categorized as low, moderate, and high, respectively [Higgins et al., 2003]. Subgroup analyses were performed to identify the potential sources of heterogeneity from five aspects, including age (young/ middle-age), overweight/obese (BMI<25/ BMI≥25), menopausal status (postmenopausal/ premenopausal), country, and ethnicity. Publication bias was assessed using Egger's test and funnel plots for PA category for at least ten studies [Egger et al., 1997]. Finally, we conducted sensitivity analysis by removing studies with low quality.

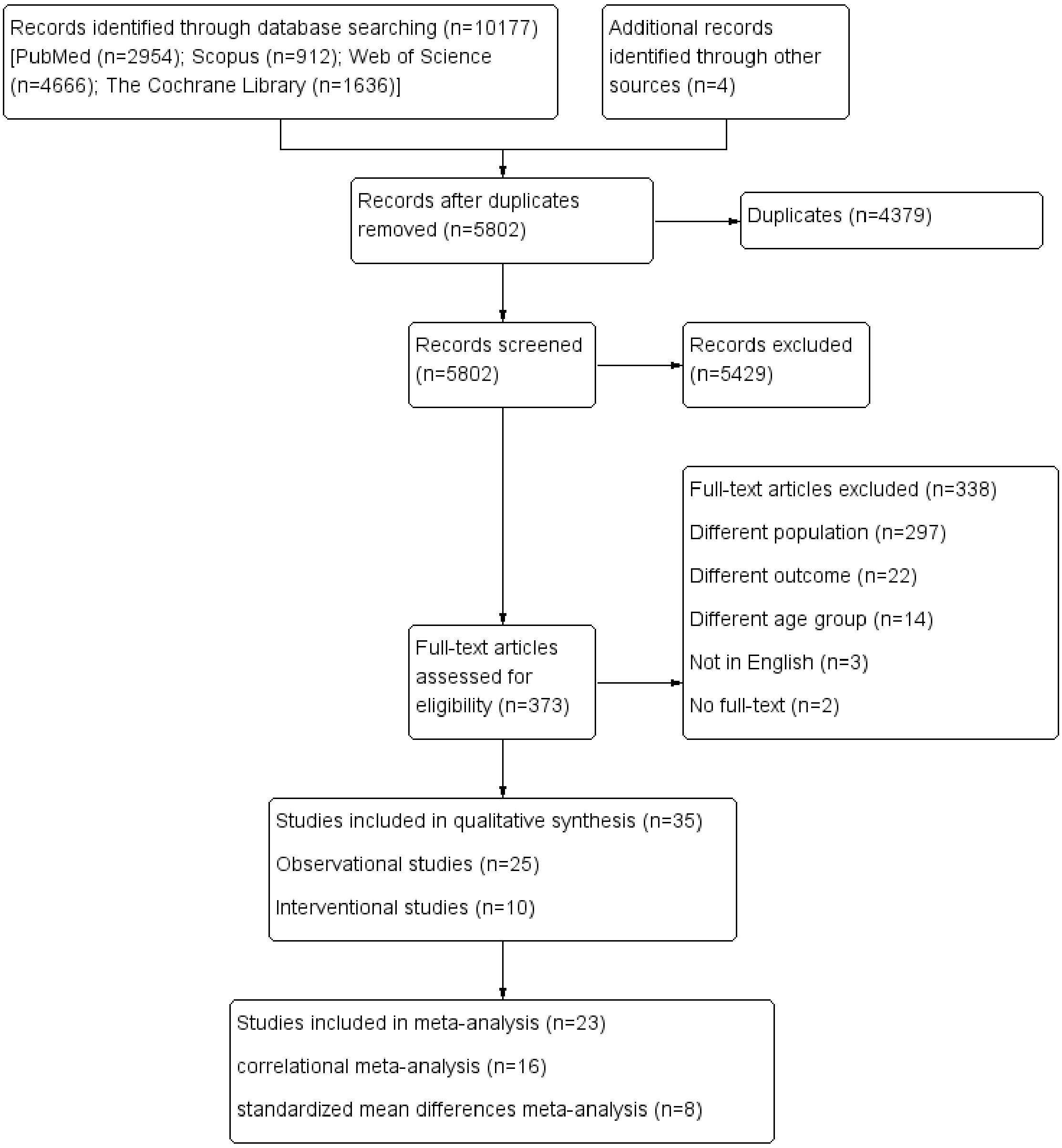
Statistical analyses were performed with Review Manager (RevMan), version 5.4.1 (The Cochrane Collaboration, 2020).

3. Results

3.1 Study identification and selection

A total of 10177 records were identified from the database search between 1 January 1990 and 31 January 2022 from PubMed, Scopus, Web of Science, and the Cochrane Library. Additionally, 4 records were identified through reference list screening. After removing the duplicate records (n=4379), 5802 studies were further screened based on title and abstract. Exclusion of irrelevant studies resulted in 373 records. After examining the full text, finally, 35 eligible studies were included in the present review. The processes of study selection followed the PRISMA guidelines and are presented in Figure 5.

Figure 5: PRISMA process of study selection



3.2 Study characteristics

Out of 35 studies, 25 were observational studies, with 24 using a cross-sectional design and 1 longitudinal design (20-month follow-up), reporting cross-sectional findings [Bailey et al., 2007]. Detailed characteristics of observational studies are illustrated in Table 7. 10/35 were intervention studies (RCTs: 3 and non-RCTs: 7), with the intervention length ranging from 9 weeks [Hasan et al., 2018] to 24 weeks [Bailey et al., 2019; Holliday et al., 2018; Moreau et al., 2001]. A detailed description of the intervention studies is presented in Table 8.

Among observational studies, linear regression was the most used method to assess any associations (10/25), correlation analysis was used in 8 studies, ANOVA was used in 8 studies, and the t-test/U-test/K-S test was used in 4 studies. While in intervention studies, ANOVA was commonly used (9/10), with 1 study also including correlation analysis [Cayir et al., 2015]. The rest one used a combination of t-test and correlation [Hasan et al., 2018].

Dietary intakes were analyzed in 4/35 observational studies [Graff et al., 2012; Hornbuckle et al., 2005; Park et al., 2011; Tucker et al., 2003] and 8/10 intervention studies [Bailey et al., 2019; Hasan et al., 2018; Holliday et al., 2018; Hornbuckle et al., 2012; Moreau et al., 2001; Musto et al., 2010; Pal et al., 2011; Swartz et al., 2003].

Table 7: Characteristics of observational studies

Reference	Study design	Country	Sample size	PA measure	Health Outcome	Association
Ayabe et al. 2013	cross-sectional	Japan	42	A: Lifecorder-Ex; uniaxial **Duration (min/d), frequency (bouts/d)** MVPA, MVPA bout (32s, 1min, 3min, 5min); VPA, VPA bout (32s, 1min, 3min, 5min).	**VAT,** by computed tomography (CT)	Regression: 1) Frequency of MVPA bout (1min,3min), TPA bout (3min, 5min) were favorable associated with VAT; 2) Duration of MVPA bout (1min) was favorable associated with VAT; 3) VPA was favorable associated with VAT; 4) No significant relationship between MVPA and VAT;
Bailey et al. 2015	cross-sectional	USA	343	A: ActiGraph GT3x; triaxial **Duration (min/d):** LPA, MPA, VPA; **Intensity** of PA (METs)	**%BF; Obese (%BF≥32%)** by BODPOD	Regression: adjusted for age and seasonality. 1) Duration of MPA, VPA was favorably associated with %BF, LPA had no association with %BF; 2) For every 10 minutes spent in MVPA per day, the odds of being obese reduced by 29%. 3) For PA intensity (≤ 4 METS), %BF decreased as duration increased; For PA intensity (≥4.9 METS), no benefit of accumulating more than 30 minutes per week. ANOVA: 1) Group (VPA ≥ 30min/w) had significantly lower %BF than Group (VPA < 30min/w); 2) Group (MVPA ≥ 30min/d) had significantly lower %BF than Group (MVPA < 30min/d); 3) Group (MVPA ≥ 90min/d) was associated with the lowest %BF;
Bailey et al. 2014	cross-sectional	USA	186	P: Omeron HJ-720-ITC **Steps (n/d)** Aerobic steps (n/d) (60/min for a minimum of 10 min)	**%BF, WC, BMI; Overweight (25≤BMI<30), Obese (%BF≥32% or BMI≥30)** by BODPOD	Regression: adjusted for age, average daily temperature, and menstrual cycle. 1) Every increase of 1000 steps/d was associated with a 2.4% lower %BF; 2) For every increase of 1000 steps/d, the odds of being obese reduced by 22%; 3) For Group (≥10000 steps/d), the odds of being overweight reduced by 65% and the odds of being obese were reduced by 80% compared with Group (< 10000 steps/d) Correlation: 1) Steps/d was favorably associated with %BF; has no association with WC, BMI; 2) Aerobic steps/d has no association with body composition index;
de Hoed et al. 2008	cross-sectional	Netherlands	80	A: Tracmor IV, triaxial **TPA** (Mcnts/d)	**%BF** by underwater weighing	Regression: adjusted for BM, height, and seasonality 1) TPA was favorably associated with %BF;

Diniz et al. 2015	cross-sectional	Brazil	49	A: ActiGraph GT3x; triaxial **Duration (min/w)**: MVPA **TPA** (counts/min) **meet/ not meet MVPA (Duration)**	**%BF, BMI** by dual-energy X-ray absorptiometry (DXA)	U-test: 1) Group (MVPA < 150 min/w) had a higher %BF compared to (MVPA ≥ 150 min/w); 2) No differences in BMI between Group (MVPA < 150 min/w) and Group (MVPA ≥ 150 min/w); 3) Group (NAF) had a higher TPA compared to Group (HAF); 4) No differences in %MVPA between Group (NAF) and Group (HAF).
Graff et al. 2012	cross-sectional	Brazil	68	P: BP 148 Steps (n/d)	**%BF, BMI, WC** by calculation	t-test and U-test: 1) Group (Steps/d < 6000) had higher BMI, WC, %BF than Group (Steps/d ≥ 6000);
Green et al. 2014	cross-sectional	USA	50	A: ActiGraph GT3X+; triaxial **Duration (min/d)**: LPA, MVPA; **Duration (min/w)**: MVPA bout (10min)	**WC** by anthropometric tape	Correlation: adjusted for SB, VO2peak, and BM 1) LPA, MVPA and MVPA bouts had no association with WC;
Hornbuckle et al. 2005	cross-sectional	USA	69	P: New Lifestyles Digi-Walker SW-200 Steps (n/d)	**BMI, %BF, WC** by BODPOD	Correlation: adjusted for age and caloric intake 1) Steps/d was favorably associated with BMI, %BF, WC;
Koniak-Griffin et al. 2014	cross-sectional	USA	210	A: Kenz Lifecorder Plus; uniaxial **Duration (min/d)**: MVPA, MVPA bout (10min) **Steps (n/d)**	**BMI, WC** by calculation and anthropometric tape	Correlation: 1) Steps/d was favorably associated with BMI, WC; 2) MVPA was favorably associated with WC; had no association with BMI; 3) MVPA bouts had no association with BMI, WC;
Panton et al. 2007	cross-sectional	USA	35	P: Yamax Digi-Walker SW-200, sealed **Steps (n/d)**	**BMI, WC** by calculation and anthropometric tape	Correlation: 1) Steps/d was favorably associated with BMI; had no association with WC. ANOVA: 1) Group (Steps/d<5000) had higher BMI compared to Group (Steps/d≥5000); 2) No differences in WC between Groups;
Park et al. 2011	cross-sectional	Japan	100	A: Lifecorder EX, uniaxial **Duration (min/d)**: LPA, MPA, VPA **Steps (n/d)**	**BMI, FM, %BF** by underwater weighing	Regression: 1) Steps/d was favorably associated with BMI, FM and %BF; 2) LPA had no association with BMI, %BF or FM; 3) MPA was favorably associated with BMI and FM; had no association with %BF; 4) VPA was favorably associated with BMI, FM and %BF;

Pelclová et al. 2012	cross-sectional	Czech Republic	167	A: ActiGraph GT1M, uniaxial **Duration (min/w)**:MPA meet MPA/do not meet MPA (Duration, Frequency) **Steps (n/d)**	**BMI, FM, VAT** by bioelectrical impedance	Correlation: 1) MPA and steps/d were favorably associated with BMI, FM, and VAT; ANOVA: 1) Group (150≤MPA≤300min/w) had higher FM than Group (MPA>300min/w); no differences in BMI and VAT between groups; 2) Group (not meet MPA 5x30min/week) had higher BMI, FM, VAT than Group (meet MPA 5x30min/week); 3) The frequency of performing 10,000 steps/day in a week was favorably associated with BMI, FM, VAT;
Phelan et al. 2007	cross-sectional	USA	237	A: RT3; triaxial **Duration (min/d):** LPA, MPA, VPA, MVPA	**BMI** by calculation	K-S test: 1) MVPA was higher in Group (weight-loss-maintainer) than Group (always-normal-weight); 2) VPA was higher in Group (weight-loss-maintainer) than Group (always-normal-weight); 3) no differences in MPA and LPA between groups. 4) Most Group (always-normal-weight) engaged in 30–60 MVPA min/d; 5) Most Group (weight-loss-maintainer) engaged in > 60 MVPA min/d;
Slater et al. 2021	cross-sectional	New zealand	275	A: ActiGraph w-GT3X, Acti-Watch; triaxial **Duration (min/d):** MVPA TPA (cpm/d)	**%BF, WC, BMI, VAT** by DXA	Regression: adjusted for age and socioeconomic level 1) TPA was favorably associated with %BF and VAT; had no association with WC or BMI; 2) MVPA was favorably associated with %BF, VAT, WC and BMI;
Smith et al. 2013	cross-sectional	USA	201	A: Actigraph AM7164, uniaxial **Duration (min/d):** LPA, MVPA TPA (min/d≥100 counts)	**VAT** by CT	Regression: adjusted for age, BMI, race-ethnicity, education, SB 1) LPA, MVPA had no association with VAT; 2) TPA was favorably associated with VAT;
Sternfeld et al. 2005	cross-sectional	USA	248	A: CSA; uniaxial **Duration (min/d):** MPA, VPA; TPA (cpm/d)	**%BF, WC** by DXA	Regression: age, menopausal status, education, and health status 1) TPA and MPA had no association with %BF or WC in both ethic groups; 2) VPA was favorably associated with %BF and WC in Group (White); had no association in Group (Chinese)
Strath et al. 2008	cross-sectional	USA	1594	A: AM-7164; uniaxial **Duration (min/d):** MVPA bout (10min), MVPA non-bout	**BMI, WC** by calculation and anthropometric tape	Regression: adjusted age, age-squared, race/ethnicity, smoking, and health status. 1) MVPA bouts was favorably associated with BMI and WC; 2) MVPA non-bouts had no association with BMI and WC; 3) The strength of association with decreased BMI was nearly 7 times greater for MVPA bout than for MVPA non-bouts; 4) The strength of association with decreased WC was nearly 5 times greater for MVPA bout than for MVPA non-bouts;

Thompson et al. 2004	cross-sectional	USA	80	P: Yamax Digi-Walker SW-200 Steps (n/d)	**BMI, %BF, WC** by BODPOD	Correlation: adjusted for age 1) Steps/d was favorably associated with BMI, %BF, WC; ANOVA: 1) Group (< 6000steps/d) had higher BMI than Group (6000-9999) and Group (≥10000); 2) Group (≥10000) had the lowest %BF, and WC among three groups.
Tolonen et al. 2018	cross-sectional	Finland	837	P: Walking style One, HJ-152R-E Steps (n/d)	**BMI** by calculation	ANOVA: 1) Group (steps/d>8765) had lower BMI than Group (Steps/d<6317);
Tucker et al. 2003	cross-sectional	USA	278	A: CSA; uniaxial TPA (counts) (min/w) Intensity and duration of PA (counts/10min)	**%BF** by BODPOD	Regression: adjusted for BM, and energy intake 1) TPA was favorably associated with %BF; 2) The intensity and duration were favorably associated with %BF.
Tudor-Locke et al. 2009	cross-sectional	Australia	158	P: Yamax Digiwalker SW700 Steps (n/d)	**BMI** by calculation	ANOVA: 1) Group (Fewer Steps/day) had higher BMI.
Vella et al. 2011	cross-sectional	USA	60	A: Actigraph GT1M; uniaxial meet MVPA/do not meet MVPA (duration)	**BMI, FM, %BF, WC** by BODPOD	t-test: 1) No differences in BMI, FM, %BF or WC between groups;
Vella et al. 2009	cross-sectional	USA	60	A: Actigraph GT1M; uniaxial Steps (n/d)	**WC** by anthropometric tape	correlation: 1) Steps/d had no association with WC
Van Dyck et al. 2015	cross-sectional	multi-country	3027	A: ActiGraph 7164/71256, GT1M, ActiTrainer, GT3X; uniaxial&triaxial **Duration (min/d):** MVPA TPA (cpm/d)	**BMI** by calculation	Regression: socio-demographic status and accelerometer wear time 1) MVPA and TPA was favorably associated with BMI with country-specific associations.
Bailey et al. 2007	cohort study/ cross-sectional	USA	228	A: ActiGraph; uniaxial The LPA, MPA, VPA groups based on the average of the highest 7 epochs (10min); The increased-, maintained- and decreased- intensity groups based on changes of PA intensity group from baseline to follow-up	**%BF** by BODPOD	ANCOVA: adjusted for age and TPA 1) Group (VPA) had lower BF% than Group (MPA) or Group (LPA); 2) no difference in BF% between Group (MPA) and Group (LPA); 3) Group (decreased intensity) had a higher proportion of having a higher %BF at follow-up than Group (maintained intensity) and Group (increased intensity);

Note: A: accelerometer; BMI, body mass index; FM, fat mass; HAF, high abdominal fat; METs, metabolic equivalents; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; NAF, normal abdominal fat; P, pedometer; PA, physical activity; SB, sedentary behaviors; TPA, total physical activity; VAT, visceral adipose tissue; VPA, vigorous physical activity; WC, waist circumference; %BF, percentage body fat.

Table 8: Characteristics of intervention studies

Reference	Study design	Country	Sample size	Intervention	PA measure	Health Outcome	Association
Bailey et al. 2019	random experiment	USA	92	24-week incremental walking program; Group 1 (n=34): asked to walk 10000 steps/d, 6 days/week; Group 2 (n=34): asked to walk 12500 steps/d, 6 days/week; Group 3 (n=24): asked to walk 15000 steps/d, 6 days/week;	A: ActiGraph GT3x; triaxial P: Omeron HJ-720-IT; Duration (min/d): LPA, MVPA Steps, Aerobic steps (n/d)	**BMI, %BF, FM, VAT (mass, volume)** by DXA	ANOVA: 1) Steps/d increased from baseline in all three Groups, with a significant intervention effect between groups; 2) LPA increased from baseline only in Group 3, with no effect for groups; 3) MVPA and aerobic steps/d increased from baseline in all three Groups, with a significant main effect for groups between Group 2&3 and Group 1; 4) BMI increased from baseline only in Group 1; 5) %BF and VAT mass and volume had no change in all three groups; 6) FM increased from baseline in Group 2&3; 7) no follow-up differences in all parameters between groups.
Cayir et al. 2015	randomized controlled trial	Turkey	84	3-month pedometer-based walking program Group 1 (n=45): with pedometer CONT (n=39): without pedometer	P: Voit 3d Steps (n/d)	**BMI, %BF, WC** by anthropometry	ANCOVA: baseline BM, BMI, %BF 1) BMI, %BF, WC decreased in Group 1; had no change in CONT; 2) ΔBMI, Δ%BF, ΔWC were larger in Group 1 compared to CONT;
Hasan et al. 2018	Quasi-experimental design	UAE	52	9-week pedometer-based walking program, asked to walk 10,000 steps per day	P: KenzLifeCoder e-step Steps (n/d)	**BMI, %BF, VAT (area), FM, WC** by InBody	Correlation: 1) After intervention, steps/d was favorably associated with BMI, FM, and %BF; had no association with VAT or WC; t-test: 1) After intervention, FM, BMI, %BF, VAT, WC decreased; 2) In Group (18≤BMI<25), after intervention, BMI and FM decreased; no changes in %BF, VAT or WC; 3) In Group (BMI≥25), after intervention, BMI, FM, %BF, WC, and VAT decreased.

Holliday et al. 2018	randomized controlled trial	UK	58	24-week PA intervention Group 1 (n=20): asked to undertake 5x30 min of moderate-intensity exercise/week; Group 2 (n=22): a points score allocated per 10-minutes of activity, Participants were instructed to accumulate 30 points per week, equating to 5x30 min of brisk walking; CONT (n=16): asked to maintain their current lifestyle	A: ActiGraph GT3X+; triaxial %duration of LPA, MVPA	**FM, VAT (area), WC** by DXA	<u>ANOVA:</u> 1) Changes in WC was significantly greater in Group 2 at 24 weeks, compared with CONT; 2) There was a trend for greater reductions in FM in Group 2 vs. CONT (p=0.075); 3) There was a trend for greater reductions in VAT in Group 2 vs. CONT (p=0.053); 4) Parameters were unchanged in Group 1;
Hornbuckle et al. 2012	random experiment	USA	44	12-week exercise intervention Group 1: asked to walk 10000 steps/d Group 2: asked to walk 10000 steps/d + RT 2d/w (3 sets of 8–12 repetitions of 10 resistance exercises for the lower and upper body)	P: New Lifestyles Digi-Walker SW-200 Steps (n/d)	**BMI, WC, %BF, FM** by DXA	<u>ANOVA:</u> 1) Steps/d increased from baseline in both groups; 2) No changes in all parameters after intervention in Group 1; 3) WC, %BF and FM decreased after intervention in Group 2;
Moreau et al. 2001	randomized controlled trial	USA	24	24-week pedometer-based walking program Group 1: provided with a target number of steps that would lead to a 3-km increase in daily walking; CONT: maintain current physical activity and subsequently wore a pedometer 1 week each month to document their walking	P: Yamax SW200 pedometer Steps (n/d)	**%BF** by BODPOD	ANOVA: 1) Steps/d increased from baseline in Group 1 compared with CONT; 2) %BF had no change in either group after intervention.
Musto et al. 2010	Quasi-experimental design	USA	77	12-week incremental walking program; asked to increase steps/d by 10% per week; the progression was reduced to a 3% when steps/d reached 10000 Group 1: improved steps/d by 3000 or greater; CONT: stopped participating or did not achieve step improvement level	P: Sportline 330 Steps (n/d)	**BMI, WC** by calculation	ANOVA: 1) BMI decreased after intervention in Group 1 compared with CONT; 2) WC decreased after intervention in Group 1;

Pal et al. 2011	random experiment	Australia	28	12-week walking program; Group 1: asked to undertake 30 minutes of walking/day; with sealed pedometer Group 2: asked to accumulate 10,000 steps/d, with unsealed pedometer	P: Yamax Digi-Walker SW-200 Steps (n/d)	**BMI, %BF, WC** by BIA	ANOVA: 1) Steps increased in both groups after intervention with between-group effects. 2) no changes in BMI, %BF, WC in either group after intervention.
Sugawara et al. 2006	random experiment	Japan	17	12-week cycling training Group 1 (n=8): 180-300 kcal/session, 3-5 sessions/week at 40% HRR Group 2 (n=9): at 70% HRR	A: Lifecorder; uniaxial Intensity LPA (<4METs), MPA (4-6METs), VPA (>6METs) (min/d)	**BMI** by calculation	ANOVA: 1) BMI decreased after intervention in Group 2;
Swartz et al. 2003	Quasi-experimental design	USA	18	4-week control period followed by 8-week walking program	P: Yamax Digi-Walker SW-200 Steps (n/d)	**BMI, %BF, WC** by BODPOD	ANOVA: 1) Steps/d increased during intervention period; 2) BMI, %BF, and WC had no change;

Note: A: accelerometer; BMI, body mass index; CONT, control group; FM, fat mass; HRR, heart rate reverse; METs, metabolic equivalents; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; P, pedometer; PA, physical activity; RT, resistance training; SB, sedentary behaviors; TPA, total physical activity; VAT, visceral adipose tissue; VPA, vigorous physical activity; WC, waist circumference; %BF, percentage body fat.

3.3 Sample characteristics

The total sample size was 9176, ranging from 17 [Sugawara et al., 2006] to 3027 [Van Dyck et al. 2015] participants. The mean age of the women ranged from 18.2 [Bailey et al., 2019] to 64.2 [Pelclová et al., 2012] years. 11/35 studies focused on young female adults, while 21/35 studies focused on middle-aged women. 8/35 studies reported menstrual status, with 2 studies focusing on post-menstruation [Moreau et al., 2001; Diniz et al., 2015], 6 including pre-menstruation [Graff et al., 2012; Green et al., 2014; Slater et al., 2021; Sternfeld et al., 2005; Tucker et al., 2003; Bailey et al., 2007]. Moreover, 10/35 studies focused on overweight/obese females and 1 study consisted of a sample of weight-loss-maintainers [Phelan et al., 2007]. 10/35 studies described the lifestyle of participants as physically inactive. 14/35 studies reported smoking status, with 8 studies utilizing participants who never smoked, 4 studies reported participants refrained from tobacco in the last 6 months, and 2 studies included mostly non-smokers (80-83%). Regarding education level, 8/35 studies indicated the percentage of participants who attended college or university, ranging from 37-100%. Social-economic levels were presented as low-income in 3 studies [Koniak-Griffin et al., 2014; Panton et al., 2007; Slater et al., 2021], college students in 4 studies [Hasan et al., 2018; Bailey et al., 2019; Bailey et al., 2014; de Hoed et al., 2008], the Third Age University students in 1 study [Pelclová et al., 2012], part-time employees in 1 study [Ayabe et al., 2013], and full-time employees in 2 studies (43-63%) [Tudor-Locke et al., 2009; Cayir et al., 2015].

Included studies were conducted in 11 countries. 4/35 studies included a sample from Asia (i.e., Japan, Turkey, and UAE), 4/35 from Europe (i.e., UK, Netherlands, Czech Republic, and Finland), 20/35 from North America (i.e., USA), 2/35 from South America (i.e., Brazil), and 3/35 from Oceania (i.e., New Zealand and Australia). Additionally, 1 study included a sample from 12 different countries [Van Dyck et al., 2015]. Moreover, 20/35 studies reported the race of participants, with 9 studies including Caucasian mainly (73%-96%), 4 studies included Asian [Ayabe et al., 2013; Park et al., 2011; Sternfeld et al., 2005; Sugiura et al., 2002], 3 studies included African American [Hornbuckle et al., 2005; Panton et al., 2007; Hornbuckle et al., 2012], and others reported ethnicities including Hispanic [Vella et al., 2011; Vella et al., 2009], Latina [Koniak-Griffin et al., 2014] and Pacific women [Slater et al., 2021]. Detailed characteristics of participants are illustrated in Supplementary Table C

3.4 Physical activity assessment

21/35 studies used accelerometers, with 1 study also using a pedometer [Bailey et al. 2019]. 14/35 studies used pedometers. The intensity of PA was categorized using various cut-points. Detailed ascertainment and measurement characteristics of objectively measured PA are illustrated in Supplementary Table D.

Most studies (19/35) assessed daily steps, with 2 studies including aerobic steps [Bailey et al., 2019; Bailey et al., 2014]. 7 studies assessed TPA, 7 studies measured the duration of LPA, 7 studies included MPA, 5 studies included VPA, and 10 studies included MVPA. 4 studies examined PA in bouts [Ayabe et al., 2013; Green et al., 2014; Koniak-Griffin et al., 2014; Strath et al., 2008]. Furthermore, 4 studies examined PA intensity [Bailey et al., 2015; Bailey et al., 2007; Tucker et al., 2003; Sugawara et al., 2006], 2 studies evaluated the frequency of PA [Ayabe et al., 2013; Pelclová et al., 2012], and 3 studies examined the adherence to PA guidelines [Pelclová et al., 2012; Vella et al., 2011; Diniz et al., 2015].

3.5 Physical health outcome assessment

Of the 35 included studies, 23/35 studies reported BMI, 20/35 examined %BF, 18/35 measured WC, 7/35 investigated FM, and 6/35 included VAT.

3.6 Risk of bias assessment and the quality of evidence

Details of the risk of bias assessment for included studies is reported in Supplementary Table B 1&2. Out of 28 observational and non-RCTs design, 19 were categorized as high quality and 9 as low quality. 14/29 studies did not control for age, which was the most important covariate that we deemed for quality assessment. Among 7 RCTs, 3 were of high quality and 4 were unclear. The lack of presenting random sequence generation was the most common reason for risk of bias.

Moreover, according to the GRADE framework, very low to moderate quality of evidence were reported, with no upgrades. Supplementary Table B.3 outlines the details of the quality of evidence by study design and the PA measures.

3.7 Qualitative synthesis of associations between PA and adiposity outcomes

Adiposity variables were reported as BMI, %BF, WC, FM, and VAT, which were objectively measured by bioelectrical impedance, underwater weighting, computed tomography (CT), BODPOD, dual-energy X-ray absorptiometry (DXA) or calculation based on objectively measured variables. A favorable association or effect was considered when increased PA resulted in improved adiposity indicators or vice versa. An unfavorable association or effect was considered when increased PA resulted in poorer adiposity indicators or vice versa.

For a total of 10 interventional studies, 8 studies investigated the effects of participating in a long-term walking program on BMI (n=7), %BF (n=7), WC (n=6), FM (n=3) and VAT (n=2). 5 studies (2 quasi-experiment and 3 random experiment) reported a significant improvement in at least one adiposity measure [Cayir et al., 2015; Moreau et al., 2001; Musto et al., 2010; Bailey et al., 2019; Hasan et al., 2018], while 3 studies (1 quasi-experiment and 2 random experiment) reported no significant changes [Hornbuckle et al., 2012; Pal et al., 2011; Swartz et al., 2003]. One random experiment examined the effects of MPA and VPA on BMI and reported a decrease in BMI only after participating VPA [Sugawara et al., 2006]. One randomized controlled trial reported that there were no significant improvements on any adiposity variables after engaging in a 24-week moderate intensity exercise protocol at a volume of 30 minutes per day for 5 days per week. [Holliday et al., 2018].

Among 25 observational studies, 11 cross-sectional studies assessed the association between daily steps and adiposity measures. There were consistent results across studies of a favorable association with %BF, FM, and VAT. Evidence pertaining the association with BMI was equivocal, with 9/10 studies reporting a favorable association and 1/10 indicating null association in college female students [Bailey et al. 2014]. The most inconsistent evidence was shown for WC, with 3/7 studies finding a beneficial association and 4/7 reported null. 7 studies evaluated the association between TPA and adiposity, with 6 (85.7%) reporting a favorable association. TPA was consistently reported to be favorably associated with VAT and to have no association with WC. While equivocal evidence was found for BMI and %BF.

3.8 Influence of PA intensity, duration, and frequency on adiposity outcomes

In observational studies (n=5), LPA had no influence on adiposity. A total of 5 observational studies focused on MPA and there were consistent findings of favorable associations with FM and VAT, and no association with WC. The equivocal result was found for %BF, with a beneficial association reported in 1/3 studies and no association found in 2/3 studies. Additionally, 2/3 studies found that MPA was favorably associated with BMI and the remaining one study reported no differences between weight-loss-maintainer and always-normal-weight women. VPA was found to be beneficially associated with all adiposity outcomes, with 1 study reporting ethnic-specified association that favorable relationships between VPA with %BF and WC were not observed among Chinese women [Sternfeld et al. 2005]. With regards to MVPA, findings were particularly inconsistent with adiposity outcomes such as VAT, %BF, BMI, and WC. Findings that the intensity of PA was significantly associated with adiposity outcomes were evidenced in experimental [Sugawara et al., 2006], longitudinal [Bailey et al., 2007] and cross-sectional studies [Tucker et al., 2003; Bailey et al. 2015].

For PA in bouts, 3 studies investigated the association between 10-min MVPA bouts with BMI or WC, with 2 studies [Green et al., 2014; Koniak-Griffin et al., 2014] reporting null association and 1 study reporting a favorable association [Strath et al., 2008]. One study reported that MVPA bouts lasting more than 1minute was beneficially associated with VAT [Ayabe et al., 2013]. Furthermore, a favorable association between PA frequency and adiposity was found in all included studies based on cross-sectional evidence [Pelclová et al., 2012; Ayabe et al., 2013].

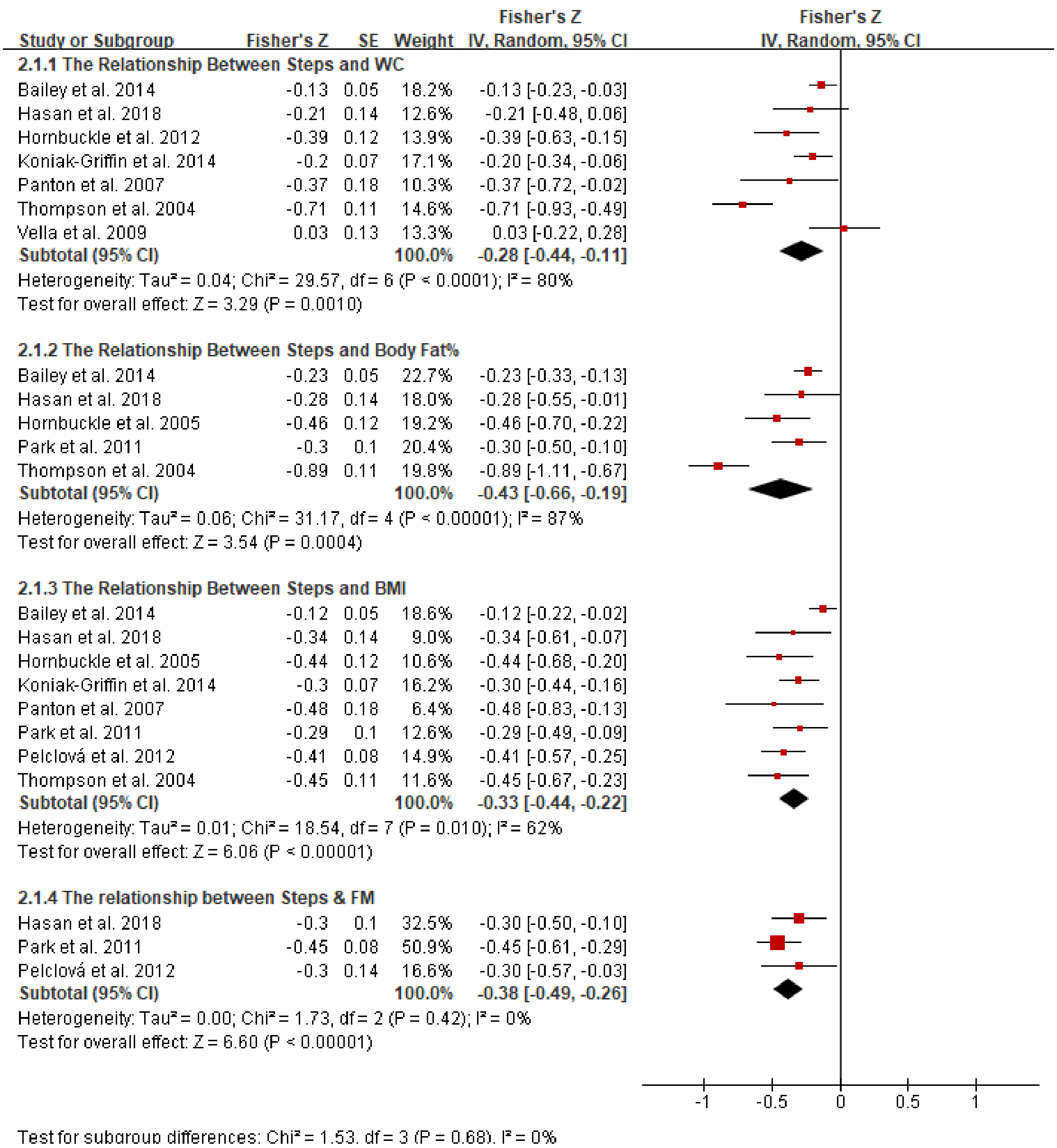
Finally, 3 studies examined the effect of PA recommendations for engaging in at least 150 minutes MVPA a week, with 1 study reporting a favorable association with %BF [Diniz et al., 2015] and the other 2 reporting no association [Vella et al., 2011; Pelclová et al., 2012].

3.9 Meta-analysis

15 observational studies and 1 intervention study [Hasan et al., 2018] were included in the correlational meta-analysis (Figure 6). The pooled analysis revealed that daily steps had moderate associations with BMI ($r = -0.32$; 95% CI: -0.44, -0.22; $p<0.001$; Figure 6.1), %BF ($r = -0.41$; 95% CI: -0.66, -0.19; $p<0.001$; Figure 2.1), and FM ($r = -0.36$; 95% CI: -0.49, -0.26; $p<0.001$; Figure 5.1). The between-study heterogeneities were moderate for BMI ($I^2 = 62\%$, $p=0.01$), high for %BF ($I^2 = 87\%$, $p<0.001$), however, no heterogeneity was shown for FM ($I^2 = 0\%$, $p=0.42$). Furthermore, there was a significant but mild association between daily steps and WC ($r = -0.27$; 95% CI: -0.44, -0.11; $p=0.001$; Figure 5.1), with a high heterogeneity ($I^2 = 80\%$, $p <0.001$). The subgroup analysis revealed that daily steps were significantly associated with BMI and WC in older, but not younger

females, with no heterogeneity for BMI (I^2 = 0%, p=0.68) and high heterogeneity for WC (I^2 = 81%, p=0.001). Furthermore, overweight/obese women showed stronger relationships between steps with BMI, %BF, and WC, with reduced heterogeneity for BMI (I^2 = 0%, p=0.78), %BF (I^2 = 85%, p=0.001) and WC (I^2 = 76%, p=0.003). Age and obesity differences were not shown in FM. The magnitude of association between steps with BMI, %BF and WC varied between race, with the strongest associations noted for African American women and weakest in Caucasian women.

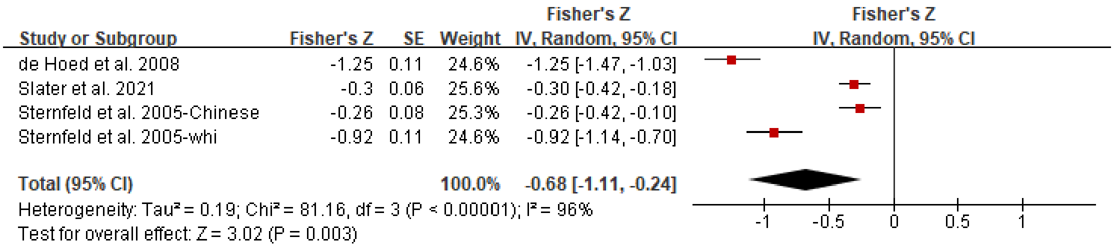
Figure 6.1: Forest plot of correlation between steps and adiposity outcomes. Overall pooled correlation for random effects model represented by black diamond



Note: BMI, body mass index; FM, fat mass; WC, waist circumference.

There was a more robust and favorable correlation between TPA and %BF (r = -0.59; 95% CI: -1.11, -0.24; p=0.003, n=4; Figure 6.2), with a high heterogeneity of 90%. Subgroup analysis demonstrated that TPA was significantly associated with %BF in Caucasian women, but not Pacific or Chinese women, with a high heterogeneity (I^2 =91%, p <0.001). The high heterogeneity between studies could be explained by subgroup analysis according to ethnicity.

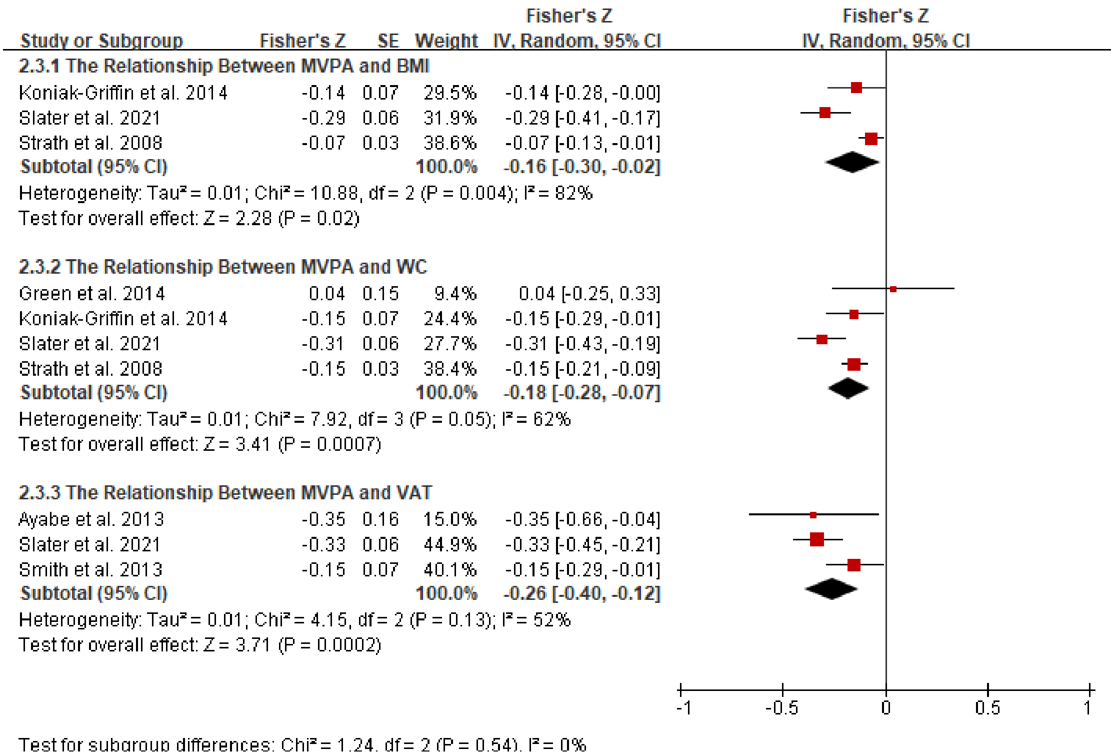
Figure 6.2: Forest plot of correlation between TPA and %BF. Overall pooled correlation for random effects model represented by black diamond



Note: TPA, total physical activity.

Correlational meta-analysis was possible for studies assessing the association between minutes in MVPA with BMI, WC, and VAT (Figure 5.3). There was a significant but weak correlation between minutes in MVPA and BMI (r = -0.16; 95% CI: -0.30, -0.02; p=0.02; Figure 5). However, the heterogeneity was shown to be high (I^2 = 82%, p=0.004). Likewise, MVPA was significantly associated with VAT (r = -0.25; 95% CI: -0.4, -0.12; p<0.001) and WC (r = -0.18; 95% CI: -0.28, -0.07; p<0.001), with moderate but not significant between-study heterogeneity for VAT (I^2 = 52%, p=0.13) and for WC (I^2=62%, p=0.05). After performing subgroup analysis, age was the potential source of heterogeneity.

Figure 6.3: Forest plot of correlation between MVPA and adiposity outcomes. Overall pooled correlation for random effects model represented by black diamond



Note: BMI, body mass index; MVPA, moderate to vigorous physical activity; VAT, visceral adiposity tissue; WC, waist circumference.

In addition, meta-analysis was possible for intervention studies investigating the effect of walking intervention on BMI, %BF, VAT and WC (Figure 7). Overall, the walking program resulting in an increase in daily steps had a significant reduction in WC (SMD = -0.35; 95% CI: -0.65, -0.05; p=0.02), with a significant and moderate heterogeneity (I^2 = 58%, p=0.02). This heterogeneity was driven by the inclusion of women with extremely large mean WC of 106.5 cm [Cayir et al., 2015]. Excluding this study resulted homogeneous (I^2 = 0%) in remaining studies. However, the pooled effect on WC was not significant. Furthermore, there was no significant pooled effect on BMI, %BF or VAT. Subgroup analysis showed that walking intervention had a significant effect on WC in middle-aged women but not in young women, with a moderate heterogeneity (I^2 = 60%, p=0.02). Subgroup analysis based on age, obesity, menstrual status, country, and ethnicity did not modify the effects of walking protocols on other adiposity indicators. None of the pooled effects was altered by the subsequent sensitivity analysis.

Figure 7: Forest plot of the effects of walking program on adiposity outcomes based on the post- and pre- intervention. Overall pooled effect for random effects model represented by black diamond

Figure 7.1: The difference between post- and pre- walking intervention on body mass index

	Post-intervation			Pre-intervation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bailey et al. 2019-10000 steps/d	23.9	2.2	34	23.5	2.7	34	9.8%	0.16 [-0.32, 0.64]
Bailey et al. 2019-12500 steps/d	23.2	2.2	34	22.7	2.1	34	9.8%	0.23 [-0.25, 0.71]
Bailey et al. 2019-15000 steps/d	23.7	2	24	23.2	2.6	24	9.0%	0.21 [-0.36, 0.78]
Cayir et al. 2015	32.1	2.7	45	35.7	2.3	45	9.9%	-1.42 [-1.89, -0.96]
Hasan et al. 2018	27.2	5.49	52	27.5	5.6	52	10.7%	-0.05 [-0.44, 0.33]
Hornbuckle et al. 2012-10000 steps/d	36.5	7.5	25	36.5	7.6	25	9.1%	0.00 [-0.55, 0.55]
Hornbuckle et al. 2012-10000 steps/d + RT 2d/w	34.7	5.8	19	34.8	5.9	19	8.3%	-0.02 [-0.65, 0.62]
Musto et al. 2010	30.2	5.3	43	30.4	5.5	43	10.3%	-0.04 [-0.46, 0.39]
Pal et al. 2011-30 minutes of walking/day	29.68	1.11	15	29.7	1.05	15	7.6%	-0.02 [-0.73, 0.70]
Pal et al. 2011-accumulate 10,000 steps/d	29.08	1.03	13	28.9	1.2	13	7.2%	0.16 [-0.61, 0.93]
Swartz et al. 2003	35.4	1.2	18	35	1.2	18	8.1%	0.33 [-0.33, 0.98]
Total (95% CI)			**322**			**322**	**100.0%**	**-0.06 [-0.37, 0.25]**

Heterogeneity: Tau² = 0.20; Chi² = 37.70, df = 10 (P < 0.0001); I² = 73%
Test for overall effect: Z = 0.37 (P = 0.71)

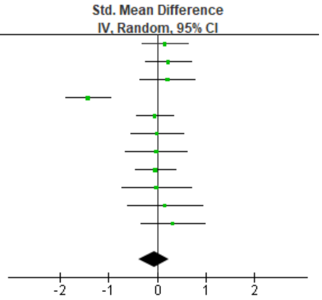


Figure 7.2: The difference between post- and pre- intervention on body fat %

	Post-intervation			Pre-intervation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bailey et al. 2019-10000 steps/d	34	4.5	34	34.1	5.3	34	10.6%	-0.02 [-0.50, 0.46]
Bailey et al. 2019-12500 steps/d	33.1	4.1	34	32.7	4.4	34	10.6%	0.09 [-0.38, 0.57]
Bailey et al. 2019-15000 steps/d	33.5	3.9	24	32.9	5.2	24	9.2%	0.13 [-0.44, 0.69]
Cayir et al. 2015	38.3	3.9	45	42.7	3.6	45	11.1%	-1.16 [-1.61, -0.71]
Hasan et al. 2018	38.7	8.23	52	39.8	7.79	52	12.3%	-0.14 [-0.52, 0.25]
Hornbuckle et al. 2012-10000 steps/d	45.6	5.9	25	45.8	5.8	25	9.3%	-0.03 [-0.59, 0.52]
Hornbuckle et al. 2012-10000 steps/d + RT 2d/w	45.3	6.2	19	45.8	6.2	19	8.1%	-0.08 [-0.72, 0.56]
Moreau et al. 2001	42	2.1	15	42.1	2.2	15	7.1%	-0.05 [-0.76, 0.67]
Pal et al. 2011-30 minutes of walking/day	38.59	2	15	39.03	1.68	15	7.1%	-0.23 [-0.95, 0.49]
Pal et al. 2011-accumulate 10,000 steps/d	38.14	1.62	13	38.34	1.86	13	6.5%	-0.11 [-0.88, 0.66]
Swartz et al. 2003	49.2	1.4	18	49.6	1.3	18	7.9%	-0.29 [-0.95, 0.37]
Total (95% CI)			**294**			**294**	**100.0%**	**-0.19 [-0.44, 0.06]**

Heterogeneity: Tau² = 0.09; Chi² = 21.90, df = 10 (P = 0.02); I² = 54%
Test for overall effect: Z = 1.46 (P = 0.14)

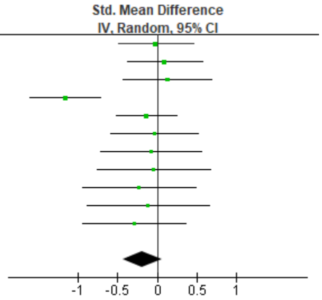


Figure 7.3: The difference between post- and pre- intervention on waist circumference

	Post-intervation			Pre-intervation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cayir et al. 2015	98.3	7.7	45	106.5	7.3	45	15.0%	-1.08 [-1.53, -0.64]
Hasan et al. 2018	79.55	12.43	52	80.9	13.68	52	16.4%	-0.10 [-0.49, 0.28]
Hornbuckle et al. 2012-10000 steps/d	99.3	11.8	25	99.3	12.1	25	12.7%	0.00 [-0.55, 0.55]
Hornbuckle et al. 2012-10000 steps/d + RT 2d/w	92.9	12	19	94.8	12.3	19	11.2%	-0.15 [-0.79, 0.48]
Musto et al. 2010	86.1	10.9	43	86.7	11.3	43	15.5%	-0.05 [-0.48, 0.37]
Pal et al. 2011-30 minutes of walking/day	95.38	2.36	15	96.48	2.07	15	9.7%	-0.48 [-1.21, 0.25]
Pal et al. 2011-accumulate 10,000 steps/d	93.45	3.32	13	94.46	2.34	13	9.0%	-0.34 [-1.12, 0.43]
Swartz et al. 2003	1.01	0.03	18	1.03	0.03	18	10.5%	-0.65 [-1.32, 0.02]
Total (95% CI)			**230**			**230**	**100.0%**	**-0.35 [-0.65, -0.05]**

Heterogeneity: Tau² = 0.10; Chi² = 16.76, df = 7 (P = 0.02); I² = 58%
Test for overall effect: Z = 2.30 (P = 0.02)

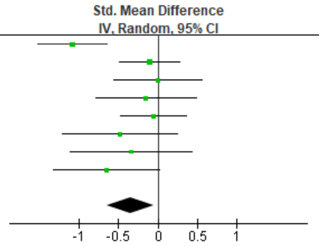
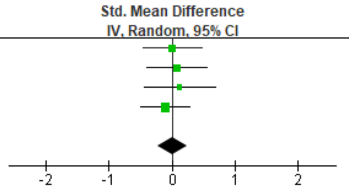


Figure 7.4: The difference between post- and pre- intervention on visceral adiposity tissue

	Post-intervation			Pre-intervation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bailey et al. 2019-10000 steps/d	163.3	158.1	34	162.2	148.4	34	23.6%	0.01 [-0.47, 0.48]
Bailey et al. 2019-12500 steps/d	135.7	136.1	34	125.4	100.2	34	23.6%	0.09 [-0.39, 0.56]
Bailey et al. 2019-15000 steps/d	177.8	115.2	24	163.2	119	24	16.7%	0.12 [-0.44, 0.69]
Hasan et al. 2018	94.94	29.3	52	98.15	32.3	52	36.1%	-0.10 [-0.49, 0.28]
Total (95% CI)			**144**			**144**	**100.0%**	**0.00 [-0.23, 0.24]**

Heterogeneity: Tau² = 0.00; Chi² = 0.58, df = 3 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)



4. Discussion

This systematic review and meta-analysis synthesized studies that investigated the association between objectively measured PA and adiposity in adult women. This was the first study to qualitatively and quantitively synthesize the evidence from both observational and interventional studies.

4.1 Association between steps and adiposity outcomes

Meta-analytical evidence (n=15 cross-sectional, n=1 interventional) indicated the favorable association between daily steps and adiposity outcomes such as BMI, %BF, FM, and WC. It is worth noting that, meta-analysis of intervention studies suggested that walking programs were effective in reducing the majority of adiposity indicators including BMI, %BF, and VAT in adult women, but the improvements were not statistically significant. However, a systematic review synthesized the effects of walking on adiposity from RCTs and reported improved outcomes for %BF, WC, and BMI [Murtagh et al., 2015]. Likewise, Gao et al. (2016) pooled effects of walking on body composition from 8 RCTs and reported significantly lower BMI, %BF and WC after intervention.

The insignificant effects of walking interventions shown in our meta-analytical findings might be explained by age. According to our subgroup analysis based on the age range, there was difference regarding the effect of walking program on WC. The effect on WC was significant in middle-aged women but not in young women. Likewise, the association between steps with BMI and WC was only significant in middle-aged women. However, this result must be interpreted with caution because the small number of studies represented the young subgroup. Despite this limitation, other studies offered some support that age was associated with the effects of walking program. A systematic review assessed the association of pedometer use with PA and health. The authors reported that the use of pedometers had benefits on increasing steps and participants with older age significantly reduced BMI from baseline [Bravata et al., 2007]. Moreover, the positive pooled effect of walking intervention on adiposity was based on mostly middle-aged women in the study by Murtagh et al. (2015) and was concluded by both perimenopausal and postmenopausal women in the study by Gao et al. (2016). It seems that the number of steps required to improve adiposity was not the same for young and middle-aged women. Accumulating 10,000 steps per day was recommended for middle-aged women [Thompson et al., 2004], while 12,000 daily steps was associated with a healthy BMI in young women [Tudor-Lock et al., 2008]. The decrease in recommended daily steps was probably due to the decline in energy intake with age.

However, evidence from our intervention study demonstrated that a step recommendation of 12,000 was not effective in weight control among young women. In a study of female university students, there was no significant difference in weight or fat gain among three groups with recommendations of 10,000, 12,500, and 15,000 steps per day respectively [Bailey et al., 2019]. This was supported by another intervention study. In an 8-week walking program with a target of 12,000 steps per day conducted in young adult, no improvement in BMI was observed at post-measurement [Chiang et al., 2019]. Likewise, 10,000 steps per day was ineffective on the reduction of BMI or %BF for middle-aged women [Pal et al., 2011; Swartz et al., 2003; Moreau et al. 2001; Hornbuckle et al. 2012]. One of the potential explanations was the walking intensity. The walking program with pedometer was not able to assess the intensity of walking and therefore, slow walking and brisk walking were counted the same by pedometer during the intervention. The increased daily steps seemed to be accumulated from light intensity walking, which was not sufficient to induce a deficit energy balance resulting in weight loss [Bailey et al., 2019]. Therefore, in addition to the age-specified recommendation for daily steps, walking intensity also needs consideration when prescribing PA in terms of walking.

4.2 Association between TPA and Adiposity

The meta-analytical result suggested that the total volume of PA was significantly associated with %BF with a moderate effect size. It was consistent with findings from cross-sectional studies [de Hoed et al., 2008; Slater et al., 2021; Tucker et al., 2003]. Likewise, a favorable association between TPA and abdominal fat was reported in a cross-sectional study [Diniz et al., 2015]. This was supported by a cohort study with a 20-month follow-up, in which authors reported a reduced risk of increasing abdominal fat among women who increased TPA [Davidson et al., 2010]. Additionally, Smith et al. (2013) investigated the relationship between accelerometer-derived PA and regional adiposity and found that the amount of TPA was inversely associated with VAT in women.

TPA was defined by the total accelerometer counts in the studies included and it appeared to play an important role in the association with adiposity. de Hoed et al. (2008) reported an additional significant 4% for TPA to explain the variation in %BF when the model was already controlled for age, BMI, and gender. In a cross-sectional study conducted by Tucker et al. (2003), the duration and intensity of PA were both associated with %BF. However, the association was weakened when controlling for TPA. Likewise, another cross-sectional study found that the relationship between higher intensity PA and %BF was negated when adjusting for TPA [Bailey et al., 2015]. This could be attributed to the fact that TPA was a cumulative measure insusceptible to the unstandardized cut-points and were able to capture all movements above zero [Van Dyck., 2015]. Therefore, TPA provided a lower level of error when investigating the association with adiposity outcomes.

Furthermore, we observed that the association between TPA and adiposity measures was influenced by ethnicity. Findings from subgroup analysis indicated that Caucasian women were more likely to improve their %BF by increasing TPA. In was consistent with other cross-sectional results. In the study by Slater et al. (2021), TPA was favorable associated with %BF in Caucasian women, however, such associations were not significant in Pacific women. Similarly, Sternfeld et al. (2005) reported that TPA was inversely related to %BF and WC only in White subjects, but not in Chinese populations. Results from Ayabe et al. (2013) supported this ethnicity-related difference, at least in part, that TPA was not associated with VAT in Japanese women. The insignificant association observed might be due to the low level of TPA. Although few research investigating ethnicity-specified relationship between TPA and adiposity, numerous previous studies supported our results of Caucasian women, reporting favorable associations between TPA and adiposity outcomes [Wolff-Hughes et al., 2015; Guo et al., 2015; Wanner et al., 2017]. Further research is required to explore the impact of ethnicity on the relationship between TPA and adiposity.

4.3 Association between PA intensities and adiposity

There was consistent evidence that the increased intensity of PA had favorable effects on adiposity outcomes. In an RCTs conducted by Sugawara et al. (2006), vigorous intensity aerobic exercises were evidenced to be more effective than moderate intensity exercises on lowering BMI in postmenopausal women. Evidence from the longitudinal study also corroborated the findings. Bailey et al. (2007) performed a prospective study to investigate the extent to which intensity of PA was associated with changes in %BF. The author also reported a cross-sectional finding that women in a VPA group had lower BF% than those in groups participating in MPA and LPA. Furthermore, women who increased the intensity of PA at follow-ups had reduced risk of fat gains over time. Cross-sectional evidence also supported that %BF was strongly and negatively correlated with the intensity of PA [Tucker et al., 2003; Bailey et al., 2015].

The meta-analysis showed a significant association between MVPA with BMI, WC, and VAT, with a slightly potent association to be shown with fat indicators such as VAT and WC. Hamer et al. (2013) provided longitudinal evidence on the more significant association with WC than with BMI. Furthermore, cross-sectional findings from the present review demonstrated that MVPA had inconsistent effects on BMI and %BF. Women participated in more MVPA did not have a significantly lower BMI but had a more favorable %BF [Diniz et al., 2015; Koniak-Griffin et al., 2014]. This was supported by experimental evidence that participating in moderate intensity exercises was able to reduce VAT without weight loss [Lee et al., 2005; van der Heijden et al., 2010]. Although BMI was generally used to measure overall adiposity, it provided limited information about the variability of body fat, which appeared to be more important in predicting health, especially reginal fat such as WC and VAT. Despite equivocal evidence for BMI, the favorable effect of MVPA on VAT and WC offered some support for the conclusion that MVPA benefits adiposity.

However, cross-sectional evidence from the present review consistently suggested that there was no relationship between LPA and adiposity [Bailey et al., 2015; Green et al., 2014; Smith et al., 2013]. This was supported by a previous review, in which little evidence was reported for the role of LPA to improve body composition [Batacan et al., 2015]. Longitudinal evidence from a study examined the association between PA with BMI and WC over 10 years demonstrated that LPA was not associated with changes in BMI or WC [Hamer et al., 2013]. Although there was emerging evidence that LPA had benefits for health [Migueles et al., 2021; Ballin et al., 2021], these findings were based on elderly. Our results did not find any relationship between LPA and adiposity outcomes in young women, and the possible health promotion mechanism of LPA need further investigation.

Compared to LPA, VPA had been more consistently shown to be beneficial for all adiposity indicators measured in this review [Ayabe et al., 2013; Sternfeld et al., 2005; Park et al., 2011]. This finding again supported the notion that PA intensity was favorably associated with adiposity. Additionally, VPA played a critical role in maintaining weight and preventing weight regain [Phelan et al., 2007]. This relationship was corroborated in a cohort study that examined PA and 4-year changes in body mass in 52,498 non-obese people. The study reported that only VPA was effective for weight control among young adults [Byambasukh et al., 2021], suggesting again that MVPA was not associated with better WC amongst young women. Further research is needed to investigate whether age influenced the relationship between PA intensity and obesity.

4.4 Association between PA duration and adiposity

The evidence from qualitative synthesis in the current review regarding to the association between PA in bout and adiposity was inconsistent. A cross-sectional study examined MVPA accumulated in bouts and non-bouts and reported that MVPA in bouts was significantly associated with the reduction of BMI and WC, while such association was not significant in MVPA non-bout [Strath et al., 2008]. It was supported by a cohort study conducted by White et al. (2015), in which the incidence of adiposity was significantly associated with MVPA in 10-minute bouts rather than short bouts of MVPA lasting less than 10 minutes. However, two cross-sectional studies reported opposite findings that the MVPA bouts lasting at least 10 minutes was not associated with better BMI or WC [Koniak-Griffin et al. 2014; Green et al., 2004]. Nonetheless, the favorable association between PA in bouts and adiposity was well documented by previous studies [Pate et al., 1995; Shiroma et al., 2019]. The absence of the positive effect of bouts PA might be partially because women often engaged in short bouts of PA, which was normally less than 10 minutes [Green et al., 2004]. This was supported by a previous study, in which nearly two-thirds of MVPA were accumulated by bouts lasting less than 10 minutes [Cameron et al., 2017]. Moreover, the authors indicated that PA in non-bouts was more strongly associated with adiposity than long-sustained PA.

Recent studies tended to offer some support to the notion that every MVPA minute counts. Jefferis et al. (2016) found that there was no difference between MVPA lasting less than 10 minutes and at least 10 minutes. Similar findings were also reported by Loprinzi and Cardinal (2013). However, the effect of non-bouts MVPA was not found in our review. This could be explained by the inclusion of lower intensity of PA, which resulted an attenuation of overall effect for non-bouts MVPA. In Strath et al. (2008)'s study, the cut-point used for identifying MVPA was 760 counts per minute (cpm), which was much lower than the most recent recommendation of 2020 cpm by Troiano et al. [2008] and 1952 cpm by Freedson et al. [1998]. However, for very short bouts of PA lasting less than 1 min, no significant association was reported with abdominal fat distribution [Ayabe et al., 2013].

Collectively, the association between bouts PA and adiposity outcomes was unclear as the sample women in our review engaged in too little bouts of PA. Although the total amount of MVPA was associated with most adiposity indicators, further research is required to determine whether MVPA accumulated by bouts or non-bouts differed in its effect on adiposity.

5. Implications for practice

The current review suggests that higher daily steps is associated with improvement in indicators of adiposity. Therefore, interventions that target the increase PA may improve adiposity. Meanwhile, if the PA promotion intervention was delivered by walking protocols, walking intensity should be emphasized. In order to improve adiposity, moderate to vigorous intensity was required, while vigorous intensity was preferred.

Additionally, the effect of PA on adiposity indicators was not consistent. BMI appeared to be an unreliable marker to exam the effect of PA on obesity, therefore, adiposity indicators such as %BF, FM and VAT should be considered.

6. Strengths, limitations, and future directions

Strengths of the current study include the use of different types of study designs, the inclusion of objectively determined PA, as well as the wide range of adiposity indicators. This review was the first to analyze the evidence qualitatively and quantitatively from all kinds of study designs, and to explore the association between different PA patterns and the comprehensive adiposity indicators in adult women.

It was important to note that there were some limitations. First, the majority evidence synthesized were of very low to low quality. This was mainly due to the non-randomized study design and the concern with inconsistency in the results across different indicators. Although we compared low-quality evidence to those with high-quality in the discussion, additional research with high quality is required to increase the confidence of findings.

Secondly, most studies included were cross-sectional designs, and most of them assessed associations without controlling for potential confounders such as age and dietary intake. Therefore, the causality and dose-response relationships could not be ascertained. Furthermore, the absence of these confounders weakened the association between PA and adiposity, and our results should be interpreted with caution.

Thirdly, the heterogeneity in the different definition of PA categories, including different cut-points of counts, METs, and vertical acceleration peaks, was a potential source of inconsistent findings and led to indirect comparation of PA intensity. Furthermore, the use of different epochs might contribute to overestimations or underestimates in the amount of PA at a particular intensity. For instance, studies using the longer epochs (e.g., 10min) were more likely to underestimate the higher intensity PA than those using 60s epochs. Finally, accelerometer-determined PA was unable to quantify fitness activities such as resistance training, yoga, and Tai chi, as well as unable to precisely calculate the energy expenditure of PA. To deal with these limitations, standardized cut-points, shorter epochs, and pattern recognition should be applied.

In addition, findings from subgroup analyses were limited and should be considered preliminary due to the small number of studies included in each category of subgroup.

7. Conclusion

Findings from the present systematic review and meta-analysis provide substantial evidence that objectively derived PA in terms of daily steps, TPA and MVPA is favorably association with most adiposity indicators. TPA has a more potent effect on adiposity, however, this association was influenced by ethnicity. There is no association between LPA and adiposity measures and adiposity is more likely to be benefited from PA performed at higher intensity. These findings must be interpreted with caution since most of the evidence is rated as low, and findings are predominantly derived from cross-sectional analysis. Further high-quality intervention studies are still needed to confidently inform PA recommendations on the volume, intensity, and duration.

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Chapter 5: Associations between Objectively Determined Physical Activity and Cardiometabolic Health in Adult Women: A Systematic review and Meta-analysis (Study 1 Part 2)

1. Introduction

The rising prevalence of physical inactivity is one of the greatest public health concerns. Physical inactivity has been epidemiologically evidenced to be associated with cardiovascular diseases (CVD), which remains the leading cause of mortality [Katzmarzyk, 2010; Ekelund et al., 2019]. Since physical inactivity is among the major modifiable risk factors for CVD, there is a growing need for the promotion of physical activity (PA). The latest PA guidelines recommend at least 150-300 min of moderate intensity physical activity (MPA) or 75-150 min of vigorous intensity physical activity (VPA) a week for adults to maintain cardiometabolic health [Bull et al., 2020; Piercy et al., 2018]. Substantial observational evidence suggests that higher level of PA is associated with a lower risk of CVD [Piercy et al., 2018; Hajna et al., 2018; Dipietro et al., 2020; Huang et al., 2021]. Intervention studies also report favorable changes in cardiometabolic risk factors after exercise interventions [Amaro-Gahete et al., 2019; Jung et al., 2020; Goodpaster et al., 2010].

However, most of the evidence comes from moderate to vigorous intensity physical activity (MVPA). Moreover, the global and national guidelines on PA specify recommended volumes for MPA, VPA and MVPA, with little consideration for other patterns of PA, such as light intensity physical activity (LPA), total physical activity (TPA) and the amount of daily steps. Emerging evidence indicates a dose-response relationship between total physical activity (TPA) and the incidence of CVD [Arem et al., 2015; Kubota et al., 2017; Verswijveren et al., 2021]. Furthermore, a recent meta-analysis reported the beneficial effect of LPA on cardiometabolic health [Chastin et al., 2019]. Despite the health benefits of PA, 27.5% of adults fail to follow the lowest level of recommended PA and women are more physically inactive, with 30.7% inactivity in women compared to 23.4% inactivity in men [Guthold et al., 2018]. Although the recommended PA is the same for both genders, women have specific anatomical, hormonal, and cardiovascular features, suggesting gender differences in the risk factors and management of CVD. For example, women have smaller size of vessel than men and suffer the higher age-related risk of hypertension, especially among postmenopausal with decreased estrogen [Saeed et al., 2017]. Furthermore, physical inactivity in women is more likely to be diagnosed with obesity [Vainshelboim et al., 2019; Cooper et al., 2021]. Therefore, there is a need to explore the association between PA and cardiometabolic health in women.

Furthermore, previous studies and PA guidelines mostly relied on the PA questionnaire, which is less accurate in women [Ferrari et al., 2007] and is difficult to provide precise measures of LPA [Skender et al., 2016]. Although objective measures of PA have been used widely, there is a paucity of evidence on the associations between objectively determined PA and clinically relevant cardiometabolic biomarkers in healthy adult women. Therefore, the purpose of this systematic review and meta-analysis is to qualitatively synthesize and quantitatively assess the association between objectively determined PA and cardiometabolic health among adult women.

2. Methods

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [Page et al., 2021].

2.1. Inclusion criteria and study selection

The Participants, Interventions, Comparisons, and Outcomes (PICO) [Schardt et al., 2007] format-ted research question was used to clarify the inclusion criteria.

Participants

Apparently healthy women with a mean age of 18-64 years. Women with the presence of cardiovascular disease risk factors (e.g., overweight/obesity, hypertension, elevated fasting glucose, and dyslipidemia) were included. Exclusion criteria included: 1) diagnosed CVD, diabetes, physical or psychological disorders, or other conditions that were barriers to physical activities; 2) pregnant, postpartum, or lactating women; 3) elite athletes.

Interventions

Accelerometer and pedometer assessed PA volume was identified as interventions, including steps, counts, the amounts of LPA, MPA, VPA, MVPA, PA bouts, and TPA. Energy expenditure was not included because the accelerometer derived data showed poor accuracy in estimating energy expenditure [Kossi et al., 2021].

Comparisons

Various steps and volumes of objectively measured physical activities were identified as comparisons.

Outcomes

According to the literature review, both traditional cardiometabolic risk factors and novel CVD biomarkers were included. These indicators were classified into six categories: 1) blood pressure (BP) 2) lipid profile; 3) carbohydrate metabolism; 4) endocrine regulators; 5) inflammation marker; 6) metabolic syndrome (MetS).

2.2 Study design

Both observational (cross-sectional and longitudinal) and experimental (randomized and non-randomized) studies investigating the relationship between accelerometer or pedometer measured PA and cardiometabolic health biomarkers were included.

2.3 Other criteria

Only original articles published in English and in a peer-reviewed journal were included. Reviews, abstracts, conference proceedings, short reports were all excluded. Furthermore, studies focusing on cardiac rehabilitation and secondary CVD prevention programs were excluded. Studies included participants of both genders and were eligible for inclusion only when separate data for women were available. When more than one article was from the same study, the following hierarchy was applied for inclusion: 1) the largest sample size, 2) the longest following period, and 3) the most de-tailed data.

2.4 Literature search

Four electronic databases including PubMed, Web of Science, Scopus, and the Cochrane Library were searched from 1 January 1990 to 31 January 2022 in accordance with the search strategy developed by two researchers with expertise in systematic reviews. Firstly, keywords such as “accelerometer”, “pedometer”, “objectively”, “physical activity”, and terms of CVD biomarkers were applied to titles and abstracts. Since there was no standardized keyword to fully capture the studies including women-specified associations. Secondly, we conducted a manual search to screen the full text for eligible studies. Thirdly, the reference list from included studies was manually screened to ensure completeness of records. Finally, search results were all imported in Endnote (Endnote 20, Wintertree Software Inc., China). The detailed search strategy is provided in Supplementary Table E.

2.5 Data extraction

For each included study, descriptive data, intervention, and correlational find-ings were extracted independently by two reviewers (Yining Lu and Qiaojun Wang) and inputted into Excel (Microsoft Corp.). Any disagreements were resolved through discussion and all results were checked by a third reviewer (Shanshan Ying). The relationship between PA and cardiometabolic health outcomes was included if it was measured by t-test/Mann-Whitney U-test (U-test)/Kolmogorov-Smirnov test (K-S test), analysis of variance (ANOVA), correlation, regression, and the relative risks.

2.6 Risk of bias and quality assessment

The Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias in nonrandomized studies (nonrandomized interventions and observational studies) [Wells et al., 2022]. For the comparability domain, we considered age to be the most important confounder. The maximum number of stars was seven for the cross-sectional design and nine for the longitudinal design. High quality was defined as 4 or more stars in cross-sectional designs, and 5 or more in longitudinal designs. Those below the cut-off point were de-fined as low quality [Ramsey et al., 2022]. The Cochrane collaboration tool was used to assess the risk of bias for random experiments [Higgins et al., 2011].

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was used to evaluate the quality of evidence for each category of biomarkers [Guyatt et al., 2011].

Each included study was rated independently by two reviewers (Yining Lu and Shanshan Ying). Any discrepancy in rating was resolved by discussion and the results were checked by a third reviewer. Details of the risk of bias and quality assessment are presented in Supplementary Table F.

2.7 Statistical Analysis

Comparable PA exposures included steps, minutes in LPA, MPA, VPA, MVPA and PA bouts, TPA, meeting/not meeting the guideline. Although different cut-off points and definitions were used, LPA, MPA, VPA, MVPA and TPA were defined as reported in the studies [Ramakrishnan et al., 2021]. If studies measured physical activity in metabolic equivalent tasks (METs), we used the cut-points proposed Ainsworth et al. (2011) (e.g.,1.6–2.9 METs was defined as LPA, 3-5.9 METs as MPA, and ≥6 METs as VPA) [Ainsworth et al., 2011]. When more than one statistical analysis was used, the following hierarchy was applied: 1) regression, 2) correlation, 3) ANOVA, 4) t-test/U-test/K-S test [Ramsey et al., 2022]. When more than one adjusted model was used, the most adjusted models were applied [Aune et al., 2015].

Meta-analysis was planned if more than two studies were eligible for comparable PA measures and biomarkers. Fisher's z transformation and Hedge's g was used for correlational and standardized mean differences meta-analysis respectively [Peterson and Brown, 2005]. The effect size was classified as low (r=0.1/SMD=0.2), moderate (r=0.3/SMD=0.5), or high (r=0.50/SMD=0.8) according to Cohen's recommendations [Cohen, 1988].

The random-effects model was used because of the diversity of the methodologies. To evaluate the impact of heterogeneity on the meta-analysis,

inconsistency was measured using the Higgins' I^2 statistic. Specifically, $I^2 = 0$ indicated no heterogeneity and the low, moderate, and high heterogeneity was identified when $I^2 < 25\%$, 25-75%, and > 75% respectively [Higgins et al., 2003]. Publication bias were assessed through Egger's test and funnel plots using at least ten studies [Egger et al., 1997]. Subgroup analyses were conducted to ex-amine the potential sources of heterogeneity from age [young (18-39 years old) / middle-age (40-64 years old) / both] [Murray et al., 2021], BMI (BMI<25/BMI≥25), menopausal status (postmenopausal/ premenopausal/both), country, and ethnicity. All Statistical analyses were performed with Review Manager, version 5.4.1 (The Cochrane Collaboration, 2020).

3. Results

3.1 Study selection and characteristics

A total of 5112 records were yielded from the database and manual search. After screening 126 full texts, 23 eligible studies were finally included in the precent review. The most common reason for exclusion was unavailability of female-specific data. Figure 8 presents the PRISMA system outlining the study process. The characteristics of the included observational and intervention studies are detailed in Table 9 and Table 10 respectively. Publication dates ranged from 2001 to 2021. Out of 23 studies, 14 studies were cross-sectional designs and 9 were interventional studies (5 random experiments and 4 non-random experiments). Intervention length ranged from 1 week to 24 months.

3.2 Sample characteristics

The total sample size was 2105, ranging from 10 to 535 participants. The mean age ranged from 21.4 to 62.8 years, with 8 studies focused on the young and 10 studies focused on the middle-aged. There were 11 studies reported menstrual status, with 4 including post menstruation, 5 including pre-menstruation, and 2 including both. Moreover, there were 11 studies focused on over-weight/obese females, 10 studies included physically inactive participants, 12 studies reported smoking status, with 5 included non-smokers, 4 reported participants refrained from tobacco in the last 6 months, and 3 studies included mostly non-smokers (60-83%). Education level were reported in 4 studies, and social-economic levels were presented as low-income in 4 studies.

Included studies were conducted in 8 countries. There were 3 studies included a sample from Asia (i.e., Japan and UAE), 2 from Europe (i.e., Italy and Poland), 13 studies from North America (i.e., USA), 3 studies from South America (i.e., Brazil), and 2 studies from Oceania (i.e., New Zealand and Australia). The race reported in the studies included Caucasian, Asian, Latina, African American, Hispanic, Pacific, Mexican American, Euro-pean. See Table 11 for details of sample characteristics.

3.3 Physical activity assessment

Accelerometers were used in 12 (85.7%) observational studies and 2 (22.2%) experimental studies. 2 (14.3%) observational studies and 7 (77.8%) experimental studies used pedometers.

From 14 observational studies, objectively assessed PA included minutes in LPA, MPA, VPA, MVPA and PA bouts, steps, TPA, and met or did not meet the PA guideline. Steps were assessed in 7 (77.8%) interventional studies. The intensity of PA was categorized using various cut-points, including accelerometer counts and metabolic equivalents (METs). Detailed ascertainment and measurement characteristics of objectively measured PA are illustrated in Supplementary Table H.

Figure 8: The PRISMA system for study process

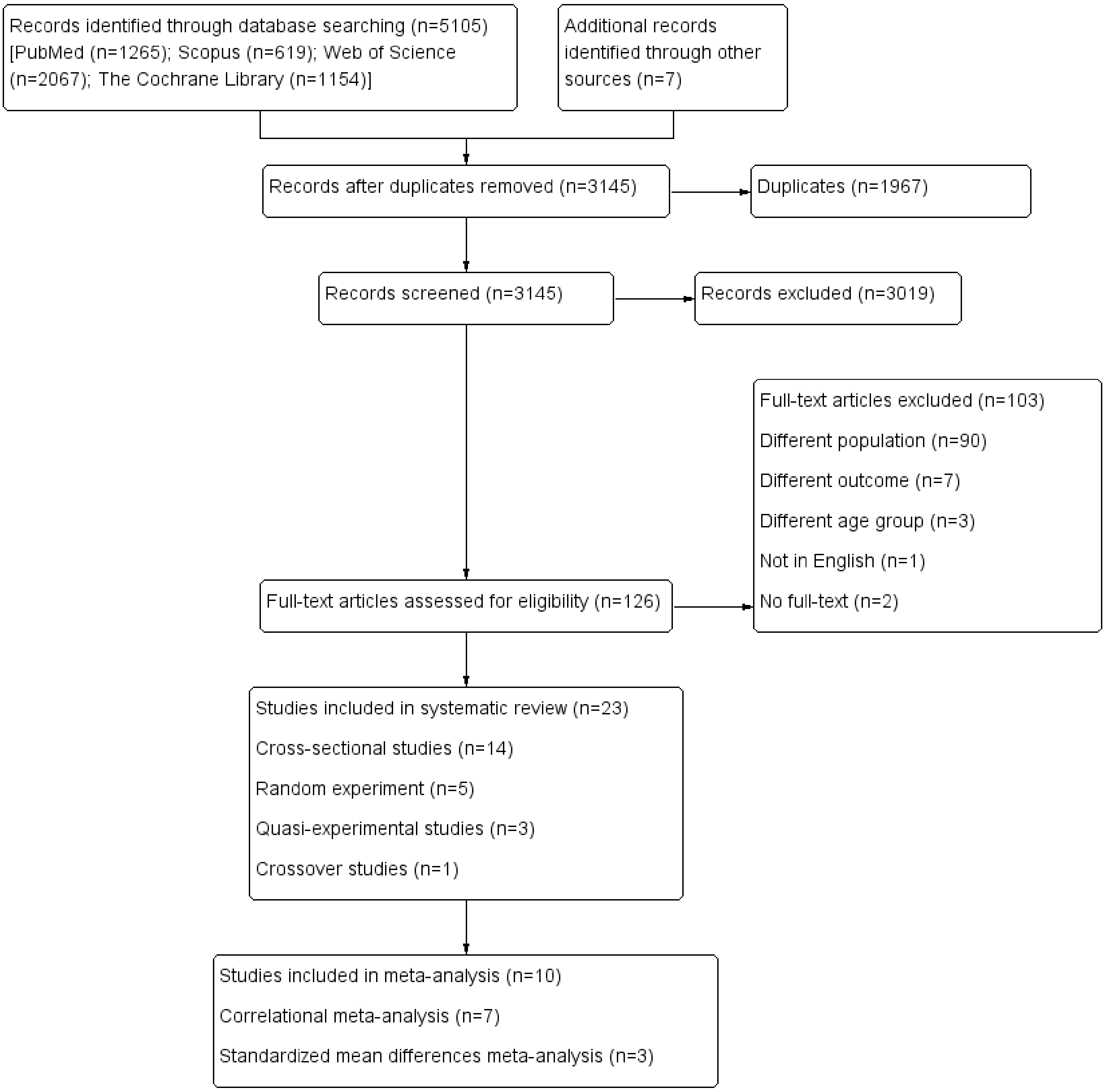


Table 9: Characteristics of observational studies

Reference	Study design	Sample size	PA measure	Health outcome	Association
Camhi et al., 2015	cross-sectional	46	ACC: ActiGraph GT3X+; triaxial Volume (min/d): LPA, MPA, VPA, MVPA, MVPA bout (10min); TPA (counts/d); Steps (n/d).	MS	t-test: 1) MHO group had significantly higher levels of LPA compared to MUO; 2) No differences of MPA, VPA, MVPA, MVPA bouts, TPA, and steps between MHO and MUO groups.
Diniz et al., 2015	cross-sectional	49	ACC: ActiGraph GT3x; triaxial meeting/not meeting MVPA (150min/w)	TNF-alpha, Fasting insulin, HOMA-IR	U-test: 1) Meeting MVPA volume had no effect on TNF-alpha, fasting insulin, and HOMA-IR;
Graff et al., 2012	cross-sectional	68	PED: BP 148 Steps (n/d)	TC, LDL, HDL, TG, FPG, PPG, Fasting insulin, Postprandial insulin, HOMA-IR	t-test and U-test: 1) no differences in TC, LDL, HDL, TG, FPG, PPG between Group (Steps/d < 6000) and Group (Steps/d ≥ 6000); 2) Group (Steps/d < 6000) had higher fasting insulin, postprandial insulin and HOMA-IR than Group (Steps/d ≥ 6000).
Green et al., 2014	cross-sectional	50	ACC: ActiGraph GT3X+; triaxial Volume (min/d) of LPA, MVPA, MVPA bout (10min)	FPG, SBP, DBP, TG, TC, HDL, LDL, HOMA-IR, Fasting insulin, CRP, IL-6, TNF-alpha	Regression: 1) MVPA had no association with TG (adjusted for SB, VO_{2peak}, BM) 2) LPA was favorably associated with TG, had no association with HOMA-IR (adjusted for MVPA, VO_{2peak}, BM). Correlation: 1) LPA was favorably associated with TG, TC, HOMR-IR; had no association with FPG, SBP, DBP, HDL, LDL, fasting insulin, CRP, IL-6, TNF-alpha; 2) MVPA was favorably associated with CRP, TNF-alpha; had no association with FPG, SBP, DBP, TG, TC, HDL, LDL, HOMR-IR, fasting insulin, IL-6; 3) MVPA bouts was favorably associated with HOMA-IR, fasting insulin, CRP; had no association with FPG, SBP, DBP, TG, TC, HDL, LDL, IL-6, TNF-alpha.
Koniak-Griffin et al., 2014	cross-sectional	210	ACC: Kenz Lifecorder Plus; uniaxial Volume (min/d) of MVPA, MVPA bout (10min) Steps (n/d)	SBP, DBP, LDL, HDL, TC, TG, FPG	Correlation: 1) Steps/d was favorably associated with TG; had no association with SBP, DBP, LDL, HDL, TC, FPG; 2) MVPA was favorably associated with HDL; unfavorably associated with TC; had no association with SBP, DBP, LDL, TG,

					FPG; 3) MVPA bouts had no association with SBP, DBP, LDL, HDL, TC, TG, FPG.
Lecheminant and Tucker, 2011	cross-sectional	264	ACC: Actigraph; uniaxial Volume (min/w) of MPA, VPA meeting/ not meeting MPA (150min/w)	HOMA-IR	ANCOVA: age, weight, BMI, %BF, and ACi 1) Meeting MPA guideline had favorable effect on HOMA-IR when adjusted for age or BM; 2) Meeting MPA guideline had no effect on HOMA-IR when adjusted for %BF, BMI, or ACi; 3) Taking VPA≥60min/w had favorable effect on HOMA-IR when adjusted for age, BM or BMI; 4) Taking VPA≥60min/w had no effect on HOMA-IR when adjusted for %BF or ACi;
Loprinzi and Cardinal 2012 [42]	cross-sectional	535	ACC: n/r Volume (min/d) of MVPA	MS	Regression: adjusted for age, race and smoking 1) MVPA was favorably associated with the odds of being MS;
Macena et al., 2021	cross-sectional	58	ACC: ActivPAL; triaxial Sitting/lying down (1.25METs), Standing (1.4METs), Walking 120 steps/min (4METs) (h/d) Steps/d	HOMA-IR	ANOVA: 1) Sitting/lying down, standing, walking, and steps/d had no association with HOMA-IR;
Panton et al., 2007	cross-sectional	35	PED: Yamax Digi-Walker SW-200, sealed Steps (n/d)	SBP, DBP; HbA1c, TC, HDL, LDL, TG, CRP	ANOVA: 1) Group (Steps/d<5000) had lower TC, LDL compared to Group (Steps/d≥5000); 2) No differences in SBP, DBP, HbA1c, HDL, TG, CRP between Groups.
Slater et al., 2021	cross-sectional	275	ACC: ActiGraph w-GT3X, Acti-Watch; triaxial Volume (min/d) of MVPA TPA (cpm/d)	HbA1c, FPG, HOMA-IR, TC, TG, HDL, LDL, SBP, DBP, Fasting insulin, CRP	Regression: adjusted for age, socioeconomic, %BF 1) In Group (Pacific), TPA was positivelyunfavorably associated with SBP; 2) In Group (European), TPA was unfavorably associated with HbA1c and CRP; 3) In Group (Pacific), MVPA was unfavorably associated with fasting insulin; 4) In Group (European), MVPA was favorably associated with HDL and HOMA-IR, unfavorably associated with fasting insulin and CRP;

					5) In all, TPA was unfavorably associated with CRP and fasting insulin; MVPA was favorably associated with HOMA-IR and HDL, unfavorably associated with CRP and fasting insulin.
Tabozzi et al., 2020	cross-sectional	13	ACC: ActiGraph GT3X + BT; triaxial %Volume: LPA, MPA, VPA Volume (min/d) of MVPA Steps (n/d)	FPG, PPG	Regression: adjusted for age, SB 1) MVPA was favorably associated with peak PPG; Correlation: 1) %LPA, %MPA, %VPA, MVPA, Steps had no association with FPG; 2)%MPA, %VPA, MVPA were negatively associated with PPG; 3)%LPA and Steps had no association with PPG;
Vella et al., 2011	cross-sectional	60	ACC: Actigraph GT1M; uniaxial meeting/not meeting MVPA (30min/d)	FPG, Fasting insulin, HOMA-IR, TC, HDL, LDL, TG, CRP, SBP, DBP	t-test: 1) meeting MVPA guideline had favorable effects on TC and TG;
Vella et al., 2009	cross-sectional	60	ACC: Actigraph GT1M; uniaxial Steps (n/d)	FPG, HDL, TG, SBP, DBP	correlation: 1) Steps/d was favorably associated with FPG; Regression: adjusted for age, FFM, FM 1) Steps/d was favorably associated with HDL and TG;
Zając-Gawlak et al., 2017	cross-sectional	85	ACC: ActiGraph GT1M; uniaxial Steps (n/d)	MS	U test: 1) Group (Steps/d≥12500) had less number of MS criteria than Group (10000-12500) and Group(<10000); 2) no differences in the number of MS between Group (10000-12500) and Group(<10000); Odds ratios: Group (Steps/d≥12500) was 3.84 times lower risk of being MS than Group (Steps/d<12500);

Note: ACC: accelerometer; ACi, abdominal circumference; ANOVA, analysis of variance; CRP, C-reactive protein; DBP, diastolic blood pressure; FFM, fat-free mass; FPG, fasting glucose; FM, fat mass; HbA1c, glycosylated hemoglobin; HDL, high density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; IL-6, interleukin-6; LDL, low density lipoprotein; LPA, low intensity physical activity; METs, metabolic equivalents; MHO, metabolically healthy overweight/obese; MPA, moderate intensity physical ac-tivity; MS, metabolic syndrome; MUO, metabolically unhealthy overweight/obese; MVPA, moderate to vigorous intensity physical activity; PA, physical activity; PED, pedometer; PPG, postprandial glucose; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TNF-alpha, tumor necrosis factor-α; TPA, total physical activity; U-test, Mann-Whitney U-test; VO_{2peak}, peak oxygen uptake; VPA, vigorous physical activity.

Table 10: Characteristics of intervention studies

Reference	Study design	Sample size	Intervention	PA measure	Health Outcome	Association
Hasan et al., 2018	Quasi-experimental design	52	9-week walking program asked to walk 10,000 steps per day	PED: KenzLifeCoder e-step Steps (n/d)	SBP, DBP, TC, TG, HDL, LDL, FPG, Fasting insulin, HOMA-IR, MS	t-test: 1) After intervention, LDL decreased; 2) In Group (18≤BMI<25), no intervention effect on cardiometabolic parameters; 3) In Group (BMI≥25), after intervention, TG and fasting insulin decreased; 4) In Group (Steps/d>7056), after intervention, TG decreased; 5) In Group (Steps/d<7056),no intervention effect on cardiometabolic parameters; Correlation: 1) After intervention, Steps/d was favorably associated with MS Score; 2) After intervention, in Group (18≤BMI<25), steps/d had no association with all parameters; 3) After intervention, in Group (BMI≥25), steps/d was favorably associated with MS Score; unfavorably associated with SBP and DBP;
Hornbuckle et al., 2012	Random experiment	44	12-week exercise intervention Group 1: asked to walk 10000 steps/d Group 2: asked to walk 10000 steps/d + RT 2d/w	PED: New Lifestyles Digi-Walker SW-200 Steps (n/d)	SBP, DBP, HDL, TG, TC, HbA1c, CRP	ANOVA: 1) No changes in all parameters after intervention in Group 1; 2) HbA1c decreased after intervention in Group 2;
Moreau et al., 2001	Randomized controlled trial	24	24-week incremental walking program Group 1: 3km increase in daily walking; CONT: maintain current physical activity	PED: Yamax SW200 pedometer Steps (n/d)	SBP, DBP, Fasting insulin, FPG, HOMA-IR	ANOVA: 1) SBP decreased after intervention in Group 1 compared with CONT; 2) no changes in other parameters in either group after intervention.
Musto et al., 2010	Quasi-experimental design	77	12-week incremental walking program; asked to increase steps/d by 10% per week; the progression was reduced to a 3% when steps/d reached 10000	PED: Sportline 330 Steps (n/d)	SBP, DBP, TG, FPG, HDL	ANOVA: 1) SBP and FPG decreased after intervention in Group 1;

			Group 1: improved steps/d by 3000 or greater; CONT: stopped participating or did not achieve step improvement level			
Pal et al., 2011	Random experiment	28	12-week walking program; Group 1: asked to undertake 30 minutes of walking/day; with sealed pedometer Group B: asked to accumulate 10,000 steps/d, with unsealed pedometer	PED: Yamax Digi-Walker SW-200 Steps (n/d)	SBP, DBP	ANOVA: 1) no changes in SBP and DBP in either group after intervention.
Rodriguez-Hernandez et al., 2018	Crossover design study	10	3-condition multiple walking breaks Condition 1: 4-h SB; Condition 2: 4-h SB with 2-min of moderate-intensity walking every 30 minutes; Condition 3: 4-h SB with 5-min of moderate-intensity walking every 30 minutes.	ACC: ActiGraph GT3X; triaxial %Volume: LPA, MVPA	PPG, AUCglucose	ANOVA: 1) there was between-condition differences for both %LPA and %MVPA during experiment between all conditions; 2) there was between-condition differences for the 4h-PPG between Condition 1 and Condition 3; 3) no between-condition differences for 1h-, 2h-, and 3h-PPG; 4) no between-condition differences for peak PPG; 5) 2h-AUCglucose was lower in Condition 3, compared to Condition1;
Sugawara et al., 2006	Random experiment	17	12-week cycling training Group 1 (n=8): 180-300 kcal/session, 3-5 sessions/week at 40% HRR Group 2 (n=9): at 70% HRR	ACC: Lifecorder; uniaxial LPA (<4METs), MPA (4-6METs), VPA (>6METs) (min/d)	SBP, DBP	ANOVA: 1) no changes in SBP or DBP in eigher group after intervention.
Sugiura et al., 2002	Randomized controlled trial	27	24-month exercise intervention Group 1 (n=14): 90-min exercise (40-60%VO_{2max}) 1d/w + asked to increase at least 2000-3000 steps/d CONT (n=13): maintain current physical activity	PED: n/r Steps (n/d)	TC, HDL, TG, LDL	ANOVA: 1) TC decreased after intervention in Group 1; 2) HDL increased after intervention in Group 1 compared with CONT; Regression: age, BMI, menopausal status 1) Steps/d had no association with TC and HDL in Group 1 before intervention; 2) Steps/d was favorably associated with TC, HDL, ΔTC and ΔHDL in Group 1 after intervention;
Swartz et al., 2003	Quasi-experimental design	18	4-week control period followed by 8-week walking program	PED: Yamax Digi-Walker SW-200	SBP, DBP, FPG, PPG, Fasting insulin, Postprandial insulin,	ANOVA: 1) SBP, DBP, 2h-PPG, 2h-AUCglucose decreased after intervention;

	Steps (n/d)	HOMA-IR, AUCglucose, AUCinsulin	

Note: ACC: accelerometer; ANCOVA, analysis of covariance; ANOVA, analysis of variance; AUC, the area under the curve; CONT, control; CRP, C-reactive protein; DBP, dias-tolic blood pressure; FPG, fasting glucose; HbA1c, glycosylated hemoglobin; HDL, high density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; HRR, heart rate reserve; LDL, low density lipoprotein; LPA, low intensity physical activity; METs, metabolic equivalents; MPA, moderate intensity physical activity; MS, metabolic syn-drome; MVPA, moderate to vigorous intensity physical activity; PA, physical activity; PED, pedometer; PPG, postprandial glucose; SB: sedentary behavior; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TPA, total physical activity; VO_{2max}, maximal oxygen uptake; VPA, vigorous physical activity.

3.4 Cardiometabolic health outcomes assessment

Cardiometabolic biomarkers assessed in the studies included BP (systolic blood pressure (SBP), diastolic blood pressure (DBP)), lipid profile (total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG)), carbohydrate metabolism (fasting glucose (FPG), postprandial glucose (PPG), glycosylated hemoglobin (HbA1c), homeostasis model assessment of insulin resistance (HOMA-IR)), endocrine regulators (fasting insulin, postprandial insulin), inflammation marker (C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-alpha) and MetS.

3.5 Risk of bias assessment and the quality of evidence

The risk of bias assessment for included studies is presented in Supplementary Table F1 & F2. Out of 18 observational or non-randomized design, 13 were categorized as high quality and 5 of low quality. 10 (55.6%) studies did not control for age, which was the most important covariate that we deemed for quality assessment. The majority of random experiments were unclear quality (80%), with only 1 high quality. The most reported risk of bias came from the lack of random sequence generation.

Moreover, according to the GRADE framework, very low to moderate quality of evidence were reported, with none upgraded. The small sample size of intervention studies was the most common reason for the downgrade and the lower quality for observational studies was mostly due to the inconsistency findings. Supplementary Table F3 presents the details of the quality of evidence by study design and the categories of cardiometabolic health outcomes.

3.6 Association between PA and cardiometabolic health outcomes

From 23 studies, 13 studies assessed the association between PA and BP, 11 studies assessed lipid profile, 16 assessed carbohydrate metabolisms, 8 assessed endocrine regulators, 6 assessed inflammation markers, and 4 assessed MetS.

Blood pressure

Observational studies reported consistent findings that there was no relationship between PA and BP [Green et al., 2014; Koniak-Griffin et al., 2014; Panton et al., 2007; Slater et al., 2021; Vella et al., 2009; 2011]. However, intervention studies found some favorable effects. One of the four random experiment reported an improvement on SBP with an average of 9700 steps/d across the 24-week walking program [Moreau et al., 2001]. Out of 3 quasi-experimental studies, one indicated significantly decreased SBP and DBP after the 8-week intervention, during which an average of 85% increased to 9213 steps per day [Swartz et al., 2003]. While another one reported that only SBP was significantly improved after a 12-week incremental pedometer program [Musto et al., 2010].

Lipid profile

Both observational and intervention studies reported some favorable relationships with lipid outcomes. One quasi-experimental study found a favorable effect on LDL after a 9-week walking program with average daily steps of 7056 [Hasan et al., 2018]. However, from three random experiments, only one study conducted a 24-months of moderate intensity exercise intervention reported the favorable effects on HDL and TC [Sugiura et al., 2002]. The other two random experiments studies showed no effect of increased daily steps on HDL, TG, or TC [Hornbuckle et al., 2012; Musto et al., 2010].

From 9 studies reported cross-sectional evidence, 3 studies (75%) reported favor-able associations between daily steps with HDL [Vella et al., 2009] and TG [Vella et al., 2009; Koniak-Griffin et al., 2014]. Furthermore, LPA [Green et al., 2014] and meeting the recommended 150 min MVPA weekly [Vella et al., 2011] were reported to be beneficial to TG and TC. Two studies (66.7%) suggested a favorable association be-tween MVPA and HDL [Koniak-Griffin et al., 2014; Slater et al., 2021]. Of note, an unfavorable but small relationship with TC in overweight Latin women was found [Koniak-Griffin et al., 2014]. Likewise, unfavorable relationships with LDL or TC were reported in obese African American women with lower socio-economic status [Panton et al., 2007].

Table 11: Characteristics of participants for included studies

Reference	Country	Race	Sample size	Age	Body mass index	Menstrual status	Diet	Education	Lifestyle	Socio-economic level	Tobacco
Camhi et al., 2015	USA	African American (61%)	46	26.7±4.7	31.1±3.7	/	no affected medications and dietary supplement s	/	/	/	non-smoker (80%)
Diniz et al., 2015 meet PA guideline	Brazil	/	25	55.8±7.2	26.9±5.1	postmenopau sal	no affected medications	/	physically active	/	/
Diniz et al., 2015 not meet PA guideline	Brazil	/	24	61.6±6.2	29.1±9.0	postmenopau sal	no affected medications	/	physically inactive	/	/
Graff et al., 2012	Brazil	Caucasian (73%)	68	28.0±6.0	28.0±6.0	premenopaus al	no affected medications	/	/	/	/
Green et al., 2014	USA	Caucasian (92%)	50	24.0±4.8	27.0±4.8	premenopaus al	no affected medications	collage (84%)	/	college student (84%)	no smoke for 6 months
Koniak-Griffin et al., 2014	USA	Latina	210	44.6±7.9	32.6±5.7	/	/	college or more (4%)	/	low income	/
Lecheminant and Tucker, 2011	USA	Caucasian (90%)	264	40.1±3.0	31.7±6.9	premenopaus al	/	college or more (50%)	/	/	non-smoker
Loprinzi and Cardinal, 2012	USA	Caucasian (73%)	535	49.3±0.9	28.8±0.3	/	/	/	/	/	non-smoker (60%)
Macena et al., 2021	Brazil	/	58	31.0±7.0	33.3±4.1	premenopaus al	no affected medications	/	/	low income	/
Panton et al., 2007	USA	African American	35	48±8	42.3±9.8	/	no affected medications	/	/	low income	non-smoker (83%)
Slater et al., 2021 Pacific normal	New Zealand	Pacific	61	25.0±7.0	25.9±3.9	premenopaus al	/	/	/	low income	/
Slater et al., 2021 Pacific obesity	New Zealand	Pacific	55	26.0±6.0	35.6±6.1	premenopaus al	/	/	/	low income	/
Slater et al., 2021 European normal	New Zealand	European	85	30.0±7.0	22.5±2.1	premenopaus al	/	/	/	less deprived	/
Slater et al., 2021 European obesity	New Zealand	European	74	33.0±7.0	33.7±3.8	premenopaus al	/	/	/	less deprived	/
Tabozzi et al., 2020	Italy	/	13	32.5±16.1	24.0±3.3	/	no affected medications	/	physically inactive	university nurse students/research staff	/
Vella et al., 2011 no meet PA Guideline	USA	Hispanic	42	25.2±5.6	23.8±4.0	/	no affected medications	/	/	/	no smoke for 6 months
Vella et al., 2011 meet PA Guideline	USA	Hispanic	18	24.4±4.9	23.0±4.6	/	no affected medications	/	/	/	no smoke for 6 months

Vella et al., 2009	USA	Mexican and Mexican American	60	24.9±0.7	23.6±0.5	/	no affected medications	/	/	/	no smoke for 6 months
Zając-Gawlak et al., 2017	Poland	/	85	62.8±5.9	27.6±4.5	postmenopausal	/	/	physically active	the Third Age University student	/
Hasan et al., 2018	UAE	/	52	21.4±4.8	27.5±5.6	/	no affected medications	college	/	college student	/
Hornbuckle et al., 2012	USA	African American	44	49.0±5.5	34.7±6.4	/	/	/	physically inactive	/	no smoke for 6 months
Moreau et al., 2001	USA	/	24	54.0±1.0	/	postmenopausal	/	/	physically inactive	/	non-smoker
Musto et al., 2010 Control	USA	/	34	45.7±9.5	29.5±5.0	/	/	/	physically inactive	/	/
Musto et al., 2010 Active	USA	/	43	46.3±10.4	30.4±5.5	/	/	/	physically inactive	/	/
Pal et al., 2011 10000 steps	Australia	/	13	41.4±2.7	28.9±1.2	/	no affected medications	/	physically inactive	/	non-smoker
Pal et al., 2011 30min walking	Australia	/	15	45.3±2.2	29.7±1.1	/	no affected medications	/	physically inactive	/	non-smoker
Rodriguez-Hernandez et al., 2018	USA	/	10	36.0±5.0	38.0±1.6	/	no affected medications	/	physically inactive	/	/
Sugawara et al., 2006 moderate intensity training	Japan	Asian	8	58.0±4.0	25.5±3.6	postmenopausal	/	/	physically inactive	/	non-smoker
Sugawara et al., 2006 vigorou intensity training	Japan	Asian	9	59.0±6.0	24.2±3.0	/	/	/	/	/	/
Sugiura et al., 2002 intervention	Japan	Asian	14	48.6±4.2	22.3±1.6	both	no affected medications	/	physically inactive	/	/
Sugiura et al., 2002 control	Japan	Asian	13	48.0±3.6	22.6±1.9	both	no affected medications	/	physically inactive	/	/
Swartz et al., 2003	USA	/	18	53.3±7.0	35.0±5.1	both	/	/	physically inactive	/	non-smoker

Carbohydrate metabolism

Observational studies reported consistent findings that there was no association between PA with FPG or HbA1c [Green et al., 2014; Koniak-Griffin et al., 2014; Macena et al., 2021; Panton et al., 2007; Slater et al., 2021; Tabozzi et al., 2020; Vella et al., 2009; 2011]. HOMA-IR was found to be favorably associated with daily steps [Graff et al., 2012] and MVPA bouts [Green et al., 2014]. Likewise, there was a favorable association between MVPA and peak PPG [Tabozzi et al., 2020].

Although two random experiments reported no effects on FPG or HbA1c, which was consistent with findings from observational studies, HOMA-IR was improved as a result of engaging in a walking program [Hornbuckle et al., 2012; Moreau et al., 2001]. These findings were not replicated in quasi-experimental studies as a favorable effect on FPG [Musto et al., 2010], and PPG [Swartz et al., 2003] was observed following walking programs. In addition, one study using a crossover design to examine the effects of three conditions on carbohydrate metabolism and found that increasing the percentage volume of MVPA had a favorable effect on PPG, while LPA had no effect [Rodriguez-Hernandez et al., 2018].

Endocrine regulation

One randomized controlled trial and two quasi-experimental studies consistently indicated no effects on fasting insulin or postprandial insulin after engaging in the walking program [Hasan et al., 2018; Moreau et al., 2001; Swartz et al., 2003]. However, some favorable associations were found in cross-sectional observational studies. One study found favorable associations between daily steps with fasting insulin and postprandial insulin [Graff et al., 2012]. Furthermore, fasting insulin was shown to be favorably associated with 10min MVPA bouts [Green et al., 2014]. It was worth noting that one study reported an unfavorable association between TPA and fasting insulin [Slater et al., 2021].

Inflammation markers

Only one random experiment examined the effect on inflammation markers and reported that increasing daily steps had no effect on CRP after a 12-week exercise intervention [Hornbuckle et al., 2012]. However, one observational study reported favorable associations be-tween CRP with MVPA and MVPA bouts [Green et al., 2014]. Opposite results were reported by Slater et al. (2021) that both TPA and MVPA were detrimental to CRP [Slater et al., 2021]. There was no relationship between PA with TNF-alpha [Diniz et al., 2015] or IL-6 [Green et al., 2014].

Metabolic syndrome

Findings regarding to MS were unequivocal between intervention and observational studies. One quasi-experimental study reported a positive effect on MS score after participating a 9-week walking program [Hasan et al., 2018]. Cross-sectional studies found the incidence of MS was favorably associated with daily steps [Zając-Gawlak et al., 2017], the volume of LPA [Camhi et al., 2015] and MVPA [Loprinzi and Cardinal, 2012].

3.7 Meta-analysis

There were six studies (4 cross-sectional, 1 quasi-experimental and 1 RCT), providing correlational data that could be pooled to conduct the meta-analysis. Table 12 and Figure 9 illustrate the correlational meta-analysis for included studies.

Table 12: The meta-analysis of the association between physical activity and cardiometabolic health outcomes (all analyses were performed using the random-effect model).

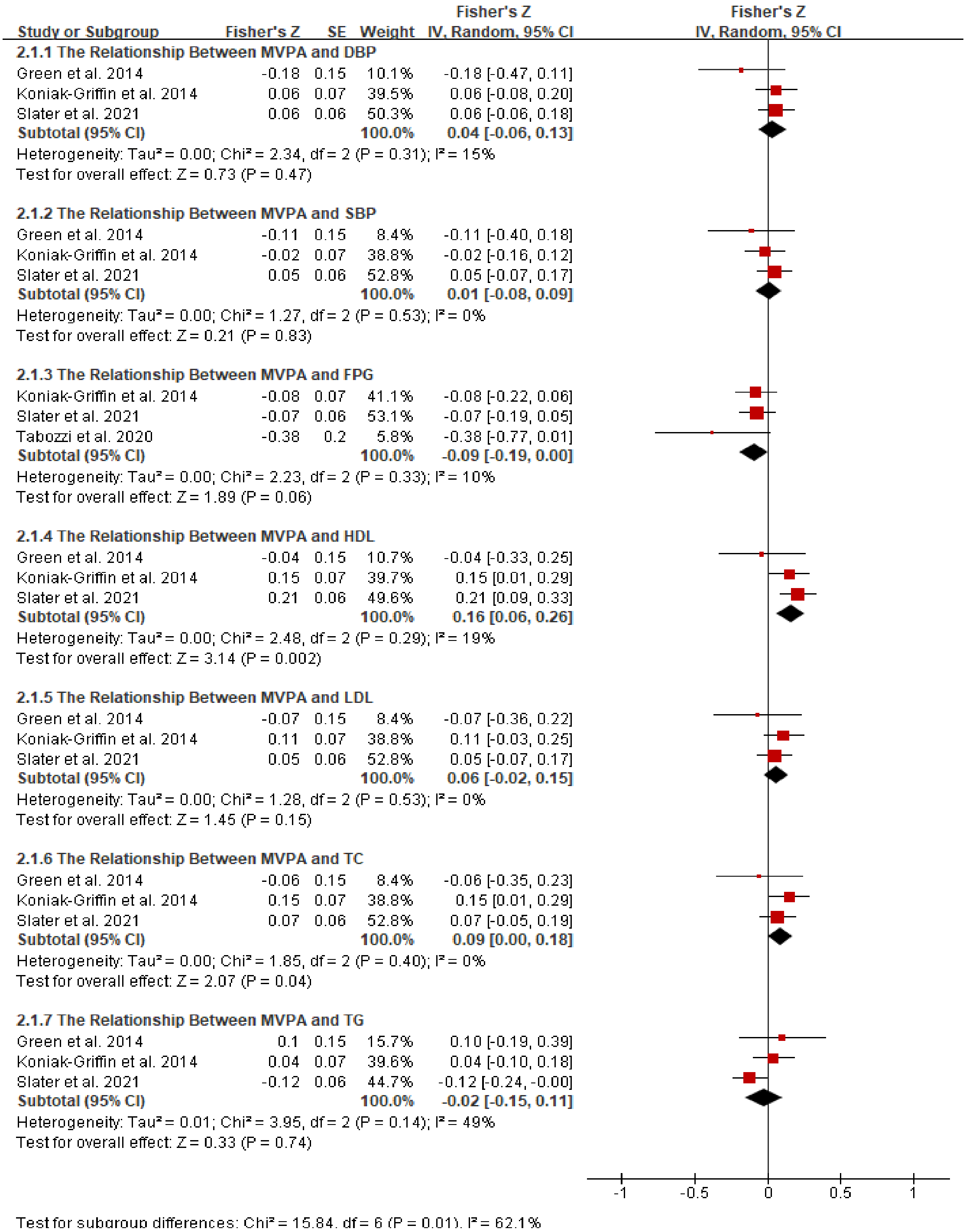
Study Group Variables	No. Studies	Meta-analysis r (95%CI)	p	Heterogeneity I^2 (%)	p
MVPA (min/day)					
DBP	3	0.04 (-0.06, 0.13)	0.47	15	0.31
SBP	3	0.01 (-0.08, 0.09)	0.83	0	0.53
FPG	3	-0.09 (-0.19, 0)	0.06	10	0.33
HDL	3	0.16 (0.06, 0.25)	0.002	19	0.29
LDL	3	0.06 (-0.02, 0.15)	0.15	0	0.53
TC	3	0.09 (0, 0.18)	0.04	0	0.4
TG	3	-0.02 (-0.15, 0.11)	0.74	49	0.14
Steps/day					
Glucose	3	-0.12 (-0.24, 0.01)	0.06	0	0.48

HDL	4	0.24 (-0.07, 0.49)	0.13	81	0.001

Note: DBP, diastolic blood pressure; FPG, fasting glucose; HDL, high density lipoprotein; LDL, low density lipoprotein; MVPA, moderate to vigorous intensity physical activity; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

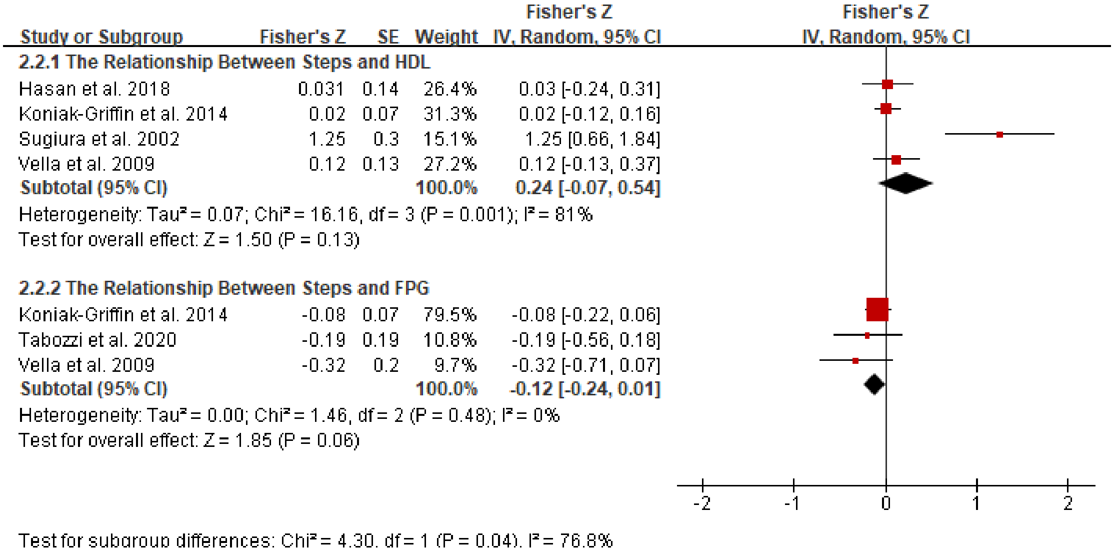
Figure 9: Forest plot of correlation between physical activity and cardiometabolic health outcomes. Overall pooled correlation for random effects model represented by black diamond.

(a) The relationship between MVPA and cardiometabolic indicators



Note: DBP, diastolic blood pressure; FPG, fasting glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TC, Total-cholesterol; TG, triglyceride.

(b) The relationship between steps and cardiometabolic indicators



Note: FPG, fasting glucose; HDL, high-density lipoprotein.

Results from three studies assessed MVPA could be pooled into a meta-analysis (n = 545). The pooled results showed a significantly favorable but small relationship be-tween MVPA and HDL (r = 0.16; 95% CI: 0.06, 0.25; p<0.01), with a low heterogeneity between studies (I^2 = 19%, p = 0.29). However, according to subgroup analysis, no significant relationship between MVPA and HDL was detected in young (n = 2) and premenopausal (n = 2) women. Studies conducted in the US (n = 2) and Caucasian (n = 1) women also showed no relationship between MVPA and HDL.

In contrast, there was a pooled unfavorable but small relationship between MVPA and TC (r = 0.09; 95% CI: 0.00, 0.18; p<0.05), with no between-study heterogeneity (I^2 = 0%, p = 0.40). The subgroup analysis showed that the unfavorable association could be explained by obesity (n = 1) and Latin ethnicity (n = 1).

According to pooled analysis, there were not any significant associations between MVPA with DBP, SBP, LDL, FPG, and TG. Subgroup analysis revealed that the age, BMI, menstrual status, country, and ethnicity had no effect on the association.

There was no significant correlation between daily steps and FPG (n = 313) (r = -0.12; 95% CI: -0.24, 0.01; p = 0.06, n = 3). The between-study heterogeneity was low (I^2 = 42%, p = 0.18). The subgroup analysis based on the age, BMI, menstrual status, country, and ethnic did not modify the association.

The pooled analysis of four studies (n = 349) revealed that daily steps was not as-sociated with HDL (r = 0.24; 95% CI: -0.07, 0.54; p = 0.13), with a high heterogeneity be-tween studies (I^2 = 84%, p<0.05). However, subgroup analysis (n = 14) revealed a significantly stronger association in middle-aged women in studies conducted in Japan (r = 0.85; 95% CI: 0.58, 0.95; p<0.001; n = 1). The between study heterogeneity was mostly explained by the subgroup analysis of BMI.

Additionally, we also conducted a meta-analysis to examine the effect of meeting PA guidelines on HOMA-IR since there were three comparable studies (Table 13 and Figure 10). The mean and standard deviation were extracted from those who meet the 150 minutes of MPA and those who not to calculate the standardized mean differences. The pooled results showed that following the recommended MVPA level had no significant effect on HOMA-IR (SMD = -0.22; 95% CI: -0.46, 0.02; p = 0.08), with a low heterogeneity (I^2 = 11%, p = 0.32). According to subgroup analysis, meeting PA guidelines was significantly associated with lower HOMA-IR in studies conducted in the USA (n = 2) and in Caucasian women (n = 1).

Table 13: The meta-analysis of the effect of meeting physical activity guideline on HOMA-IR (all analyses were performed using the random-effect model)

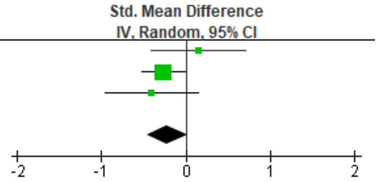
Variables	No. Studies	Meta-analysis		Heterogeneity	
HOMA-IR		**SMD (95%CI)**	**p**	**I^2 (%)**	**p**
Meet vs. Not meet	3	-0.22 (-0.46, 0.02)	0.08	11	0.32

Note: HOMA-IR, homeostasis model assessment of insulin resistance.

Figure 10: Forest plot of the effect of meeting physical activity guideline on HOMA-IR. Overall pooled effect for random effects model represented by black diamond

	Meet			Not meet				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Diniz et al. 2015	2.59	3.98	25	2.05	2.86	24	17.4%	0.15 [-0.41, 0.71]
Lecheminant et al. 2011	1.36	0.77	88	1.63	1.1	177	64.9%	-0.27 [-0.53, -0.01]
Vella et al. 2011	1.1	0.7	42	1.4	0.8	18	17.7%	-0.41 [-0.96, 0.15]
Total (95% CI)			**155**			**219**	**100.0%**	**-0.22 [-0.46, 0.02]**

Heterogeneity: Tau² = 0.01; Chi² = 2.25, df = 2 (P = 0.32); I² = 11%
Test for overall effect: Z = 1.76 (P = 0.08)



Note: HOMA-IR, homeostasis model assessment of insulin resistance

4. Discussion

This systematic review and meta-analysis are the first to synthesize studies that investigated the association between objectively determined PA volume and clinically relevant cardiometabolic biomarkers in adult women across a range of study designs. Although relatively limited in the small number included, the evidence examining the association between objectively assessed PA and cardiometabolic indicators points towards a favorable association between MVPA and HDL. Evidence of a beneficial effect on other cardiometabolic outcomes seems to be limited.

4.1 Meta-analytic findings

Findings from the meta-analysis revealed that spending more minutes in MVPA were significantly associated with healthier HDL, however the pooled effect size was small. No significant associations were observed between MVPA and most cardiometabolic biomarkers, including SBP, DBP, LDL, FPG, and TG.

Subgroup analysis showed significant differences in the association between steps and HDL, across various ages, countries of studies and ethnicities. However, it was noteworthy that the number of studies included in the subgroup was small, which calls for caution in drawing conclusions from subgroup analyses.

4.2 Association between steps and cardiometabolic biomarkers

The observational and experimental evidence examining the associations be-tween daily steps and cardiometabolic health indicate no effects in improving cardiometabolic biomarkers, including BP, lipids, glucose, insulin, and inflammation markers. This was supported by the meta-analytic findings that daily steps were not significantly associated with HDL or FPG.

Even though most studies reported no association between steps and BP, three studies conducted a long-term walking program in obese women and observed de-creases in SBP after the intervention [Moreau et al., 2001; Musto et al., 2010; Swartz et al., 2003]. Participants in these three studies were all obese with elevated or stage I high SBP at baseline, and moreover, their daily steps doubled to about 10,000 after the intervention. This favorable effect was sup-ported by a systematic review, in which the decreased SBP was found to be associated with higher baseline values and the magnitude of change on steps per day [Bravata et al., 2007].

Experimental evidence suggests that increasing daily steps after intervention had no effects on HDL, LDL, TG or TC [Hornbuckle et al., 2012; Musto et al., 2010]. A pedometer-based walking intervention reported no effects on HDL, TG, or TC, while LDL improved at the end of the intervention [Hasan et al., 2018]. The improved LDL was mainly due to weight loss and improved body composition [Albright et al., 2006]. However, one intervention study reported favorable associations be-tween steps with HDL and TC after the intervention [Sugiura et al., 2002]. It was supposed that the improved lipid profiles were mostly due to additional moderate intensity aerobic training rather than the increased steps since aerobic exercise interventions had a more consistent and potent effect on improving HDL and associated cardiometabolic health indicators [Leon et al., 2001; Swift et al., 2021].

Cross-sectional evidence revealed that there was no association between steps and most blood lipids [Graff et al., 2012; Koniak-Griffin et al., 2014; Panton et al., 2007; Vella et al., 2009]. This was supported by a cross-sectional study, in which, no differences were observed for TC, LDL, HDL, and TG between the group with more than 7500 steps per day and the group with less than 7500 [Woolf et al., 2008]. However, body composition affected this relationship as steps was significantly associated with HDL and TG after adjusting for fat mass and fat-free mass [Vella et al., 2009]. Interestingly, opposite findings were reported by Panton et al. (2007) that women who walked at least 5000 steps per day had worse LDL and TC than those walking less than 5000 steps [Panton et al., 2007]. A potential explanation was that for obese women, more steps were needed to improve lipid markers.

There was consistent evidence from experimental and observational studies that steps had no effects on carbohydrate metabolism [Graff et al., 2012; Koniak-Griffin et al., 2014; Tabozzi et al., 2020; Vella et al., 2009; Hasan et al., 2018; Hornbuckle et al., 2012; Moreau et al, 2001]. Results from other intervention studies also supported that walking programs had no effect on im-proving FPG [Huffman et al., 2014; Yates et al., 2015]. Although most studies reported no improvement on FPG, a favorable effect on PPG was observed after increasing daily steps during the 8-week walking program [Swartz et al., 2003]. This finding was consistent with a prospective study that there was a weak favorable correlation between previous daily steps and 2h-PPG, but no correlation with FPG [Yates et al., 2015].

Experimental studies reported consistent findings that increased daily steps after intervention had no effects on insulin sensitivity [Hasan et al., 2018; Moreau et al., 2001; Swartz et al., 2003], while a cross-sectional study observed the lower level of fasting insulin and HOMA-IR in more active women [Graff et al., 2012].

Despite no relationship between daily steps and cardiometabolic health outcomes suggested by most of the studies, consistent beneficial effects were observed for MetS score, which was defined as the sum of the number of individual MetS indicators [Zając-Gawlak et al., 2017; Hasan et al., 2018]. Both observational and intervention studies found a favorable association be-tween steps and MetS score, which could be supported by longitudinal studies. Huffman et al. (2014) conducted an observational study from NAVIGATOR and found baseline steps were independently associated with reductions in MS score, which was calculated by summing each standardized MetS component [Huffman et al., 2014]. Ponsonby et al. (2011) followed 458 adults with normal glucose and found that a higher level of daily steps was associated with a lower risk of the incidence of abnormal glucose metabolism 5 years later [Ponsonby et al., 2011].

Walking is incidental to daily life and the accumulated number of steps was mostly at a low intensity. Walking intensity was more important than walking volume in the association with cardiometabolic health, and this might explain why the beneficial effects on cardiometabolic biomarkers were hardly observed [Summer et al., 2020]. In addition to walking intensity, evidence from experimental studies indicated that the baseline value of biomarkers and magnitude of changes on daily steps affected the relationship between walking and cardiometabolic health outcomes. Likewise, body composition variables suggested by observational cross-sectional evidence could also mediate this relationship. Therefore, more controlled experimental and prospective studies with high quality experimental designs are needed in the future.

4.3 Association between TPA and cardiometabolic biomarkers

Evidence from the current review revealed that there was no association between TPA and most cardiometabolic markers, expect fasting insulin and CRP [Slater et al., 2021]. Among obese women, there was no significant difference in TPA between metabolically healthy and metabolically unhealthy women [Camhi et al., 2015]. However, a cross-sectional finding revealed that TPA displayed stronger associations with cardiometabolic biomarkers, including HDL, TG, FPG, fasting insulin, CRP, and SBP [Wolff-Hughes et al., 2015]. One potential explanation for the contradictory result might be the discrepancy of TPA between genders as women engage in less TPA than men. Additionally, the relationship varied by ethnicity of the subjects. TPA was associated with fasting insulin in Pacific women but not European women, and the relationship between TPA and CRP was reversed between the two ethnicities. This may be because fasting insulin was nearly two times higher in Pacific women and CRP was positively associated with visceral fat, which was higher in Pacific women.

4.4 Association between volume of PA at different intensity and health outcomes

Both cross-sectional and intervention evidence supported that there was no relationship between LPA and cardiometabolic health markers [Green et al., 2014; Macena et al., 2021; Rodriguez-Hernandez et al., 2018]. Our findings were consistent with a previous review [Batacan et al., 2015]. This review summarized the effect of exercise protocols delivered at light intensity and showed little support for the role of LPA to improve cardiometabolic health and moreover, it indicated that the applied dose of LPA was low among included studies. However, there was emerging evidence that LPA had benefits to health [Loprinzi, 2017; Migueles et al., 2021; Ballin et al., 2021]. In a cross-sectional study, LPA was shown to be significantly associated with TG and TC. These associations were independent of MVPA but were attenuated by peak oxygen uptake (VO_{2peak})

and body composition outcomes, indicating that VO_{2peak} and body composition might be important contributors to cardiometabolic health [Graff et al., 2012]. It was evidenced by previous cross-sectional studies that VO_{2peak} was associated with risk factors of CVD with a moderate to strong correlations [Abdulnour et al., 2010]. Likewise, Kodama et al. (2009) conducted a meta-analysis to quantitatively define the relationship between cardiorespiratory fitness and the incidence of CVD. The authors indicated that those with low cardiorespiratory fitness had a risk ratio for CVD events of 1.56 compared to those with high cardiorespiratory fitness [Kodama et al., 2009]. Therefore, the cardiorespiratory fitness appeared to be an important confounder when investigating the relationship between PA and cardiometabolic health. Furthermore, the cardiorespiratory fitness should be taken into consideration when developing exercise protocols aiming to improve cardiometabolic health. Since high in-tensity exercises were well documented to be effective and efficient on improving cardiorespiratory fitness [Sultana et al., 2019; O'Donoghue et al., 2021; Wen et al., 2019; Kong et al., 2016], in this regard, PA performed at higher intensity was recommended.

Moreover, a recent systematic review identified 24 cross-sectional and 6 longitudinal studies and found that LPA appears to be independently associated with better WC, TG, fasting insulin, and the presence of MS [Amagasa et al., 2018]. Additionally, replacing sitting with LPA had also been found to be an effective way to improve health [Drenowatz et al., 2016]. It was plausible that there is a threshold for PA at which health outcomes improved, and the threshold for LPA would be much higher due to the lower effects by the low intensities accumulated. This statement is supported by findings from a recent systematic re-view examining the relationship between LPA and cardiometabolic health and mortality in adults. The authors pointed toward beneficial effects of LPA, however, LPA had two to four times less effect than MVPA for the same duration [Chastin et al., 2019]. Moreover, the current PA guidelines recommended at least 150-300 min/week of MPA were required to observe the benefits [Bull et al., 2020]. Studies that investigated MPA exclusively were sparse. Limited evidence from the present review supported that MPA had no association with HOMA-IR [Lecheminant and Tucker, 2011; Macena et al., 2021].

It was generally believed that MVPA appeared to be more potently associated with cardiometabolic biomarkers. However, cross-sectional evidence from the present review suggests that there are no associations between MVPA and cardiometabolic risk indicators [Green et al., 2014; Koniak-Griffin et al., 2014; Slater et al., 2021; Tabozzi et al., 2020]. Only one study founded a favorably association with the odds of being MS after controlling for age, ethnicity, and smoking [Loprinzi and Cardinal, 2012]. In this study, MetS was defined if participants meet three or more of the following criteria: 1) WC $\geq$ 88 cm; 2) TG $\geq$ 150 mg/dL or self-reporting on treatment; 3) HDL $<$ 50 mg/dL or self-reporting on treatment; 4) SBP $\geq$ 130 mm Hg and DBP $\geq$ 85 mm Hg or self-reporting on treatment); and 5) FPG $\geq$ 100 mg/dL or self-reporting on treatment). Cross-sectional evidence suggested effects on cardiometabolic health seemed to be limited, while some prospective studies reporting beneficial associations. A 10-year longitudinal study investigated the independent association of changes in MVPA and objectively measured cardiometabolic health and concluded that a greater decrease in MVPA was associated with a greater decrease in HDL and increases in clustered cardiometabolic risk score [Knaeps et al., 2021]. However, MVPA was self-reported. Mielke et al. (2021) investigated the prospective association between accelerometer determined MVPA and cardiometabolic health in the transition to adulthood [Mielke et al., 2021]. The authors suggested that young women who increased MVPA from 18 to 22 years old showed improvements in cardiometabolic health at age 22, and moreover, MVPA in 10min bouts showed a stronger interaction than MVPA in 1min. Similarly, a previous study con-ducted by Strath et al. (2008) analyzed data from the 2003-2004 National Health and Nutrition Examination Survey and found that the bout MVPA appeared to be a time-efficient strategy [Strath et al., 2008]. However, evidence from qualitative synthesis in the current re-view pointed towards no differences in beneficial effects between bouts MVPA that measured more than 10 consecutive minutes and non-bout MVPA [Green et al., 2014; Koniak-Griffin et al., 2014]. One potential explanation was that women often engaged in short bouts of MVPA, which was normally less than 10 minutes [Koniak-Griffin et al., 2014]. Consistent findings were also reported by recent cross-sectional research that the impact of accumulated PA obtained from several short bouts of exercise is the same as benefits obtained from longer duration activities [Marschollek, 2015; Millard et al., 2021; Loprinzi and Cardinal, 2013; Jefferis et al., 2016]. These results were in agree with findings from prospective studies that short spurts of MVPA could provide protection against the onset of hypertension [White et al., 2015] and all-cause mortality [Saint-Maurice et al., 2018]. Although MVPA in 10 min bouts were generally recommend-ed for health benefits, the accumulated evidence from cross-sectional and prospective studies showed that short-lived MVPA was associated with health outcomes. As such, the move towards recommending MVPA of any bout duration through the lasted PA guideline tended to be a pragmatic change [Bull et al., 2020; Piercy et al., 2018].

Research focusing on total volume suggested that there was emerging evidence that it was the total volume of PA, not the minutes accumulated in bouts, that was important in relation to health [Wolff-Hughes et al., 2015; Loprinzi and Cardinal, 2013; Jefferis et al., 2016; White et al., 2015]. Moreover, PA of sufficient volume was favorably associated with cardiometabolic health independent of PA intensity [LaMonte et al., 2017]. In a cross-sectional study assessing the relationship between PA and cardiometabolic health in overweight Latina women, minutes in bout MVPA was shorter than overall minutes in MVPA and moreover, the effect size of the correlation with cardiometabolic indicators was smaller with minutes in bout MVPA than overall minutes in MVPA [Koniak-Griffin et al., 2014]. Likewise, Green et al. (2014) found that overall minutes of MVPA was a stronger variable than the bout MVPA regarding to the association with markers of cardiometabolic health in young women [Green et al., 2014]. Despite that most evidence was from cross-sectional analysis; it was encouraging that the promotion of short bouts MVPA was more likely to be feasible for most women. From the public health perspective, it had significant implications for inactive individuals as health benefits could be achieved by simply being more physically active without emphasizing the exercise duration.

We also examined the effects of meeting PA recommendation that adults should undertake at least 150 min of MPA a week and overall, meeting PA recommendation had an unclear impact on cardiometabolic health. Few significant differences were found between women who were meeting the recommendations and those who were below the recommended levels [Diniz et al., 2015; Lecheminant and Tucker, 2011; Vella et al., 2011]. This was supported by the meta-analytic findings that there was no effect on HOMA-IR when meeting the recommended level. Only TG and TC were found to be improved by meeting the PA recommendation [Vella et al., 2011]. On the contrary, several previous studies based on large-scale populations showed that following the PA guideline was strongly associated with lower risk of cardiometabolic disease [Hamer et al., 2009; Sofi et al., 2007]. Discrepancies among these findings may be explained by the mediating roles of body composition variables on the relationship between PA and insulin resistance [Lecheminant and Tucker, 2011; Reaven, 2011]. Other research also suggested that greater adiposity was associated with higher concentrations of inflammatory markers [Rubin and Hackney, 2010; Dring et al., 2019].

It is worth noting that most large-scale studies included self-reported PA rather than objectively measured ones, which were believed to attenuate the credibility of the findings. Furthermore, the current guidelines were developed in accordance reviewed evidence to assess associations between PA and a set of health outcomes, however, most of the evidence was based on subjectively determined PA. Despite limitations of our relative low-quality evidence, the results of the current review showed some support that objectively measured PA was not beneficial to most cardiometabolic out-comes. However, the majority of studies using subjectively determined PA consistently reported a favorable association with health outcomes [Schultz et al., 2020; Pitanga et al., 2019; Crichton and Alkerwi, 2015]. This discrepancy was mainly due to the weak correlation between subjective and objective methods for assessing the intensity and duration of PA [Nascimento-Ferreira et al., 2018]. We were unable to judge which one was superior because both had several limitations. Therefore, a combination of subjective and objective methods would be expected to further clarify some of the issues revealed by this study.

5. Strengths, limitations, and future directions

Strengths of the current study include the use of different types of study designs and the inclusion of objectively determined PA volumes. This review was the first to analyze the evidence both qualitatively and quantitatively from different study de-signs and to explore the association between PA volume and clinical health indicators in adult women.

It was important to note that there were some limitations. First, most of the evidence synthesized was very low to low quality. This was mainly due to concerns with risk of bias and small sample sizes in the results. However, we compared low-quality evidence to those with high-quality in the discussion and additional high quality and well controlled intervention studies with a large sample will be required to increase the confidence of findings presented here.

Secondly, most of the included studies were cross-sectional in design, using t-test or ANOVA without controlling for any potential confounders such as age and body composition. An initiative to address this issue was setting age to be the most import confounder in rating the quality of studies included. Furthermore, the most adjusted data were included in the discussion and meta-analysis. In addition, although sedentary behavior was documented to be associated with cardiometabolic health, it was not assessed in the current review. Taken together, the absence of these confounders attenuated the association between PA and cardiometabolic health, and our findings should be interpreted with caution.

Thirdly, our findings must be interpreted with the methodological consideration that PA at different intensities was defined as reported in the studies. Therefore, the heterogeneity in the different definition of PA categories, including different cut-points of counts, METs, and vertical acceleration peaks, was a potential source of in-consistent findings. Furthermore, the use of different epochs might also contribute to overestimation or underestimation in the amount of PA at a particular intensity. For instance, studies using the longer epochs (e.g., 10 minutes) were more likely to under-estimate the volume of higher intensity of PA than those using 60 seconds epochs. Finally, accelerometer-determined PA was unable to quantify certain activities such as yoga, Pilates, and swimming, as well as unable to precisely calculate the energy expenditure of PA. Likewise, the pedometer was unable to quantify the intensity of walking. To deal with these limitations, standardized cut-points, shorter epochs, and pattern recognition should be applied in future.

Lastly, findings from intervention studies were synthesized with small sample size. Further large-scale intervention studies were need. Likewise, findings from sub-group analyses were limited and should be considered preliminary due to only a few studies including each category of subgroup.

6. Registration

This protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO). The registration name was physical activity and health indicator in women: a systematic review and meta-analysis, and the registration number was CRD42022307774(https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=307774). The current systematic review and meta-analysis was conducted with regard to the association between PA and cardiometabolic health.

7. Implications for practice and future research

Our systematic review and meta-analysis found that accelerometer and pedometer derived PA were not associated with most individual cardiometabolic health out-comes. These findings were inconsistent with those based on the subjectively measured PA. Improvement in objective measures in the future including the gender-specific cut-points, activity pattern recognition was more likely to improve our knowledge of the health benefits of PA.

Our review found the evidence that walking program was effective in increasing daily steps among adult women, while significant improvements in cardiometabolic indicators were hardly observed following interventions, except among obesity participants. However, some improvements on SBP were reported among obese women with higher SBP value at baseline. Furthermore, we found that increasing PA was associated with higher HDL, however, such favorable association was attenuated among young women. Further research should pay greater attention to potential confounders such as age, body composition and cardiorespiratory fitness when investigating the association between PA and cardiometabolic health in adult women.

8. Conclusion

Findings from the present systematic review and meta-analysis provide evidence that objectively measured PA is not associated with most cardiometabolic health outcomes in healthy adult women. However, it is most compelling that being more physically active is beneficial for the MS. For women, it makes more sense to emphasize the volume of PA rather than whether the volume of PA is accumulated by bouts or is sporadic. Even though low to moderate intensity PA contributes the most to PA patterns observed in women, PA performed at higher intensity is more effective to improve cardiometabolic health. The present review also highlights that meeting 150 minutes of MVPA weekly recommended is scarcely enough to observe significant beneficial effects. However, further high-quality studies with less heterogeneity are still needed to yield compelling findings of the association between PA and cardiometabolic health in women.

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Chapter 6: The Effects of Running Compared with Functional High-intensity Interval Training on Body Composition and Cardiorespiratory Fitness in Female University Students (Study 2)

1. Introduction

Regular physical activity (PA) is beneficial for health [Bermejo-Cantarero et al., 2017; Biddle et al., 2004; Hallal et al., 2006]. Despite the well documented benefits of moderate- to vigorous-intensity PA, 31% of adults worldwide do not engage in sufficient PA for health benefits as recommended by the World Health Organization (WHO) and the American College of Sports Medicine (ACSM) [Bull et al., 2020; Liguori et al., 2021; Hallal et al., 2012]. Frequently reported barriers to PA are physical exertion, time, and financial expenditure [Lovell et al., 2010; Reichert et al., 2007]. Thus, compared to traditional continuous training, which is characterized by long-duration, continuous exercises, and moderate-intensity, high-intensity interval training (HIIT) appears to be an efficient pathway to enhance PA and improve health [Gillen and Gibala et al, 2014].

HIIT involves repeated bouts of high-intensity exercises separated by a recovery using low-intensity activities or inactivity [Laursen and Jenkins, 2002]. Recent studies indicate that HIIT has a similar, or even greater positive effect on physical fitness, especially on body composition and cardiorespiratory health [Astorino et al., 2012; Dias et al., 2018; Milanović et al., 2015; Sultana et al., 2019]. From a time/benefit perspective, HIIT appears to help physically inactive individuals overcome a major time and participation barrier to maintaining a healthier lifestyle [Gaesser and Angadi, 2011].

Originally, HIIT was used to improve the performance of endurance athletes [Billat, 2001]. Cycling, running, and rowing are traditional exercise modalities adopted using HIIT protocols. While, for individuals who perform exercise for health and recreation, these traditional modalities seem too boring because there is no variation in exercise combined with repetition. It is considered as a negative impact for maintaining regular exercise and has been cited as “lack of enjoyment” when investigating barriers to exercise [Bartlett et al., 2011]. Participants’ intrinsic factors are also important to exercise adherence. [Aaltonen et al., 2014; Parfitt et al., 2006]. Meanwhile, several studies revealed that adherence was affected by exercise intensity, especially among inactive individuals [Ekkekakis et al., 2008; 2011].

HIIT utilizing functional exercises has become a popular training modality in recent years, as an alternative to traditional aerobic activities. The functional HIIT (HIIT-F) protocol consists of a variety of functional movements, executed at a relatively high intensity [Feito et al., 2018a; Haddock et al., 2016]. Recently, several investigators have studied the effects of HIIT-F on physical fitness promotion. After engaging in HIIT-F protocols, participants show significant improvements in cardiorespiratory fitness (CRF) [Heinrich et al., 2012; 2015] and body composition [Heinrich et al., 2015; Feito et al., 2018b]. Additionally, participants perceive this type of activity to be more enjoyable when engaging in HIIT-F compared to those individuals performing traditional HIIT [Fisher et al.,2017; Heinrich et al., 2014]. Moreover, most HIIT-F protocols executed using their own body weight, make exercise intensity controllable by the participants themselves. This helps improve exercise adherence [Bartlett et al., 2011; Parfitt et al., 2006; Ekkekakis et al., 2011].

Although studies show that HIIT-F has similar or superior benefits for physical fitness compared to moderate-intensity continuous training, and indicates more enjoyment compared to conventional HIIT, the question remains whether the HIIT utilizing functional exercises is as efficient as that using running for improving health-related outcomes. Moreover, there was limited data on the efficiency and feasibility of HIIT-F in a university setting for female university students.

Therefore, the objectives of this study were to (1) determine whether the HIIT-F and running based HIIT (HIIT-R) had different effects on body composition and CRF in untrained female university students following a 12-week intervention. It was hypothesized that percentage body fat (%BF) and CRF would be improved in both functional HIIT-F and HIIT-R groups; (2) explore the heart rate (HR), perceived exertion, and exercise enjoyment responses during two HIIT protocols. We hypothesized that HIIT-F had a lower HR and perceived exertion responses compared to HIIT-R, whereas HIIT-F provided more enjoyment; (3) generate the participants’ perceptions towards HIIT-F via focus groups and reported how these data were used in the refinement of the HIIT-F protocol.

2. Materials and Methods

2.1. Participants

Twenty untrained healthy females who were physical inactive volunteered to participate the study. Participants who did not exercise for more than 2 hours weekly for at least 12 months were considered as physically inactive [Brisebois et al., 2018]. All participants were from the year 2 non-physical education degree in Ningbo University. Similar self-reported menstrual cycles were required, ensuring the simultaneity of testing and training. Interventions were suspended for 1 week during menstruation because the normal menstruation period lasted 3 to 10 days [Armour et al., 2019; Motahari-Tabari et al., 2017]. A randomized controlled research design was utilized, and participants were randomly assigned into the HIIT-R (n = 10) or the HIIT-F (n = 10) group. Participants were nonsmoking and were instructed to keep their dietary intake and lifestyle habits the same throughout the intervention. Nutritional supplements and intense exercise beyond their usual exercise habits were forbidden during the intervention period [Brisebois et al., 2018]. All participants were fully familiarized with test procedures and data collection prior to the intervention. Written informed consent was provided by all participants. The study was approved by Ningbo University ethics committee. Characteristics of participants at baseline were detailed in Table 14.

Table 14: Baseline characteristics of HIIT-R and HIIT-F group.

Parameter	HIIT-R group (n=10)	HIIT-F group(n=10)	p-value
Age (yrs)	20.7 ± 0.6	20.2 ± 0.7	p = 0.14
Height (m)	161.1 ± 3.1	160.7 ± 2.8	p = 0.76
Weight (kg)	56.6 ± 6.7	57.8 ± 6.7	p = 0.69
FFM (kg)	36.5 ± 1.7	36.0 ± 2.1	p = 0.53
BMI (kg/m^2)	21.9 ± 3.1	22.4 ± 2.2	p = 0.70
WHR	0.80 ± 0.0	0.80 ± 0.0	p = 0.79
% BF	31.6 ± 4.1	32.3 ± 3.6	p = 0.71
HR resting (bpm)	70.8 ± 13.9	72.5 ± 11.2	p = 0.77
VO_{2max} (ml/kg/min)	31.3 ± 7.0	32.8 ± 5.4	p = 0.61

Notes: BMI, body mass index; bpm, beats per minute; FFM, fat-free mass; HIIT-F, functional exercise based high in-tensity interval training; HIIT-R, running based high intensity interval training; $HR_{resting}$, resting heart rate; VO_{2max}, maximal oxygen uptake; WHR, waist to hip ratio; yrs, years old; %BF, percentage body fat.

2.2. Procedures

A randomized controlled trial was used in this study. Each participant completed 12 weeks of 36 sessions of HIIT-R or HIIT-F intervention (3 sessions per week), comprising of a total of 19 min per session (10 min warm-up, 4 min work-out and 5 min cool-down). All sessions were conducted and monitored at the same indoor stadium at the same time of day between 9:00-10:00 a.m. HR data were collected by an activity wristband (Mi Smart Band 5, Xiaomi, China) during each session to ensure that the required high intensity was achieved. The reliability and validity of heart rate index and distance index was reported in a previous study [Li, 2021]. The activity wristband was required to be worn tightly on the participant's wrist. HR index is measured based on changes in light transmittance caused by blood flow density using optical sensing technology and distance index was measured by the triaxial acceleration sensor. Two time points of measurement (pre- and post-intervention) were included. Participants were instructed to abstain from drugs, alcohol and intense exercise two days prior to the baseline and post-intervention measurements. On the first measurement day, participants presented themselves at 8:00 a.m. and underwent a body composition analysis, physical and physiology measures, as well as resting heart rate ($HR_{resting}$) and BP under standardized conditions. The assessment of cardiorespiratory fitness using a 12-min running test was completed on two days with 24 hours observed between each test. The first running test was scheduled on the first measurement day following completion all other tests, and the second trial was 24 hours later. The average of the two data sets was used to assess cardiorespiratory fitness. After resting for a week [Menz et al., 2019], both groups began the training intervention. Post-intervention measurements were performed using the same methodologies at baseline and were undertaken two days following total training sessions [Astorino et al., 2012]. During the intervention period, additional exercises were suspended.

2.3. Anthropometric Assessment

Participants were instructed to arrive at the laboratory 9:00 a.m. after a normal breakfast. Height was measured using a standard stadiometer protocol. BP and $HR_{resting}$ were measured by an automatic upper arm BP monitor (HEM-1000, Omron, China). Height, BP and $HR_{resting}$ were measured in duplicate and the average of two data sets was used for analysis. Before the body composition measurement, participants were asked to empty their bladder to minimize measurement error caused by "electrically silent" [Kushner et al., 1996]. Under the guidance of two skilled operators, participants wearing normal PE clothing stood on a bioelectrical impedance analysis (BIA) (MC-180, TANITA CO., China) and data were presented from associated software, including, weight, waist and hip circumference, fat mass, fat-free mass (FFM) and %BF. Body mass index (BMI) was calculated by dividing weight (kg) by height (m) squared. Waist-to-hip ratio (WHR) was obtained by dividing waist (cm) by hip (cm).

2.4. Cardiorespiratory Fitness Test

The most reliable and effective way to measure cardiorespiratory fitness is to record individual subjects VO_{2max} [Safrit et al., 1988]. Although maximal-effort tests were commonly used to measure VO_{2max}, for untrained participants, submaximal exercises can be used as a reliable measure to estimate this value. Cooper's 12-min running test was used to assess $VO2_{max}$ in this study. All participants completed 2 trials of the running test separated by 24 hours rest. After a 5-min warm up, participants were required to wear an activity wristband (Mi Smart Band 5, Xiaomi, China) and commence running on a standard 400-metre running track. Subjects were instructed to run as many laps as possible on a standard outdoor track during the 12 minutes test period. All participants were encouraged verbally and were instructed to focus on their own pace throughout the test. The experimenter verbally provided the elapsed time at 3, 6, 9 minutes. At the end of the 12-minute period, the experimenter called "stop". All participants ceased running and stood still, until the distance recorded. The total distance run was determined by measures obtained from the activity band and the average value of 2 trials was used for analysis. An estimated VO_{2max} was calculated by Cooper's standardized equation [Cooper, 1968]. The calculated VO_{2max} was highly correlated with the laboratory-determined one and had acceptable reliability and validity ($r = 0.897$) [Cooper, 1968].

2.7. Heart rate, exercise exertion, and enjoyment responses

The mean heart rate (HR_{mean}) and peak heart rate (HR_{peak}) were recorded by an activity wristband (Mi Smart Band 5, Xiaomi, China) during each 4-minute exercise session. These data were presented as a percentage of the individual's age-predicted maximal heart rate (HR_{max}) (220 – age). A cut-point of 80% of HR_{max} for HR_{mean} was used to ensure that the required high intensity was achieved during the intervention [Gibala et al., 2014; Maillard et al., 2018].

Borg's rating of perceived exertion (RPE) was used to assess participants' exercise exertion. Prior to the test, the RPE scale was explained by a trained researcher. The 15-point scale ranged from 6 to 20, with 6 indicting no exertion and 20 indicating maximal exertion.

Enjoyment responses were assessed by the Physical Activity Enjoyment Scale (PACES). The original 18-item PACES was used, and it was a validate tool to measure exercise enjoyment in university students aged 18-24 years [Kendzierski and DeCarlo, 1991]. Before the test, the 18-item PACES scale was explained by a trained researcher to each participant. Participants were particularly informed that 11 out of the 18 questions were scored in reverse. Participants were asked to rate the scale with the instruction "Please rate how you feel at the moment about the physical activity you have been doing". The responses were scored on a 7-point bipolar rating scale, with 1 point being considered "the least enjoyable" and 7 points being "the most enjoyable". The total scores ranged from 18 to 126 with higher scores indicating higher levels of exercise enjoyment.

Participants in both groups were asked to complete the RPE and PACES scales immediately on the completion of last session of the 4^{th}, 8^{th}, and 12^{th} intervention week.

2.6. Intervention

The intervention commenced one week after the last measurement day. Both the HIIT-R and HIIT-F interventions were conducted three sessions per week on Mondays, Wednesdays, and Saturdays for 12 weeks. In the case of participants being unable to attend a scheduled exercise session, exercise was performed on the next day and monitored by the same researcher.

Participants in HIIT-R group were required to complete 144 repetitions of maxi-mal shuttle running for a total exercise time of 72 minutes. Each bout included a 30s maximal shuttle run between cones placed 20m apart with a 30s recovery period between runs. The validity and reliability of 40 m maximal shuttle run as a measure of anaerobic performance has been reported previously [Baker et al., 1993]. Participants exercised 4 bouts per session for three sessions per week. Prior to the intervention, a familiarization trial was provided to acquaint participants with the training procedure. Running and recovery times were recorded manually using a digital stopwatch by the same experimenter. Participants were encouraged to run at individual maximal speed for each bout.

Participants in the HIIT-F group performed multiple functional exercises with their own body weight according to Tabata training [Tabata et al., 1996]. According to a recent study [Domaradzki et al., 2020], eight movements were implemented in each session (Table 15).

Table 15: Details of the functional high-intensity interval training intervention.

Duration	Frequency	Exercises	Exercise bout/recovery duration
12 weeks	3 sessions/week	Jumping Jacks	20s
		Stepping	10s
		High knees	20s
		Stepping	10s
		Side to side squat	20s
		Stepping	10s
		Mountain climbers	20s
		Stepping	10s
		Forearm plank to high plank	20s
		Stepping	10s
		Burpees	20s
		Stepping	10s
		Deep squat jumps	20s
		Stepping	10s
		Butt kickers	20s
		Stepping	10s

Participants were motivated to complete as many repetitions as possible of a given movement for 20 seconds, followed by a 10 second recovery in the form of low intensity stepping. The total training time of each session was 4 minutes. All training exercises were recorded by video, which was provided to HIIT-F participants prior to intervention to make sure they were familiar with the movements and procedures. This video was played on a screen during training intervention to ensure that participants kept up with the rhythm of each movement.

All sessions began with a standardized 10-min low-to-moderate running and stretching, followed by maximal shuttle run or functional training, and ended with a 5-minute cool-down and stretching.

2.7. Post-intervention focus groups

A focus group strategy was used to explore the experience of HIIT-F intervention from the participants. The post-intervention focus group were conducted after the post-test. All participants of the HIIT-F group were invited to attend the focus group. Two trained Ningbo University researchers were presented in the focus group. They were familiar to the participants during the pre- and post-measurements but had not been the exercise supervisors before. This minimized the interference from facilitators and encouraged participants to provide their comments freely. One researcher led the focus group, and the other one was responsible for taking notes. The focus group took place in the same indoor stadium they trained before, with the main facilitator sitting amongst the participants. The discussion warmed up with questions: have you ever done HIIT before and what type of HIIT have you done before, and then the participants' experience of the HIIT-F intervention was discussed. The following prompts were used: what is participants' experience of performing HIIT-F, what are the barriers/facilitators to your participation, is it easy to perform these functional movements, which movements do they like/dislike, and what do you think to improve the intervention. The whole process of discussion was audio-recorded on the mobile phone.

2.8. Statistical analyses

Statistical analyses were performed using SPSS, version 23.0 (Chicago, IL, USA). Data were presented as means ± SD. The normality was checked using Shapiro-Wilk test. Paired t-tests were used to estimate within-group effects and independent t-tests were carried out to examine differences between groups. A two-factor analysis of variance with repeated measures was used to analyze differences in outcome variables, with time as a within-group factor and group as a between-group factor. A significant time × group interaction was used to identify training-induced changes in variables. Data were subsequently checked by Bonferroni's post hoc test if a significant interaction was revealed. The effect size was considered small if $\eta^2 < 0.01$, moderate if $0.01 \leqslant \eta^2 \leqslant 0.14$ and large if $\eta^2 > 0.14$ [Richardson, 2011]. The significance level was established as $p < 0.05$.

The directed content analysis was used to analysis raw transcription data from the focus group [Hsieh and Shannon, 2005]. The structure of analysis was informed by previous studies [Elo and Kyngäs, 2008]. The data were transcribed verbatim by one researcher and checked by another. The transcript was imported into Nvivo 12 software (QSR international Pty Ltd., Australia). In the first stage, three researchers read and re-read the transcripts in Chinese and independently coded the transcript. One the three researchers was the main facilitator in the focus group, one did not take part in the research and was blinded to the research objective, and the remaining one was the author. A pre-defined categorization was used to code the transcripts, including barriers and facilitators to the intervention participation, the frequency, the intensity, the time, the length, and the exercise modality of intervention [Burn et al., 2021]. During the inductive coding, these three researchers discussed the codes combination and interactively developed sub-categories. Any discrepancies were resolved by discussion.

3. Results

All participants completed all sessions during the twelve weeks. There were no significant between-group differences of variables measured at baseline (Table 14).

3.1 Body Composition

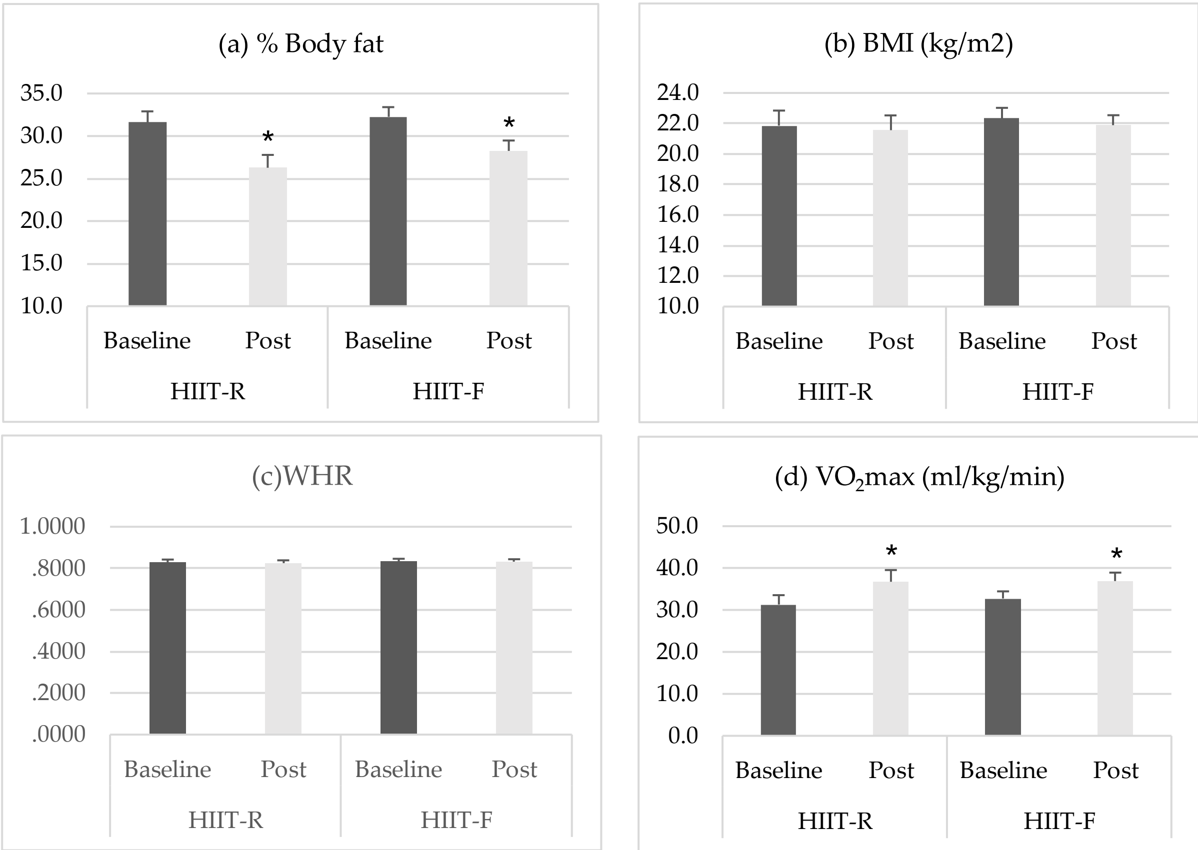
Body composition data are presented in Table 16. There was a significant decrease (17.4% ± 7.4% for HIIT-R and 12.6% ± 5.1% for HIIT-F, $p < 0.05$) in %BF for both groups (Figure 11a), with no interaction effect between HIIT-R and HIIT-F ($p > 0.05$). BMI (Figure 11b) and WHR (Figure 11c) did not change in both interventions ($p > 0.05$). FFM increased significantly in both groups (1.8% ± 1.4% for HIIT-R and 1.2% ± 1.2% for HIIT-F, $p < 0.05$).

Table 16: Body composition and cardiorespiratory fitness of HIIT-R and HIIT-F group.

	HIIT-R group (n=10)				HIIT-F group(n=10)				Interaction effect	
Variables	Baseline	Post	Δ	p-value	Baseline	Post	Δ	p-value	p-value	η^2
Weight (kg)	56.6 ± 6.7	55.8 ± 6.5	-1.3% ± 2.1%	ns	57.8 ± 6.7	56.6 ± 6.4	-1.9% ± 3.0%	ns	ns	0.020
FFM (kg)	36.5 ± 1.7	37.2 ± 1.8	1.8% ± 1.4%	p < 0.05	36.0 ± 2.1	36.4 ± 2.1	1.2% ± 1.2%	p < 0.05	ns	0.056
BMI (kg/m^2)	21.9 ± 3.1	21.6 ± 3.1	-1.3% ± 2.1%	ns	22.4 ± 2.2	21.9 ± 2.1	-1.9% ± 3.0%	ns	ns	0.018
WHR	0.8 ± 0.0	0.8 ± 0.0	-0.6% ± 0.9%	ns	0.8 ± 0.0	0.8 ± 0.0	-0.3% ± 0.5%	ns	ns	0.032
%BF	31.6 ± 4.1	26.3 ± 4.8	-17.1% ± 7.4%	p < 0.01	32.3 ± 3.6	28.3 ± 3.9	-12.6% ± 5.1%	p < 0.01	ns	0.118
HR resting (bpm)	76.5 ± 10.1	74.2 ± 7.4	-2.5% ± 5.5%	ns	77.8 ± 9.1	75.3 ± 8.6	-3.1% ± 5.3%	ns	ns	0.001
VO_{2max} (mL/kg/min)	31.3 ± 7.0	36.7 ± 8.8	17.1 ± 5.6%	p < 0.01	32.8 ± 5.4	36.9 ± 6.4	12.7% ± 6.7%	p < 0.01	ns	0.075

Note: BMI, body mass index; FFM, fat-free mass; HR, heart rate; HIIT-F, functional high-intensity interval training; HIIT-R, running based high-intensity interval training; $VO2_{max}$, maximal oxygen uptake; WHR, waist-to-hip circumference; %BF, percentage body fat; Δ (post-baseline)/baseline; ns, no significance; Partial η^2 value for effect size.

Figure 11: Changes in (a) BMI, (b) %Body fat, (c) WHR, and (d) VO_{2max}



Note: BMI, body mass index; VO2max, maximal oxygen uptake; WHR, waist-to-hip circumference; * significantly different from baseline at p < 0.05; ** significantly different from baseline at p < 0.01.

3.2 Resting Heart Rate and Blood Pressure

$HR_{resting}$ ($p < 0.05$) was improved compared to baseline in both intervention groups, while no interaction effect was observed. Resting systolic BP and diastolic BP remained unchanged ($p > 0.05$) after training in both HIIT-R and HIIT-F groups.

3.3 Cardiorespiratory Fitness

VO_{2max} data was calculated from the following equation according to Cooper's. VO2max (ml/kg/min) = (distance(m)-506)/45. There was no difference on baseline value between groups. A significant increase ($p < 0.05$) in VO_{2max} was demonstrated in both training groups compared to baseline measures, while no significant intervention × group interaction was revealed between HIIT-R and HIIT-F after intervention compared with baseline (Figure 11d). ($p > 0.05$). The percentage of changes in VO_{2max} were 17.1% ± 5.6% and 12.7% ± 6.7% in HIIT-R and HIIT-F respectively.

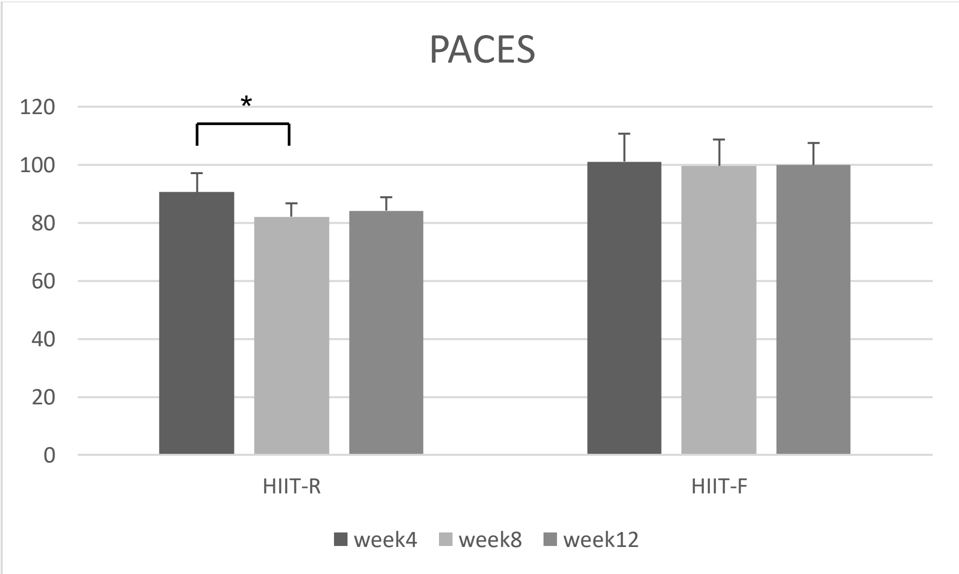
3.4 Heart rate and exercise exertion, and exercise enjoyment responses

Over the 36 sessions, the average HR_{mean} for HIIT-R was 83.5% of HR_{max}, with a between-subject SD of 1.2% and a within-subject SD of 0.9%. The average HR_{peak} for HIIT-R was 90.4% of HR_{max}, with a between-subject SD of 2.1% and a within-subject SD of 1.1%. For HIIT-F group, the average HR_{mean} for was 82.8% of HR_{max}, with a between-subject SD of 2.5% and a within-subject SD of 1.4%. The average HR_{peak} was 89.3% of HR_{max}, with a between-subject SD of 3.3% and a within-subject SD of 1.8%. Both HIIT-R and HIIT-F were delivered at a satisfied intensity for all participants throughout the intervention. There was no statistically significant difference on the HR_{mean} or HR_{peak} between groups ($p > 0.05$).

The average RPE calculated for 4^{th}, 8^{th} and 12^{th} week were 16.8 ± 0.6, 16.8 ± 0.4, and 16.6 ± 0.7, respectively for HIIT-R groups. For HIIT-F group, the average RPE were 14.4 ± 0.8, 14.2 ±0.8, and 14.3 ± 0.8, respectively. No differences on RPE between intervention weeks were observed for both groups. We found statistically significant differences on RPE between the HIIT-R and HIIT-F group on each of the three intervention weeks ($p < 0.05$), indicating that HIIT-R was perceived to be harder than HIIT-F with the similar HR responses.

The changes on exercise enjoyment in both groups were shown in Figure 12. There were significant main group effect ($p < 0.05$, $\eta^2 = 0.641$), with no interaction effect ($p > 0.05$, $\eta^2 = 0.067$) on PACES. Moreover, the main time effects were observed at week 4 ($p < 0.05$, $\eta^2 = 0.315$), week 8 ($p < 0.05$, $\eta^2 = 0.621$) and week 12 ($p < 0.05$, $\eta^2 = 0.491$). Both group and time effect were large. The enjoyment response decreased significantly from week 4 to the following weeks in HIIT-R group ($p < 0.05$), whereas it remained unchanged throughout the intervention in HIIT-F group ($p > 0.05$).

Figure 12: Scores of physical activity enjoyment scale (PACES) for HIIT-R and HIIT-F group



Note: PACES, physical activity enjoyment scale; HIIT-F, functional high-intensity interval training; HIIT-R, running based high-intensity interval training; * significant difference at $p < 0.05$.

3.5 Focus groups

One focus group was conducted that resulted in one transcript with 32 pages of raw transcription data. The main categories were described, with illustrative quotes.

Frequency: The frequency of 3 times weekly was accepted by all participants. Daily HIIT sessions would make one feel tried, while once weekly might not enough to see improvements.

"If I did HIIT once a week, it's hard to imagine any significant improvement on the fitness. If there is no gain, then I will not be interest in it anymore".

Intensity: Participants indicated that the "individual nature" of HIIT-F was important to facilitate engagement. A relative intensity, rather than an absolute one, was used. HIIT-F was executed with participant's own body weight and was performed at the highest self-selected intensity. It enabled participants with different fitness level to exercise at the same time.

"The intensity is really fit because I can slow down if I feel extremely uncomfortable".

"At first, I can only complete 4 Burpees within 20 seconds, but then I can complete 6. Although it is very hard, I see the improvement. That encourages me to complete more."

"I am not good at running and often fall behind. That makes me lose interest in running. However, during the functional HIIT, I don't have to compete with others, I only compete with myself."

Timing: A fixed time schedule of HIIT were conducted throughout the intervention. Compared to a flexible session, a fixed session is thought to be an effective way to increase exercise motivations. There was no consensus on what time of the day they would like to perform HIIT, whereas there was an agreement that it should not be done on an empty or full stomach. Moreover, some participants indicated that it should not be done before bedtime.

"Training together seemed a good idea for me. If a flexible session was conducted, I am afraid I will forget it or feel too lazy to exercise".

"Doing HIIT makes me excited all day. I don't think I would be able to sleep if I did HIIT at night".

Length: Participants highlighted that the short length of session (19 minutes) was the key to getting them to participant. The short session minimized the exercise barriers for university students since they already had too many classes and work.

"I did not have enough time to exercise before, but I am interested when I hear that this training only takes about 20 minutes".

Modality: Participants consistently rated Burpees as the least favorite. While there was no consensus on the most favorite, simple movements such as jumping jacks and high knees were the most reported. The combination of different functional movements was very attractive. More importantly, most participants suggested that it is difficult to keep the 8 different movements in mind and practice in a pre-designed order.

"We are usually asked to complete 30 or 50 high knees. I've never done high knees in this way before, and it makes me more motivated".

"Although there was a video, it was hard to follow. I often forget the next movement."

"Some of the movements are so hard to remember that I must watch videos while doing exercises. This distracts me".

Experience of HIIT-F: Participants' experiences of HIIT-F were described with the following subcategories: physiological responses and psychological responses.

Physiological responses: Exercise exertion such as breathlessness, accelerated heart rate and muscular fatigue was reported by most of participants.

"My heart beats fast. I think I can't sit down immediately when I finished the session".

"I feel my thigh and hip hurt after the training".

"I felt my heart beating fast all morning".

Psychological responses: Most participants described themselves as more energetic after participating in the intervention. Some participants described that this intervention made them feel more confident. All participants reported that they enjoyed the functional HIIT.

"I feel full of energy for the whole day".

"I feel that my shape has been improved after the intervention and this makes me more confident".

4. Discussion

The present study aimed to compare the effects of running and functional HIIT on body composition and CRF. The second objective was to investigate the physiology and psychology responses after these two HIIT protocols. Furthermore, this study was aimed to explore participants' perceptions towards HIIT-F. The primary finding was that HIIT-F was as effective as HIIT-R for the promotion of body composition and CRF in healthy inactive young females. Furthermore, HIIT-F was able to elicit similar HR responses compared to HIIT-R whereas HIIT-F was perceived to be less hard and more enjoyable. We also found that participants were satisfied with HIIT-F, while measures to improve HIIT-F protocol still need to be developed.

4.1. Body composition

Our findings that HIIT-R and HIIT-F had positive effects on body composition promotion regarding to reducing %BF were consistent with other researchers. A previous study [Racil et al., 2016] showed improved body mass, BMI, and %BF among obese females after a total of 108 minutes HIIT-R. Similarly, other research [Tjønna et al., 2009] found HIIT-R was effective in reducing BMI and %BF in overweight adults. Also, for individuals with normal BMI, body composition was improved by decreasing fat mass and increasing lean mass after the 6 weeks' HIIT-R intervention [Macpherson et al., 2011].

Not surprisingly, benefits for body composition were also found in other studies investigating HIIT-F. Improved %BF was reported after a 5-week, three times a week HIIT-F intervention [Heinrich et al., 2015], and further studies also indicated a beneficial influence of HIIT-F on body composition [Murawska-Cialowicz et al., 2015].

However, a recent study indicated that %BF was significantly improved after an 8-week HIIT-F, while body mass was unaltered [Brisebois et al., 2018]. Likewise, after 16-week of HIIT-F, a significant decrease in %BF was observed with no changes in body mass [Feito et al., 2018b]. HIIT-R studies provided similar results [Buchan et al., 2013; Weston et al., 2016]. These results were consistent with our findings that although %BF was improved, body mass and BMI was not affected by the intervention. The improved %BF might be explained by the significant increase in lean muscle mass ($p = 0.001$ for HIIT-R and $p = 0.006$ HIIT-F) without significant changes in body mass ($p= 0.064$ for HIIT-R and $p = 0.051$ for HIIT-F). The non-significant change in BMI may be due to the following reasons: the insufficient exercise duration per session (2 mins vs. 6-10 mins); the uncontrolled dietary intake during the intervention and the characteristic of participants regarding body weight. This suggestion has been highlighted in a recent systematic review [Batacan et al., 2017] which indicated that, for normal weight populations, low-volume HIIT is inefficient for body composition improvement. Furthermore, several studies indicated that HIIT-R and HIFT had a more significant effect on weight loss or body fat loss among obese individuals [Sperlich et al., 2017; Domaradzki et al., 2020; Racil et al., 2016; Tjønna et al., 2009].

Finally, no significant interaction effect was revealed for any variable of body composition. This suggests that HIIT-R and HIIT-F were equally effective in the improvement on body composition.

4.2 Cardiorespiratory fitness

VO_{2max} was assessed in the present study to estimate the effects of HIIT-R and HIIT-F on cardiorespiratory fitness. Running based HIIT had been evidenced to increase VO_{2max} in numerous previous investigations. Several studies reported significant increases in VO_{2max} after HIIT [Astorino et al., 2012; Dias et al., 2018; Batacan et al., 2017]. Furthermore, a systematic review also showed that HIIT was beneficial for VO_{2max} improvements among healthy young people [Gist et al., 2014a]. Nevertheless, there was no consensus on the effect of HIIT-F on VO_{2max}. Some studies investigating HIIT-F had shown an improvement in VO_{2max} [Menz et al., 2019; Murawska-Cialowicz et al., 2015; Nieuwoudt et al., 2017]. On the contrary, recent research found VO_{2max} improvement only in underweight and overweight boys with no change among normal weight people [Domaradzki et al., 2020]. Some studies reported no significant changes in VO_{2max} after a 6-week HIIT-F protocol [Crawford et al., 2018; Sobrero et al., 2017].

In our study, participants from both the HIIT-R and HIIT-F groups experienced improvements in VO_{2max} (17.1% ± 5.6% and 12.7% ± 6.7%, respectively). In line with the magnitude of our results, an increase of 8% in VO_{2max} was found after a low-volume HIIT-F [McRae et al., 2012]. It should be noted that, in the current study, the enhanced VO_{2max} observed in the HIIT-F group was significantly higher than that of previous studies. VO_{2max} has been reported to improve by 5% after a HIIT-F with no aerobic exercise [Gettman and Pollock, 1981]. Another study showed a moderate improvement in VO_{2max} of 6.3% [Brisebois et al., 2018]. The greater response of VO_{2max} to HIIT-F in our study could be explained by the following reasons: firstly, improvements in VO_{2max} was related to the testing modality [Magel et al., 2075]. Cooper's 12min run test demonstrated a systematic bias in favor of higher-scoring individuals [Penry et al., 2011]; secondly, a longer duration (12 weeks vs. 6-8 weeks) in the implementation of functional exercises. Short or low-volume training reported no improvements in VO_{2max}, which required continuous training [Sultana et al., 2019; Rodas et al., 2000]. However, other investigations reported that the extent of improvement was not clearly related to training duration, but to training intensity [Gist et al., 2014a; Sloth et al.,2013]; and finally, the magnitude of improvement in VO_{2max} can be attributed to the fatigue index, which was not measured in our study [Astorino et al., 2012].

Although high intensity running and functional training were both beneficial for cardiorespiratory fitness promotion, few studies compared the effectiveness of these two exercise modalities in VO_{2max} enhancement. In the current study, we controlled for the same intensity and duration of intervention and found that, surprisingly, there was no significant difference in changes in VO_{2max} between HIIT-R and HIIT-F groups. Generally, running showed higher oxygen consumption for the same intensity compared to other modalities [Viana et al., 2019]. Our finding was partially in line with a previous study [Gist et al., 2014b], that indicated no significant differences in VO_{2max} promotion between high intensity cycling and high intensity functional training. The result from the present study illustrated that functional training was as effective as running for CRF improvement when performed at the same high intensity.

4.3. Feasibility

Feasibility was essential for a practical intervention. Although the intervention was conducted on a fixed approach, the attendance was satisfactory of 100%. This was similar to a previous HIIT intervention study, in which a 99% of attendance was reported [Allison et al., 2017]. However, there was no detailed description about the time schedule of sessions. The high attendance might be due to the fact that participants were allowed to make up missed session on another day. Therefore, a fixed plus flexible mode was used in this study exactly. Furthermore, the small sample size might be contributed to the high attendance. However, given the small sample size in the current study, the feasibility of such supervised compensatory sessions in the intervention with large sample size is questioned. Instead of the fixed session, a recent the study by Burn et la. (2021) used a flexible approach. Participants were asked to attend any 3 sessions within one week. The reported attendance of HIIT session was 83% [Brun et al., 2021]. Controversy remained on the most optimal approach to schedule sessions. The goal was to enhance the attendance while maintaining a pre-determined exercise frequency.

Although the attendance was high in the present study, it did not provide further information on the exercise fidelity [Taylor et al., 2015]. For HIIT intervention, in addition to session attendance, the exercise intensity achieved should be evaluated. Both HIIT-R and HIIT-F were delivered at a high intensity ($\geqslant$ 80% of HR_{max}), with no differences between groups. Therefore, our hypothesis that HIIT-F elicited lower HR responses than HIIT-R was not supported. Contrast to our finding, HIIT-F was reported to had lower HR responses than HIIT-R in a previous study [Menz et al., 2019]. It should be noted that, at the same intensity, running resulted in high oxygen consumption compared to other exercise modalities including cycling, burpees, jumping jacks and resistance trainings [Viana et al., 2019]. It was hard to explain why these two HIIT protocols had similar HR responses. This might be because we used the shuttle run instead of the sprint. Another study compared the HR responses between sprint interval cycling and HIIT-F and there was no difference on HR_{peak} between two HIIT protocols [Gist et al., 2014b]. Although a long recovery interval of 4 minutes was used in Gist et al. (2014)'s protocol, it appeared that HIIT utilizing repeated whole-body functional exercises was able to induce cardiorespiratory stimulus, conferring physiological adaptions similar to those reported for traditional running or cycling HIIT. This was supported by our finding related to the similar CRF improvement observed between groups. Although the similar HR responses were observed in the current study, less exercise exertion were reported by participants involved in the HIIT-F group.

For HIIT-F, the between-subject SDs were 2.5% and 3.3% for HR_{mean} and HR_{peak}, respectively. It revealed that the variability of exercise intensity was small between participants. The smaller within-subject SD indicated that individual participants kept up a similar exercise intensity throughout the intervention.

4.4 Perceptions on HIIT-F

The post-intervention focus group provided participants' perception of the HIIT-F intervention as a whole. Overall, the frequency, intensity, time, and length of the HIIT-F protocol were reported to be satisfactory and acceptable. Additionally, a fixed, group-based, supervised nature of intervention were favored, which made it possible to integrate HIIT-F into physical education classes.

In line with previous studies, unpleasant affective responses were reported such as breathlessness, accelerated HR and muscular hurt [Ekkekakis, 2003]. A previous study indicated that these affective responses might have negative impact on future exercise behaviors [Rhodes and Kates, 2015]. However, this finding was based on moderate-intensity exercises and there was limited data on whether the HIIT induced unpleasant affective responses will affect future behaviors. With regard to the current study, participants reported that they were really enjoyed and felt more energetic after the intervention.

The 8 different functional movements were selected according to Tabata's recommendation. Participants highlighted the importance of involving a variety of movements in a session. This facilitated the exercise enjoyment. However, the more is not always the better. Most participants emphasized it was difficult to follow so many movements and to perform burpees. According to findings from the focus group, the HIIT-F protocol will be conducted 3 sessions per week with a fixed plus flexible, group-based and supervised manner. Furthermore, the protocol will be refined by reducing 8 movements to 4. 4 movements were performed with a pre-designed order and then repeated. Finally, jumping jacks, high knees, squat jumps, and mountain climbers were selected according to participants and PE teachers' suggestions. Physiology and psychology responses on the refined HIIT-F protocol, as well as movement behaviors after HIIT will be examined in the next study.

A general limitation in the HIIT-F investigation was the different types of functional exercises that were included. The results might be dissimilar if HIIT-F was performed with other combinations of movements. Secondly, the results of our study came from a small sample size and a non-exercising control group was not used. Thirdly, dietary intake was not controlled during the intervention, and the total calories consumed were not calculated. Finally, although the time-matched design was used to compare the training effects between HIIT-F and HIIT-R, the total exercise energy expenditure was not assessed for both groups. This made the exercise volume incomparable between groups. Since the exercise volume was vital for exercise effects, further studies should include exercise energy expenditure assessment to make the results more comparable and to confirm findings. In addition, the fatigue index was not measured during the aerobic test.

5. Conclusions

Twelve weeks of high intensity training based on functional exercises was effective on similar improvements on body composition and cardiorespiratory fitness among healthy inactive university female students. HIIT-F with self-selected intensity was able to elicit a high intensity in this population. Moreover, HIIT-F showed superior perceived exercise exertion and enjoyment compared to HIIT-R. Finally, HIIT-F revealed strong exercise adherence and was highly accepted. The feasibility of conducting a HIIT-F intervention in the university setting was largely confirmed.

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Chapter 7: Effects of Low-Volume High-Intensity Interval Exercise on 24 h Movement Behaviors in Inactive Female University Students (Study 3)

1. Introduction

Physical inactivity has been significantly associated with a wide range of adverse health outcomes, such as an increased risk of cardiovascular diseases, Type 2 diabetes, metabolic syndrome [Alessa et al., 2017; Balducci et al., 2022; Teixeira et al., 2020; Cunningham et al., 2020], as well as increased mortality [Whitlock et al., 2009]. Recently, the rising prevalence of physical inactivity worldwide has become a major public health concern, and more than one in four adults fail to follow the minimum recommended levels of participating in 150 min of moderate physical activity (MPA) per week [Guthold et al., 2018]. Reduced physical activity (PA) and increased sedentary time (ST) are also common among students, especially when they attend university [Vella-Zarb et al., 2009; Kwan et al., 2012; Kljajević et al., 2021]. Moreover, only one of five female students meet the weekly PA recommendations [Grasdalsmoen et al., 2019]. ST for students includes attending classes, studying, and sitting in front of computers. This accounts for most of the usable daytime and leaves limited time for PA among university students [Cotton et al., 2016; Carballo-Fazanes et al., 2020]. Therefore, there is a need to identify an efficient and effective type of physical activity to increase the level of PA participation in this population.

Recently, the prevalence and popularity of high intensity interval exercise (HIIE) among young adults has provided an exciting type of exercise and health promotion intervention, but its efficacy varies across studies [Dias et al., 2018; Sultana et al., 2019; Batacan et al., 2017; Jelleyman et al., 2015; Kessler et al., 2012]. The "activitystat" hypothesis may be one of the potential explanations for the varied efficacy observed [Rowland, 1998]. This hypothesis suggests that increased energy expenditure during PA must be compensated for by the conservation of energy by changing the accumulation of other movement behaviors. Such changes were defined as compensatory movement behaviors [King et al., 2007], and in the context of HIIE, indicate that participants compensate for increased PA during HIIE by being less active following HIIE [Rangan et al., 2011]. In contrast, some studies have indicated that activity synergy occurs because participating in exercise helps individuals to stay active for the rest of the day [Cooper et al., 2003; Goodman et al., 2011; Long et al., 2013].

Recently, the prevalence and popularity of HIIE among young adults have made it an exciting type of exercise and health promotion intervention, especially among females as it is promoted as a time-efficient and effective strategy to reduce fat [Maillard et al., 2018]. Although the effects of HIIE on improving health outcomes has been investigated by numerous studies [Sultana et al., 2019; Astorino et al., 2012; De Revere et al., 2021; Gibala, 2018], few studies have examined the effects on movement behaviors following high intensity exercises. A previous study evaluated the within-day changes of sedentary behaviors after vigorous physical activity and reported an in-crease in subsequent sedentary time [Skovgaard et al., 2019]. Another crossover study on overweight boys examined the behavioral changes after a single bout of moderate or vigorous exercise. The author indicated a slightly higher increase in sedentary time after vigorous exercise than moderate in the following 4 days, and furthermore, the time spent in vigorous intensity physical activity (VPA) decreased greatly after vigorous exercise [Paravidino et al., 2017]. While in the study conducted in adults, time spent in sedentary activities was significantly reduced during HIIE [Nugent et al., 2018].

When investigating movement behaviors, it is important to note that the length of the day is limited to 24 h, suggesting an increases in the time spent in one behavior must result in a decrease in the time spent in associated behaviors. There is potent evidence for sedentary behaviors [Sjöros et al., 2020; Zheng et al., 2021], sleep [Itani et al., 2017; Peltzer and Pengpid, 2016; Zhu et al., 2021], and MVPA [Bakker et al., 2021; Liu et al., 2020; Wu et al., 2017], and emerging evidence for LPA to be associated with health outcomes [Batacan et al., 2015; Chastin et al., 2019]. Moreover, the al-location of whole 24 h time is associated with health outcomes across the lifespan [German et al., 2021; McGregor et al., 2018; 2021]. Therefore, collecting data on all movement behaviors, including PA performed at all intensity categories, sedentary behaviors, and sleep over a full day (24 h) may pro-vide researchers with the best method to observe any changes in the time accumulated in other behaviors, resulting from a single or combined behavioral intervention [Tremblay et al., 2016]. Understanding the 24 h movement behavior changes after HIIE can improve our cur-rent knowledge in relation to VPA adaptations and responses and concurrently aid in prescribing PA and health promotion programs. However, there is a paucity of re-search on the effects of HIIE on 24 h movement behaviors among young women. Therefore, the main purpose of this study, therefore, was to examine changes in 24 h movement behaviors following low-volume HIIE among inactive female university students. Secondly, this study also examined the perceived exertion and fidelity to gain insight into whether such vigorous intensity exercise will be acceptable for inactive female university students. We hypothesized that ST would increase following HIIE. Furthermore, we expected to see a disparity in the magnitude of increase in ST among participants with the highest mean heart rate (HR_{mean}) during exercise. We also hypothesized that the greatest increases in VPA will be observed on the exercise day.

2. Materials and Methods

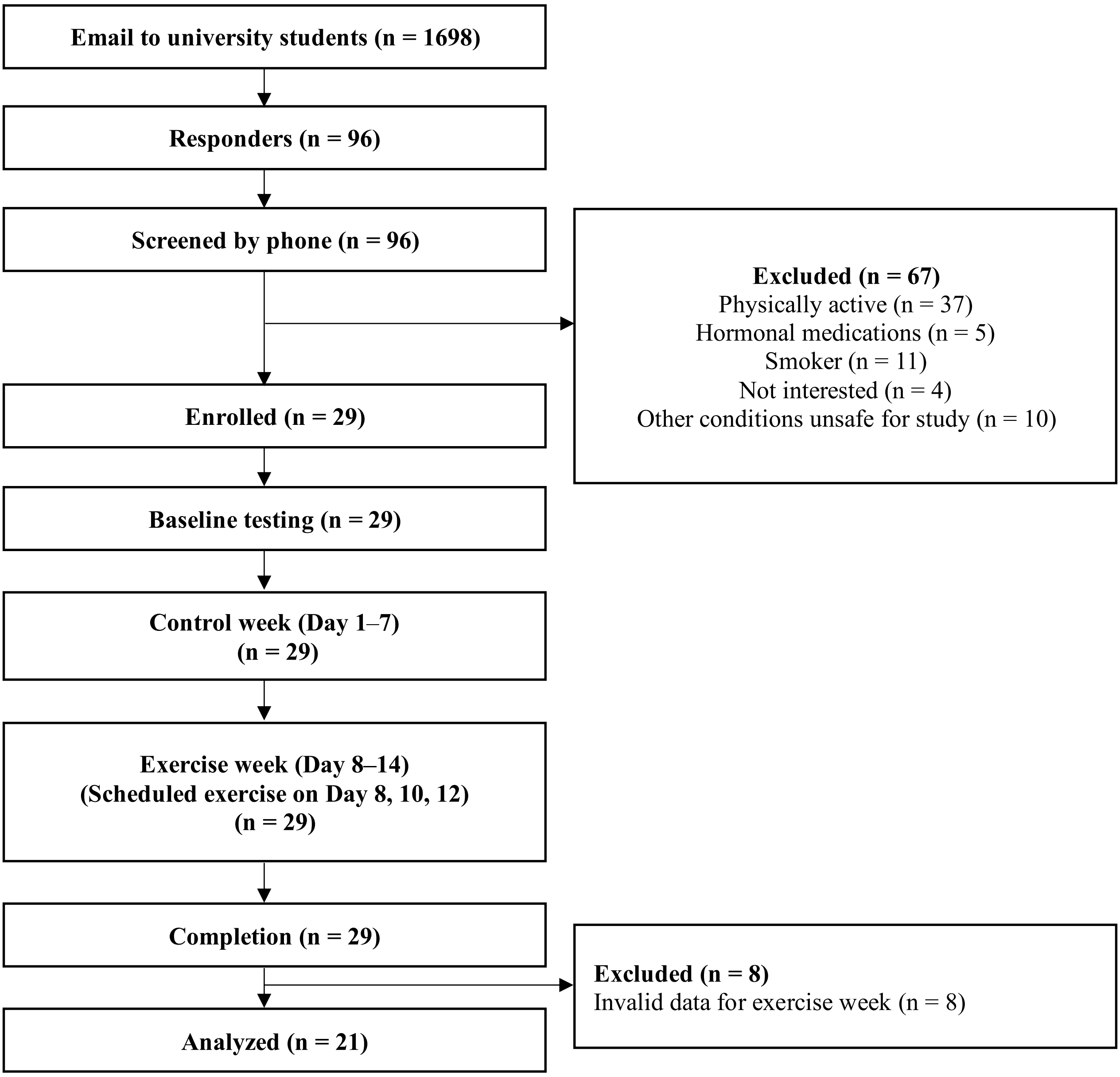
2.1. Participants

Healthy female students were recruited from a university. The inclusion criteria included having an inactive lifestyle, which was defined as engaging in less than 90 min of moderate intensity activity per week for a period longer than three months [Riebe et al., 2018]. Participants were required to complete a PAR-Q+ questionnaire for further eligibility screening. Participants who were severely obese (BMI ≥ 40), who had smoked in the past 6 months, took hormonal medications, or who were diagnosed with medical conditions were all considered unsuitable for high intensity exercises and were excluded. Finally, 29 eligible participants were included in this study. Participants were instructed to maintain their normal dietary and lifestyle habits throughout the intervention. The study was approved by Ningbo University ethics committee (RAGH20213744). Written informed consent was provided from all participants prior to the intervention and data collection.

2.2. Procedures

A quasi-experimental design was used for data collection. In this 2-week study, all participants were identified as their own controls. Previous studies recommended at least 7 consecutive days, which was required to assess habitual PA [Skender et al., 2016], and a frequency of 3 times per week was preferred for HIIE to provide health promotion [Stavrinou et al., 2018]. Therefore, to make it comparable, the protocol in this study began with a control week during which participants were asked to maintain their PA as usual. This was followed by an intervention week where each participant was required to engage in three sessions of Tabata style HIIE, with a one-day interval between each session. Because of menstrual cycle differences, the starting times (at the end of menstruation) were different between participants, with the last participant starting 20 days later than the first. On the day before the commencement of the protocol, participants were asked to at-tend the laboratory. During the visit, participants were equipped with an accelerometer to assess movement behaviors over the two weeks including the exercise sessions. Furthermore, they were instructed to record exercise and sleep time in individual logbooks. They were fully familiarized with exercise protocols, data collection procedures, and had completed baseline assessments prior to the two-week intervention. During the exercise day, the participants were required to attend the laboratory and complete the HIIE, which was supervised by a trained researcher. During each session, a heart rate monitor was used to record the HRmean and peak heart rate (HRpeak) during exercise, which was used as a measurement of exercise fidelity. Furthermore, Borg's rating of perceived exertion (Borg's RPE) was recorded after each session to assess subjective perception of effort during exercise. At the end of the two-week protocol, participants returned the accelerometer and the sleep and exercise log. Flow diagram of samples and study timeline was outlined in Figure 13.

Figure 13: Flow diagram of sample and study timeline



2.3. Measurement

Anthropometry

At baseline, body mass was determined using a calibrated bioelectrical impedance analysis (BIA) (MC-180, TANITA CO., Dongguan, China) to the nearest 0.1 kg. Height was measured using a stadiometer (HGM-6, Shanghai, China) to the nearest 0.1 cm. Body mass index (BMI) was also calculated using standard equations. Standardized procedures were used for all subjects during all measurements.

Aerobic capacity

Maximal oxygen uptake (VO_{2max}) was used to measure the aerobic capacity of participants. The modified YMCA submaximal cycle ergometer test has been used previously as a reliable measure to estimate oxygen uptake in adults (Ergoselect 100, Ergoline GmbH, Bitz, Germany) [Beekley et al., 2004]. This modified test includes 2–4 stages, with each stage lasting 3 min. After resting for 10 min, the participants began to cycle at 0.5 kg (25 W; 150 kg·m/min), which increases based on stable heart rate recordings during the last 1 min in stage 1. Participants were then asked to maintain a steady pace of 50 rpm throughout the test. Heart rate was monitored and recorded throughout the test. Stable heart rates from two consecutive stages between 110 bpm and 85% age-predicted maximal heart rate were used to predict VO_{2max}.

Movement behaviors

Participants' movement behaviors were measured for two weeks (14 consecutive days) using a triaxial accelerometer (wGT3X-BT, ActiGraph, Pensacola, FL, USA). Participants were instructed to wear the accelerometer on the non-dominant hip, which is a position used previously to measure physical activity [Trost et al., 2005]. Participants were asked to wear the accelerometer throughout all waking hours except when participating in water-based activities (e.g., swimming and bathing). All participants were provided with instructions concerning the charge and care for the device.

The ActiLife software (Version 6.13.4) was used to initialize the accelerometers and process the data using a midnight–midnight 24 h format. The device was initialized to commence at 12:00 a.m. on Day 1 and to terminate at 12:00 a.m. on Day 14. In this study, raw triaxial acceleration data was collected at a sampling rate of 30 Hz and processed at 10-s epochs with a low frequency extension applied to capture lower magnitude activities [Barreira et al., 2018]. Sleep epochs were identified using the sleep log and then removed. Additionally, in this study, the non-wear-time validation tool available in ActiLife software was applied. The software provided two defaults (Troiano 2007 and Choi 2011) with an allowance for customizing. We conducted a randomized subgroup trial (n = 5). After calculating the non-wear period using both defaults, the criteria of Choi 2011 were selected following checks from participants. The default included a minimum length of 90 min for a consecutive 0 counts with 2 min of spike tolerance in an up/down stream small-window length of 30 min [Choi et al., 2011]. After removing sleep and non-wear periods, as well as invalid data, the remaining data were used to identify the valid control week. This was defined as > 4 of 7 days, with > 10 h per day during waking time. The valid exercise week was defined as 7 days, with > 10 h per day of waking time. Data including both valid control and exercise weeks were used in the final analysis.

The time spent participating in sedentary behaviors and PA at different intensities was calculated by using the Freedson Adult algorithm. The Freedson cut-off points were applied with sedentary defined as <100 counts per minute (cpm), LPA as 100–1951 cpm, MPA as 1952–5724 cpm, VPA as 5725–9498 cpm, and MVPA as >1951 cpm. TPA was identified as the average daily vector magnitude cpm [Slater et al., 2021]. A prolonged sedentary bout was identified as a minimum of consecutive 30 min in which <100 cpm were recorded [Dunstan et al., 2012].

Exercise exertion

Borg's RPE was used to assess participants' exercise exertion. The 15-point scale ranged from 6 to 20, with 6 indicting no exertion and 20 indicating maximal exertion.

Exercise protocol

Participants were required to perform the exercise intervention on Day 8, Day 10, and Day 12 of the designated two-week period. If participants were unable to engage in a scheduled exercise, the exercise was performed on the next day and supervised by the same researcher. On the first visit, participants were instructed to follow the "Timer Plus" App and a familiarization trial was conducted to acquaint participants with exercise protocols.

All exercise sessions included a 10-min low-to-moderate warm-up, a 4-min maximal work-out, and a 5-min cool-down and stretching. The Tabata style HIIE protocol included 4 movements (jumping jacks, high knees, squat jumps, and mountain climbers in sequence) with subjects using their own body weight based on the Tabata training recommendations [Tabata, 2019]. During the 20 s exercise period, participants were encouraged to work maximally and to repeat the movements as many times as possible, and then rest for 10 s. There were 8 bouts in each session, with 4 movements completed in sequence that were repeated.

Participants were verbally encouraged to move using maximal efforts. To assess exercise fidelity, a chest strap heart rate monitor (Polar H10, Polar, Malaysia) was ap-plied during each session. Monitors were placed close to the heart and attached by a band to the chest using non-slip silicone dots and a buckle. Heart rate data per second were recorded and processed using the Polar Flow. Maximal heart rate (HRmax) was calculated using the age-predicted equation (i.e., 220-age), and according to the Tabata protocol, 90% of HRmax was required during the 6th bout.

2.4 Statistical Analysis

Sample size was estimated by G * Power (version 3.1.9.7) (Heinrich Heine University, Dusseldorf, Germany) using a priori based on the difference between paired means. The effect size was set at 0.80 and alpha was set at 0.05. After calculation, 15 participants were required to achieve 80% power.

Descriptive data were summarized as mean ± SD. Normality was checked using the Shapiro–

Wilk test. The correlation was examined using the Pearson's product moment correlation coefficient. For weekly basis analysis, a paired t-test was used to compare the mean differences of sedentary behaviors (ST, PST, BPST), physical activities (LPA, MPA, VPA, MVPA, and TPA), and sleep between the control week and exercise week. For an additional daily analysis, a repeated measures analysis of variance with the Bonferroni post hoc test was performed to analyze any differences in sedentary behaviors, physical activities, and sleep during the control week, exercise day, and the following day. Linear regression modeling was used to assess the effects of VO_{2max}, exercise exertion, and HRmean on changes in movement behaviors. SPSS for windows, version 23.0 (Chicago, IL, USA) was used for statistical analysis, and the significance level was set as $p < 0.05$.

3. Results

A total of 29 participants were involved and finally completed all sessions during the three weeks, with all participants attending the exercise on the scheduled day. 21 (72.4%) participants met the inclusion criteria for final analysis, with 19 (90.5%) recording all 14 valid days, and 2 (9.5%) recording 13 valid days (one invalid day on baseline week). The mean wear day was 6.9 ± 0.3 days during the control week and 7.0 ± 0.00 days during the exercise week. The mean daily wear time was 23.1 ± 1.4 and 23.3 ± 0.5 h for the control and exercise week respectively. Baseline characteristics are presented in Table 17. Correlation data for movement behaviors at baseline are detailed in Table 18.

Table 17: Characteristics of participants at baseline (n = 21)

Variables	Mean ± SD
Age (years)	25.4 ± 1.0
Weight (kg)	60.9 ± 4.9
Height (m)	165.4 ± 3.9
Body mass index (kg/m^2)	22.3 ± 1.9
VO_{2max} (mL/kg/min)	36.8 ± 4.3
Accelerometry (days)	13.9 ± 0.3
Wear time (h/d)	23.6 ± 0.2
Movement behaviors:	
LPA (min/d)	269.4 ± 55.5
MPA (min/d)	148.3 ± 47.4
VPA (min/d)	11.1 ± 7.2
MVPA (min/d)	159.5 ± 52.0
TPA (cpm)	1411.5 ± 381.5
ST (min/d)	446.7 ± 98.9
PST (min/d)	160.4 ± 54.4
Sleep (h/d)	9.0 ± 1.1

Note: bpm, beat per minute; cpm, counts per minute; h/d, hours per day; LPA, light intensity physical activity; min/d, minutes per day; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST, sedentary time; TPA, total physical activity; VPA, vigorous intensity physical activity.

Table 18: The correlation data between movement behaviors at baseline

		1	2	3	4	5	6	7	8	9
1	LPA	–								
2	MPA	0.666 **	–							
3	VPA	0.498 *	0.579 **	–						
4	MVPA	0.677 **	0.994 *	0.668 **	–					
5	TPA	0.430	0.911 **	0.537 *	0.907 **	–				
6	ST	−0.567 **	−0.818 **	−0.258	−0.782 **	−0.748 **	–			
7	PST	−0.060	−0.251	−0.077	−0.24	−0.365	0.398	–		
8	Sleep	−0.443 *	−0.117	−0.493 *	−0.175	0.003	−0.382	−0.325	−0.270	–

Note: LPA, light intensity physical activity; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST, sedentary time; TPA, total physical activity; VPA, vigorous intensity physical activity; * $p < 0.05$; ** $p < 0.01$.

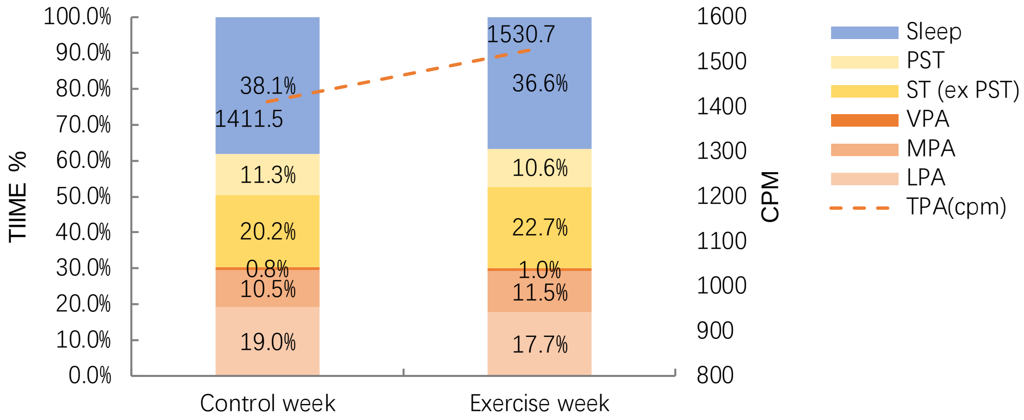
Weekly basis analysis

Daily LPA significantly decreased from 269.4 ± 55.5 min per day (min/d) during control to

246.0 ± 54.5 min/d during exercise week (p < 0.05). MPA, VPA, MVPA, and TPA showed statistically significant increases during the exercise week (p < 0.001) and the mean changes were 11.5 ± 12.6, 2.6 ± 2.7, and 14.1 ± 13.1 min/d, and 119.2 ± 70.9, cpm respectively. We found the largest increase in VPA, with a 35.2 ± 40.6% increase during the exercise week.
ST increased 4.4 ± 6.0% during the exercise week, from 446.7 ± 98.9 to 464.1 ± 95.5 min/d (p < 0.01). The time spent in prolonged sedentary activities was significantly decreased from 160.4 ± 54.4 to 148.1 ± 50.1 min/d, with a percentage decrease of 5.1 ± 20.6% (p < 0.05). No significant differences were found in BPST (p > 0.05).

Sleep durations were significantly decreased from 9.0 ± 1.1 h per day (h/d) to 8.5 ± 0.7 h/d, with a percentage decrease of 5.0 ± 7.5% (p < 0.05). See weekly changes in Figure 14 and Table 19.

Figure 14: The changes of movement behaviors between control week and exercise week



Note: cpm, counts per minute; LPA, light intensity physical activity; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST (ex PST), sedentary time except PST; TPA, total physical activity; VPA, vigorous in-tensity physical activity.

Table 19: Weekly changes of movement behaviors

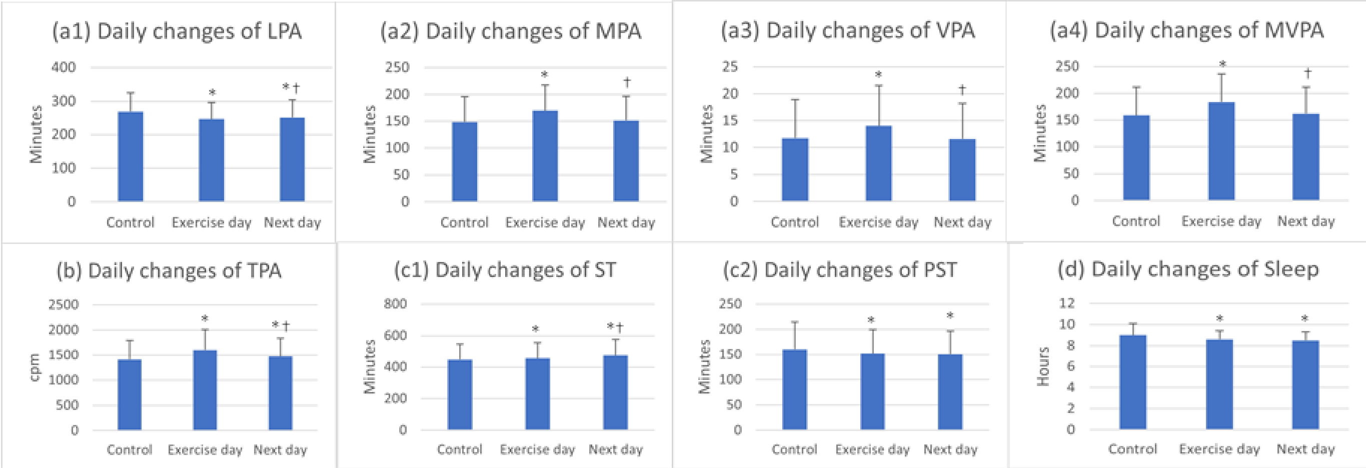
Variables	Control Week	Exercise Week	Mean Change	95% CI		% Change	*p* Value	Effect Size (Cohens'd)
LPA (min/d)	269.4 ± 55.5	246.0 ± 54.5	−23.4 ± 44.3 *	−43.5	−3.2	−7.3 ± 16.7%	*p* < 0.05	**−0.53**
MPA (min/d)	148.3 ± 47.4	159.8 ± 44.8	11.5 ± 12.6 ***	5.7	17.2	9.9 ± 11.7%	*p* < 0.001	**0.91**
VPA (min/d)	11.1 ± 7.2	13.8 ± 7.6	2.6 ± 2.7 ***	1.4	3.8	35.2 ± 40.6%	*p* < 0.001	**0.96**
MVPA (min/d)	159.5 ± 52.0	173.6 ± 49.1	14.1 ± 13.1 ***	8.2	20.1	11.1 ± 11.6%	*p* < 0.001	**1.06**
TPA (cpm)	1411.5 ± 381.5	1530.7 ± 384.3	119.2 ± 70.9 ***	86.9	151.5	9.1 ± 5.6%	*p* < 0.001	**1.68**
ST (min/d)	446.7 ± 98.9	464.1 ± 95.5	17.5 ± 25.9 **	5.7	29.3	4.4 ± 6.0%	*p* < 0.01	**0.68**
PST (min/d)	160.4 ± 54.4	148.1 ± 50.1	−12.3 ± 24.7 *	−23.5	−1.0	−5.1 ± 20.6%	*p* < 0.05	**−0.49**
Sleep (h/d)	9.0 ± 1.1	8.5 ± 0.7	−0.5 ± 0.7 **	−0.8	−0.2	−5.0 ± 7.5%	*p* < 0.01	**−0.71**

Note: cpm, counts per minute; h/d, hours per day; LPA, light intensity physical activity; min/d, minutes per day; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST, sedentary time; TPA, total physical activity; VPA, vigorous intensity physical activity. * p < 0.05; ** p < 0.01; *** p < 0.001.

Daily basis analysis

LPA decreased significantly on the exercise day from 269.4 ± 55.5 to 245.9 ± 50.8 min/d and at the day after exercise, it significantly increased to 250.9 ± 53.1 min/d but was still significantly below the control (p < 0.05) (Figure 15a1). MPA, VPA, and MVPA increased significantly on the exercise day from 148.3 ± 47.4 to 170.2 ± 46.9 min/d, 11.1 ± 7.2 to 14.0 ± 7.5 min/d, and from 159.5 ± 52.0 to 184.2 ± 51.6 min/d, respectively (p < 0.05). However, on the following day, they decreased significantly and returned to control levels (Figure 15a2–a4). TPA was 1605.8 ± 401.4 cpm on exercise day, which was significantly higher than the control (1411.5 ± 381.5 cpm), and significantly decreased the next day to 1472.8 ± 366.4 cpm (p < 0.05), staying above the control (p < 0.05) (Figure 15b).

Figure 15: Daily changes of movement behaviors

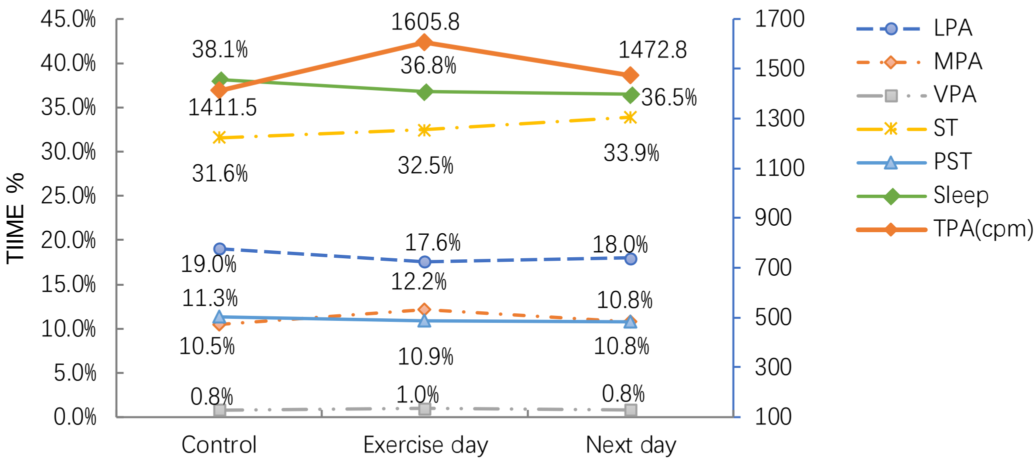


Note: cpm, counts per minute; LPA, light intensity physical activity; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST, sedentary time; TPA, total physical activity; VPA, vigorous intensity physical activity. *, statistically significant difference from control p < 0.05; †, statistically significant difference from exercise day p < 0.05.

We found that ST increased continuously after performing exercises, and on the day after exercising it demonstrated the biggest increase (446.7 ± 98.9, 454.6 ± 101.3, and 473.6 ± 103.3 min/d for the control, exercise day, and next day, respectively, $p < 0.05$, Figure 15c1). However, time spent on PST declined significantly on the exercise day from 160.4 ± 54.4 to 152.0 ± 47.5 min/d ($p < 0.05$) and then remained unchanged the next day (Figure 15c2).

Sleep duration revealed significant decreases on the exercise day from 9.0 ± 1.1 to 8.6 ± 0.8 h/d ($p < 0.05$) and remained unchanged the day after exercise (8.5 ± 0.8 h/d, $p > 0.05$, Figure 15d). See percentage daily changes in Figure 16 and details in Table 20.

Figure 16: Daily changes of movement behaviors



Note: cpm, counts per minute; LPA, light intensity physical activity; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST, sedentary time; TPA, total physical activity; VPA, vigorous intensity physical activity.

Table 20: Daily changes of movement behaviors

Variables	Control	Exercise Day	Next Day	*p*-Value	η^2
LPA (min/d)	269.4 ± 55.5	245.9 ± 50.8 *	250.9 ± 53.1 *†	<0.001	0.615
MPA (min/d)	148.3 ± 47.4	170.2 ± 46.9 *	151.0 ± 45.5 †	<0.001	0.784
VPA (min/d)	11.1 ± 7.2	14.0 ± 7.5 *	11.6 ± 6.6 †	<0.001	0.735
MVPA (min/d)	159.5 ± 52.0	184.2 ± 51.6 *	162.6 ± 48.9 †	<0.001	0.816
TPA (cpm)	1411.5 ± 381.5	1605.8 ± 401.4 *	1472.8 ± 366.4 *†	<0.001	0.784
ST (min/d)	446.7 ± 98.9	454.6 ± 101.3 *	473.6 ± 103.3 *†	<0.001	0.462

PST (min/d)	160.4 ± 54.4	152 ± 47.5 *	150.5 ± 45.8 *	<0.001	0.35
Sleep (h/d)	9.0 ± 1.1	8.6 ± 0.8 *	8.5 ± 0.8 *	<0.001	0.419

Note: cpm, counts per minute; h/d, hours per day; LPA, light intensity physical activity; min/d, minutes per day; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PST, prolonged sedentary time; ST, sedentary time; TPA, total physical activity; VPA, vigorous intensity physical activity. *, statistically significant difference from control $p < 0.05$; †, statistically significant difference from exercise day $p < 0.05$.

Exercise fidelity and exertion

The mean heart rate during exercises was 82.4 ± 1.9% of HR_{max} (ranging from 79.4% to 85.8%), and the mean peak heart rate was 92.3 ± 3.1% of HR_{max}, with the lowest being 86.3% and the highest being 97.0%. Seventeen (81.0%) participants met the high intensity requirements of 90% HR_{max}. The average peak heart rate achieved during Session 1 to Session 3 was 92.3 ± 3.0, 92.4 ± 2.8, and 92.4 ± 3.8% respectively, with no between-differences. The reported score for Borg's RPE was 15.7 ± 0.5 during exercise, ranging from 14.7 to 16.7.

Linear regression modeling

VO_{2max}, Borg's RPE score, and HR_{mean} were included in the linear regression model to explore the potential variables associated with changes in movement behaviors. Only the changes in ST from the control week to the exercise week were significantly associated with VO_{2max} ($b = -0.36$, 95% CI: -0.72, -0.01; $p = 0.047$) and HR_{mean} during exercises ($b = 0.54$, 95% CI: 0.19, 0.88; $p = 0.004$), indicating that better aerobic capacity was associated with a smaller increase in ST, and that higher exercise intensity led to more increases in ST.

4. Discussion

This study was the first to investigate the compensatory effects of HIIE among inactive female university students across an entire 24-h day. In the present study, we observed a compensatory increase in ST, with the most increases occurring on the day after exercise, with decreases in LPA. On the contrary, MPA, VPA, MVPA, and TPA increased on exercise day. Sleep duration decreased after HIIE.

Findings from the present study were partially supported by an experimental study conducted in adolescents by Paravidino et al. (2017) [Paravidino et al., 2017]. There was an increase in subsequent sedentary time after both 55 min of moderate (64–76% of HRmax) and vigorous (77–95% of HRmax) exercise sessions. Similar behavior compensations for acute exercise by increasing ST and PST and decreasing LPA were also reported among older adults [Goncin et al., 2020]. Although our results indicated that HIIE induced compensation for the increasing ST and decreased LPA occurring in inactive young women, the simultaneous decreases in MVPA following HIIE reported by previous studies were not observed in the present study.

Inconsistent to the "Activitystat" hypothesis, MPA, VPA, MVPA, and TPA were increased rather than reduced following HIIE in the current study, which was consistent with several other studies. Cooper et al. (2003), Goodman et al. (2011), and Long et al. (2013) investigated the effects of participating in PA among children and found that PA interventions may increase activity overall, indicating the occurrence of activity synergy in youth [Cooper et al., 2003; Goodman et al., 2011; Long et al., 2013]. We further found that low-volume HIIE-induced activity synergy was transient, as it was observed only on exercise day and it returned to baseline levels the next day. However, an observational study conducted by Baggett et al. (2010) showed a positive correlation between daily MVPA and MVPA on the following days among female adolescents [Baggett et al., 2010]. We hypothesized that in the present study, higher levels of PA on the exercise day were mostly accumulated as the result of in-creased exercise. Meanwhile, the transient effect of activity synergy could be potentially explained by the short workout bout and the low exercise volume in the current study. This suggestion had been highlighted in a systematic review of randomized controlled trials [Fedewa et al., 2017], in which the session duration was revealed to be significantly positively associated with compensatory behaviors.

Exercise intensity was another factor potentially influencing subsequent movement behaviors. Several studies assessed the changes of behaviors after engaging in exercises with different protocols. One study compared the compensatory effects of a single bout of moderate intensity training, high intensity exercise, and sprint training, and reported greater declines in PA following high intensity exercise and sprint training [Goncin et al., 2020]. However, in a 22-week intervention, no compensatory changes were reported in four exercise groups (strength, endurance, combined, and PA recommendations) [Castro et al., 2017]. Our study supported the findings that exercises including higher intensities were more likely to induce movement behavior compensations, since the HR_{mean} was significantly positively associated with an increase in ST after HIIE. We also found females with a better aerobic capacity had smaller increases in ST after HIIE. It was worth also noting that in our study, there was no correlation between perceived exertion and increases in ST. Participants with a higher Borg's RPE score did not subsequently spend more time sitting, sleeping, or engaging in other activities.

In contrast, several studies reported no changes in non-exercise behaviors after exercise interventions. de Moura et al. (2015) noted that compensatory effects were not observed following an 8-week moderate intensity aerobic exercise [de Moura et al., 2015]. Similar findings were indicated after an 8-month training program with a moderate to high intensity [Rangan et al., 2011]. Furthermore, in the study conducted by Church et al. (2007), non-exercise physical activities were assessed following different doses of exercises and, during 6 months of intervention, neither behavior compensation nor synergy were observed [Church et al., 2007]. One of the potential explanations of these findings was that the longer intervention length was evidenced to be favorably associated with non-exercise-based physical activities [Fedewa et al., 2017].

When investigating compensatory activities, most studies have focused on changes of MVPA and ST. As a growing number of studies have indicated the health promotion effect of LPA, we had to take LPA into consideration simultaneously when evaluating changes on LPA. Our study revealed a decrease in LPA after HIIE in both weekly and daily analyses. This finding was consistent with a study conducted by Ridgers et al. (2014), in which additional time spent in MVPA was associated with less time spent in LPA on subsequent days [Ridgers et al., 2014]. However, in an observational study, daily LPA was positively associated with MVPA [Baggett et al., 2010]. Similarly, a significantly higher LPA was revealed in the school day with physical education classes when compared to a day without physical education classes [Sigmund et al., 2014]. These controversial results might be caused by the different cut-off points, epochs, and placements applied to the accelerometer measurements, which result in differences in identifying between LPA and MVPA.

Additionally, it was interesting that total time spent in PA, including LPA, MPA and VPA, was unchanged, while TPA, measured by the vector magnitude cpm, increased significantly. Correlation analysis also indicated a significantly positive association between TPA with MPA, and VPA and MVPA but not LPA. We tested the changes of PA on the exercise day when controlling for interventions by removing exercise periods and found that time spent on MPA still increased significantly, while VPA showed a decrease. In addition to the increased non-exercise MPA, the PST accumulated in our study was significantly reduced following HIIE. Sedentary behavior that is accumulated in a prolonged manner has been independently correlated to an increased risk of cardiometabolic diseases [Zheng et al., 2021]. At this point, we believe that participating in such low-volume HIIE would make participants more active on the same day. Even though the 24 h was limited, it was an effective way to increase overall PA by replacing lower intensity PA with higher intensity.

Sleep duration was significantly decreased following HIIE. This was supported by a day-to-day study that indicated there was a negative association between steps and sleep duration [Chevance et al., 2021]. However, some studies suggested that exercises were an effective strategy to improve sleep duration. Mendelson et al. (2016) conducted a 12-week monitored exercise intervention to improve sleep duration and found it was effective, with sleep duration increasing from 6.7 to 7.4 h [Mendelson et al., 2016]. Another study examined the effects of exercises at different intensities on sleep duration and indicated a short-term increase on sleep duration only after vigorous intensity exercise [Quist et al., 2019]. Kakinami et al. (2017) reported no association between PA intensity and sleep quantity [Kakinami et al., 2017]. The contradiction in results might be due to the different characteristics of sleep at baseline. Participants in our study revealed a longer sleep duration close to the maximum of the recommended level. Both inadequate and longer sleep duration have negative effects on health in women [Smiley et al., 2019]. Even though the time spent on sleep decreased following HIIE, it was not a negative effect, but rather can be recognized as an improvement in sleep quality resulting from increased activity.

The HIIE protocol revealed an acceptable fidelity with high intensity exercise achieved by most participants. It was interesting that Borg's RPE score was not associated with changes in any movement behaviors. We estimated heart rate with the RPE score, using the equation recommended by Scherr et al. (2013): $HR = 69.34 + 6.23 * RPE$ [Scherr et al., 2013]. The estimated HR was significantly lower than the objectively measured one, suggesting that high intensity exercises might be perceived as being less strenuous when performing Tabata style exercises. Lack of time and exercise exertion was reported as the most cited barriers to exercise among females; therefore, a Tabata-style HIIE represents a viable alternative to improve PA among inactive young females

Our study has several strengths including (1) the daily average length of accelerometry data per participant being more than 23 h. This is extensively higher than previous studies and consisted of evaluating 24-h movement behaviors, therefore in-creasing the validity of findings; (2) the inclusion of daily and weekly analysis made contributions to the comparation between acute and short-term effects; (3) the discrepancy between subjectively and objectively measured intensities indicated the perceived exertion during the Tabata-style HIIE.

Several limitations also need to be mentioned. Firstly, the small sample size and participants' characteristics limit the extrapolation of our findings. Participants included in the present study were young, female, of normal weight, and inactive. Secondly, energy expenditure was not assessed due to the invalid estimation by ActiGraph [Kossi et al., 2021]. Thirdly, although the age-predicted maximal heart rate is a quick and easy estimation, it is suggested to overestimate it in young adults. Using a specialized equation would be more appropriate as age and gender might influence the accuracy of the estimation. Furthermore, sleep quality was not measured in the present study. Whether the decreases in sleep time observed in this study represented an improvement in sleep quality requires further investigation. Finally, as this trial was a pilot study, the long-term effects of HIIE on the changes of movement behaviors needs to be investigated further.

5. Conclusions

Compensatory changes in movement behaviors were recognized as being potential explanations for the varied effects on health outcomes following HIIE. The results highlighted the existence of compensatory increases in ST in response to a low-volume HIIE in inactive young females, and the magnitude of increase in ST was associated with exercise intensity and aerobic capacity. Although LPA decreased, TPA was in-creased following HIIE, and MPA, VPA, MVPA temporary improved on the exercise day. Time spent in prolonged sedentary behaviors and sleep was reduced. Overall, in the short term, participating in a low-volume HIIE made participants more active since the observation of an increase in ST may displace prolonged sitting and an overlong sleep period. Higher-intensity PA may displace lower levels of PA. Although low-volume HIIE may contribute to an increase in physical activity in a short term, further investigation is needed to develop an understanding of the long-term effects of changes in movement behaviors following HIIE.

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Chapter 8: Associations between Dairy Consumption, Physical Activity, and Blood Pressure in Chinese Female University Students (Study 4)

1. Introduction

The prevalence of hypertension (HTN) has emerged as one of the main risk factors for cardiovascular disease (CVD) worldwide [Lewington et al., 2002]. Although high blood pressure (BP) is generally observed among elderly populations, epidemiological research has reported an increase in the incidence of elevated BP in young adults [De Venecia et al., 2016; Forouzanfar et al., 2016]. A recent meta-analysis including 4.5 million young adults revealed that young adults with high BP are more likely to develop CVD in later life [Luo et al., 2020]. Moreover, an association between raised BP in young adulthood and the increased risk of premature CVDs has also been observed [Vasan et al., 2018] and this association is independent of later adult exposures [Zhang et al., 2019a]. There has been a substantial increase in HTN-related CVDs burden in young adults from 1990 to 2019 globally [Liu et al., 2021], therefore, promoting an effective HTN management method is essential.

Poor dietary habits and physical inactivity are well documented as traditional risk factors for elevated BP [De Venecia et al., 2016]. Scientific evidence from randomized controlled trials and prospective cohort studies has demonstrated beneficial effects, including the Dietary Approaches to Stop Hypertension (DASH) diet on the control of BP in middle-aged and older adults, [Moore et al., 2001; Svetkey et al., 2005; Fung et al., 2008; Blumenthal et al., 2010]. Dairy products, included as one of the components of the DASH eating pattern, have not been investigated fully in relation to beneficial effects on the BP of young women. Due to the effects that sex hormones have on BP in relation to estrogens having a protective effect on BP while androgens have a hypertensive effect [Reckelhoff, 2001], some studies suggest that these hormones result in differences in effects of dairy intake on the occurrence of HTN and that women are more likely to benefit from dairy intake [Mirmiran et al., 2016; Heidari et al., 2021]. Furthermore, a favorable association between dairy consumption and BP in young women has been observed previously [Celik et al., 2016; Skowrońska-Jóźwiak et al., 2017]. However, these findings are derived from Western experimentation and subjects. Since the pattern and the amount of dairy consumption varies between countries and ethnicities, there are geographical, regional, and ethnicity-related differences in the association between dairy intake and HTN. A recent systematic review has shown reduced BP with dairy intake among Americans, while no effects were recorded in Asian populations [Heidari et al., 2021]. DellaValle et al. (2017) reported an inverse relationship between dairy intake and SBP in white children, but not in black children. In China, the average dairy consumption increased from 25 g in 2012 to 40 g in 2021, which is still much lower than dairy consumption in Western populations [Wang et al., 2008]. In addition, this increase is still lower than the recommended daily intake of 300 g outlined in the 2016 Chinese dietary guideline [Wang et al., 2016]. Despite the low level of dairy intake, some studies observed an inverse relationship with BP in older Chinese [Sun et al., 2013, 2014], however, data for Chinese female university students is still minimal.

Also, despite the evidence strongly supporting a BP reducing effect from physical activity (PA) for adults [Bravata et al., 2007; Diaz and Shimbo. 2013; Börjesson et al., 2016; Barone Gibbs et al., 2021], this positive effect is undetectable in several studies based on adult women exclusively [Vella et al., 2011; Green et al., 2014; Koniak-Griffin et al., 2014; Slater et al., 2021]. Since this experimental evidence is derived from Western populations, including Caucasian, Hispanic, Pacific and Latina women, limited data are available for Chinese female university students.

PA and dietary behaviors demonstrate some correlations. For example, physically active individuals tend to consume more healthy food and nutrients (e.g., fruits, vegetables, fiber, calcium, and vitamins) than their less active counterparts [Gillman et al., 2001]; PA was associated with lower sugar-sweetened beverages intake among adolescent boys [Fröberg et al., 2022]. Although several studies have investigated the effects of individual behaviors such as diet and PA, little research has focused on combined associations. Previous studies have investigated the interaction between dietary patterns and physical activity for BP and report that both may attribute to more optimal BP control [Margetts et al, 1999; Silva et al., 2013], while a superior effect is observed when combining diet and PA [Elliot et al., 2018]. However, other studies have provided inconsistent results that adding exercise to diet has no further effect on reducing BP [Fagard et al., 2005].

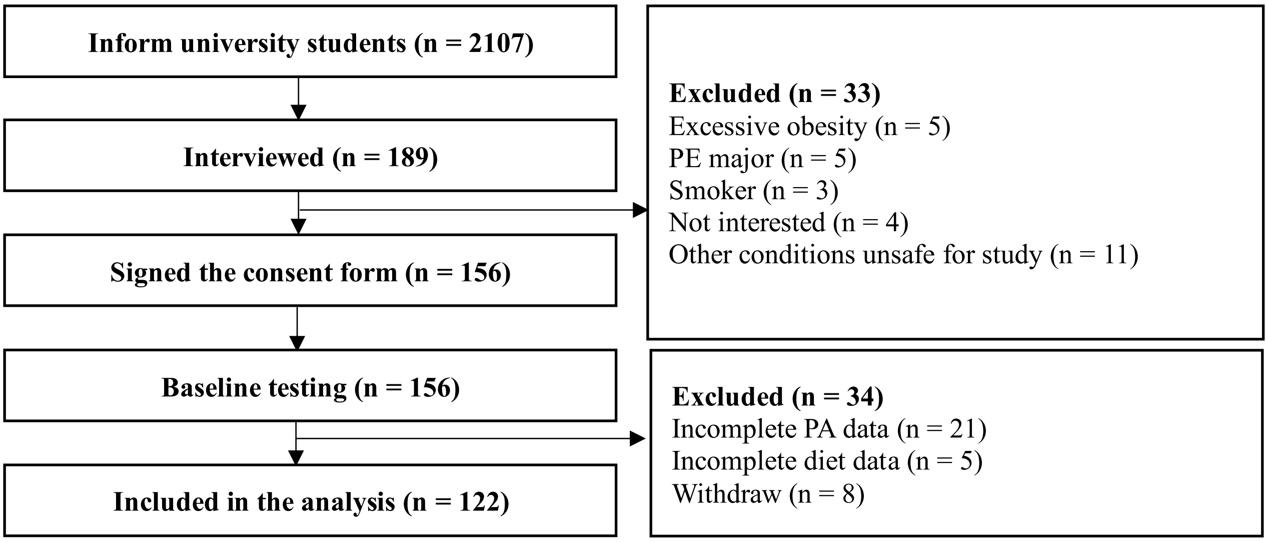
Therefore, the purpose of this study was to investigate the associations between BP with dairy consumption and PA in a sample of Chinese female university students. We hypothesized that high levels of dairy consumption and PA are independently beneficial for BP in this population. We also hypothesized that dairy intake and PA had a combined effect on healthy BP.

2. Methods

2.1 Study design and participants

This cross-sectional study was based on baseline data from a 12-week randomized controlled trial which investigated the effects of high-intensity interval training on cardiometabolic health and PA in female university students (Study 5). Female university students in the Physical Fitness in Campus (PFIC) study were invited via mobile messages and WeChat groups. The PFIC study was a prospective study of 3829 students (2107 females and 1722 males) from Ningbo University who were enrolled in September 2021. The PFIC study was designed to investigate changes in health-related physical fitness and to explore potential risk factors during campus life. Students underwent health-related physical fitness tests once a year during their 4 years of college, including body composition, cardiorespiratory fitness, flexibility, muscular endurance, and muscular strength. Introductions of the exercise intervention and the cross-sectional study were presented during weekly PE classes. During the introduction, we briefly described the project background, training requirements (19 minutes per session, 3 sessions per week for a total of 12 weeks), and the major measurements (body composition, aerobic capacity, and blood samples). Interested students went through the following procedures individually: a face-to-face interview, a medical examination, a written consent form and a pre-test. Students with diabetes, on a diet, who were pregnant, or had any other conditions that might affect PA and dietary intake were excluded (e.g., physical disability or injury, CVDs, cow's milk protein allergy and lactose intolerance). In addition, students with severe obesity (BMI ≥ 40 kg/m^2) were not included in the present study because they were not included in the regular PE classes. Instead, they were instructed to attend a weight loss intervention, which affects their daily diet and PA. Participants were required to attend the laboratory on weekday mornings in March 2022 to complete all measurements. Detailed processes of samples are presented in Figure 17. Finally, 122 female students who had complete dietary, PA, laboratory, lifestyle, and personality data were included in this cross-sectional analysis. The study was approved by the University of Ningbo institutional review board.

Figure 17: The process of sample



Note: PA, physical activity; PE, physical education.

2.2 Physical, Physiological and Body Composition Measurement

Participants were instructed to refrain from alcohol and strenuous exercise 24 hours prior to the measurements. Height was measured in duplicate, using a standard stadiometer protocol [Arboleda Serna et al., 2016]. Weight was measured using bioelectrical impedance analysis (MC-

180, TANITA CO., China) under the guidance of two trained staff. Body mass index (BMI) was calculated using standardized equations.

2.3 Blood Pressure

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by trained research staff using an automatic upper arm sphygmomanometer (HEM-1000, Omron, China). Prior to BP measurement, participants were required to sit and rest for at least 5 minutes. BP measurements were taken in a seated position from the left arm, with the upper section of the arm supported at the heart level. Three measurements were performed at 1-minute intervals and the average of the second and the third readings were used for analysis. If the two readings differed by more than 5 mm Hg, an additional measurement was taken. BP was classified based on the recommendation from the American Heart Association as normal (SBP < 120 mm Hg and DBP < 80 mm Hg), elevated (SBP = 120-129 mm Hg and DBP < 80 mm Hg), HTN stage 1 (SBP = 130-139 mm Hg or DBP = 80 - 89 mm Hg), and HTN stage 2 (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg). Participants with elevated, HTN stage 1 or stage 2 were identified as having unhealthy BP profiles.

2.4 Dietary Intake

Dietary intake was assessed by a staff-administered semi-quantitative food frequency questionnaire (FFQ). This 127-item FFQ was modified from the validated questionnaire used in the 2002 China Nutrition and Health Survey [Zhao et al., 2002]. Dairy products included fluid milk, milk power, and yogurt. The consumption frequency included: 1) never, 2) less than once per month, 3) 1 - 3 times per month, 4) once per week, 5) 2 - 3 times per week, 6) 4 - 5 times per week, 7) once per day, 8) twice per day, and 9) three or more times per day. The consumption quantity of fluid milk and yogurt was recorded as serving with the serving size consisting of 250g and 250g, respectively. Milk powder was recorded in grams, and 40g milk power was estimated as a single serving. Samples were presented to help participants to more accurately record serving sizes. Total dairy intake was calculated as the sum of these three categories. Other dietary data were recorded, and the intake of nutrients were calculated according to the Chinese Food Composition Tables [Yang et al., 2002] and manufacturer information.

2.5 Physical Activity

PA was measured using a triaxial accelerometer (ActiGraph, wGT3X-BT, Pensacola, FL, USA), which is a valid measure for university students [Peterson et al. 2015]. Participants were instructed to wear the accelerometer on the non-dominant hip for 7 consecutive days except during water-based activities [Trost et al. 2005]. A valid day was defined as not less than 75% of the wear time between 7 a.m. to 11 p.m. and participants provided at least 4 valid days including at least one weekend included in the analysis. The intensity of PA was classified according to the Freedson Adult algorithm. Sedentary was defined as < 100 counts per minute (cpm), light intensity physical activity (LPA) was defined as 100-1951 cpm, moderate intensity physical activity (MPA) was defined as 1952-5724 cpm, vigorous intensity physical activity (VPA) as > 5725 cpm, and moderate-to-vigorous intensity physical activity (MVPA) as > 1952 cpm. Total physical activity (TPA) was defined as the daily vector magnitude cpm.

2.6 Personality

Previous studies have reported that personality is associated with BP recordings [Burke et al., 1992; Sutin et al., 2019]. Therefore, personality was considered as a confounder in the current study. The “Big Five” dimensions of extraversion, neuroticism, conscientiousness, openness, and agreeableness have been commonly used as measures of personality. In this study, the Chinese Big Five Personality Inventory Shortened Version (CBF-PI-15) was used and has been proven to be a valid and reliable informative alternative when personality is not the main purpose of the study [Zhang et al. 2019b]. The CBF-PI-15 consisted of 15 items, with 3 items to measure each personality dimension.

2.7 Other variables

Other variables including demographic data, lifestyle and family history of hypertension were identified using a standardized questionnaire. Smoking, drinking, and staying up late were classified as never, sometimes, or always. The family history of hypertension was classified as yes or no.

2.8 Statistical analysis

The sample size was estimated a priori using G*Power (version 3.1.9.7) (Heinrich Heine University, Dusseldorf, Germany) under a F tests linear multiple regression designs for fixed models with R2 increase. The effect size f^2, power and alpha were set at 0.15, 0.95 and 0.05, respectively. With 3 tested predictors (dairy intake, MVPA and TPA) and the total of 18 predictors, a total of 120 participants were required.

Descriptive analyses were summarized as Means + SD and proportions for continuous and categorical variables. Normality was checked using the Kolmogorov-Smirnov test. ANOVA and Fisher's exact test were used to analyze differences between continuous and categorical variables, respectively. Least significant difference or Bonferroni post hoc test was used to detect any differences between groups. Correlations between variables were examined using the Pearson product moment correlation coefficient. Linear regression models were used to test the association between dairy consumption (servings per day), PA (MVPA and TPA), and BP (SBP and DBP). The variance inflation factor (VIF) was used to check the collinearity. The z-score method was used to standardize variables. For SBP and DBP, three models were used. The independent variable was dairy consumption in model 1, dairy consumption and MVPA in model 2, and dairy consumption, MVPA and TPA in model 3. In model 2 and model 3, the interaction terms (dairy × MVPA for model 2, dairy × MVPA and dairy × TPA for model 3) were estimated to explore the interaction effects. Additionally, we assessed interaction by the BP groups. If there was a statistically significant interaction, separate regression would be performed for healthy and unhealthy BP groups. All models controlled for age, alcohol, smoking, staying up late, family history of HTN, BMI, total calorie intake, carbohydrate, fat intake and dietary fiber intake. Furthermore, for all models, we further controlled for personality data. Statistical analyses were performed using SPSS for windows, version 23.0 (Chicago, IL, USA) and the significance level was set as $p < 0.05$.

3. Results

The characteristics of the participants according to BP ranges are presented in Table 21. Most participants had normal BP (41.80%, n = 51), with 23.77% (n = 29) classified as elevated, 29.51% (n = 36) as HTN stage 1 and 4.92% (n = 6) as HTN stage 2. There were no statistically significant differences in age (p = 0.889), BMI (p = 0.407), alcohol (p = 0.976), smoking (p = 1.000), staying up late (p = 0.775), family history of HTN (p = 0.087), personality score of conscientiousness (p = 0.296), agreeableness (p = 0.956), openness (p = 0.888), and extraversion (p = 0.870) between each category. Participants with normal BP had significantly lower scores for neuroticism and were less likely to have a family history of HTN than those with unhealthy BP.

Table 21: Characteristics of participants

	All (n=122)	Normal (n=51, 41.80%)	Elevated (n=29, 23.77%)	HTN Stage1 (n=36, 29.51%)	HTN Stage2 (n=6, 4.92%)	p value
Age (years)	20.4±1.56	20.38±1.40	20.49±1.49	20.41±1.24	20.01±0.98	0.889
BMI (kg/m2)	20.66±2.58	20.59±2.83	21.00±2.64	20.26±2.27	21.96±1.39	0.407
Alcohol						0.976
Never	105 (86.07%)	43 (84.31%)	25 (86.21%)	31 (86.11%)	6 (100%)	
Sometimes	17 (13.93%)	8 (15.69%)	4 (13.79%)	5 (13.89%)	0 (0.00%)	
Always	0	0	0	0	0	
Smoking						-
Never	122 (100.00%)	51 (100%)	29 (100%)	36 (100%)	6 (100%)	
Sometimes	0	0	0	0	0	
Always	0	0	0	0	0	
Staying up late						0.775
Never	0	0	0	0	0	
Sometimes	27 (22.13%)	11 (21.57%)	5 (17.24%)	9 (25.00%)	2 (33.33%)	
Always	95 (77.87%)	40 (78.43%)	24 (82.76%)	27 (75.00%)	4 (66.67%)	
Family history of HTN						0.087
Yes	9 (7.38%)	1 (1.96%)	2 (6.90%)	5 (16.13%)	1 (16.67%)	
No	113 (92.62%)	50 (98.04%)	27 (93.1%)	31 (83.87%)	5 (83.33%)	
Personality						
Neuroticism	10.61±3.06	9.57±2.77	10.32±2.27	11.66±1.99	13.17±1.33	<0.001
Conscientiousness	13.5±1.71	13.57±1.76	13.86±1.73	13.11±1.60	12.69±1.70	0.296

Agreeableness	14.82±2.15	14.71±2.36	14.90±2.11	14.88±1.96	14.63±1.15	0.956
Openness	9.91±2.83	9.71±2.74	10.19±2.86	9.93±2.97	10.28±3.03	0.888
Extraversion	9.35±3.44	9.55±3.53	9.40±3.29	9.18±3.48	8.33±3.94	0.870
Energy intake (kcal/day)	1679.88±518.17	1599.25±456.28	1632.26±462.69	1739.93±591.94	2235.19±537.24	0.029
Carbohydrate (% in energy)	46.99±4.71	47.14±3.92	46.24±4.28	47.58±5.53	45.81±7.61	0.633
Fat (% in energy)	36.44±3.02	35.5±2.78	36.54±2.48	37.15±3.32	39.70±2.42	0.002
Fiber (g/d)	14.01±5.03	15.22±4.57	13.08±6.24	12.98±4.56	14.48±3.49	0.138
Dairy intake (serving/d)	1.20±0.54	1.42±0.53	1.07±0.53	1.06±0.45	0.74±0.50	0.001
MVPA (min/d)	103.20±16.73	110.00±14.06	99.82±17.41	96.16±16.39	95.85±10.58	<0.001
TPA (cpm)	1192.31±252.59	1291.87±231.26	1203.36±272.97	1082.02±213.94	954.36±119.21	<0.001
SBP (mm Hg)	121.89±11.39	110.86±5.66	124.29±2.76	132.00±5.59	143.27±2.52	<0.001
DBP (mm Hg)	70.35±6.24	68.57±5.57	68.96±4.02	73.24±7.49	75.62±3.32	<0.001

Note: BMI, body mass index; DBP, diastolic blood pressure; HTN, hypertension; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TPA, total physical activity.

The average SBP for all participants was 122 ± 11 mm Hg. For the normal, elevated, HTN stage 1 and HTN stage 2 groups, the average SBP was 111 ± 6, 124 ± 3, 132 ± 6, and 143 ± 3 mm Hg, respectively, and all values were significantly different from the others ($p < 0.001$) The average DBP for all samples was 70 ± 6 mm Hg, and the normal (69 ± 6 mm Hg) and elevated (69 ± 4 mm Hg) group had significant lower values than the HTN stage 1 (73 ± 7 mm Hg, $p < 0.001$ for normal group and $p = 0.004$ for elevated group) and stage 2 (76 ± 3 mm Hg, $p = 0.006$ for normal group and $p = 0.011$ for elevated group) group.

For average daily dietary consumption, there were no statistically significant differences between groups in percentage of energy intake of carbohydrate (46.99 ± 4.71%, $p = 0.633$) and fiber (14.01 ± 5.03g, $p=0.138$). The HTN stage 2 group had significantly higher total calories (2235.19 ± 537.24 kcal/day, $p=0.029$) and percentage of fat (39.70 ± 2.42%, $p=0.020$) intake compared to other groups. The average daily dairy consumption was 1.20 ± 0.54 serving per day, which was significantly higher in the normal group (1.42 ± 0.53 serving per day, $p = 0.001$).

The average daily MVPA and TPA were 103.20 ± 16.73 min/d and 1192.31 ± 252.59 cpm, respectively. There were statistically significant differences in both MVPA ($p < 0.001$) and TPA ($p < 0.001$) between groups and those in the normal group engaged in more MVPA and TPA per day.

Furthermore, we compared healthy and unhealthy BP groups (Table 22) and found statistically significant differences in SBP ($p < 0.001$), DBP ($p = 0.007$), the score of neuroticisms ($p < 0.001$), intake of fat ($p = 0.003$), fiber ($p = 0.024$) and dairy products ($p < 0.001$), MVPA ($p < 0.001$) and TPA ($p < 0.001$).

Table 22: Characteristics of participants with healthy or unhealthy blood pressure

	All (n=122)	Health (n=51)	Unhealth (n=71)	P value
Age (years)	20.4±1.56	20.38±1.40	20.41±1.32	0.911
BMI (kg/m2)	20.66±2.58	20.59±2.83	20.71±2.40	0.808
Alcohol				0.792
Never	105 (86.07%)	43 (84.31%)	62 (87.32%)	
Sometimes	17 (13.93%)	8 (15.69%)	9 (12.68%)	
Always				
Smoking				-
Never	122 (100.00%)	51 (100%)	71 (100%)	
Sometimes				
Always				
Staying up late				0.899
Never				
Sometimes	27 (22.13%)	11 (21.57%)	16 (22.54%)	

Always	95 (77.87%)	40 (78.43%)	55 (77.46%)	
Family history of HTN				0.078
Yes	9 (7.38%)	1 (1.96%)	8 (11.27%)	
No	113 (92.62%)	50 (98.04%)	63 (88.73%)	
Personality				
Neuroticism	10.61±3.06	9.53±2.73	11.27±2.22	<0.001
Conscientiousness	13.29±1.78	13.57±1.76	13.45±1.68	0.708
Agreeableness	14.57±2.18	14.71±2.36	14.90±1.99	0.622
Openness	10.04±3.02	9.71±2.74	10.06±2.90	0.502
Extraversion	9.39±3.63	9.55±3.53	9.21±3.38	0.595
Energy intake (kcal/day)	1679.88±518.17	1599.25±456.28	1737.81±554.32	0.146
Carbohydrate (% in energy)	46.99±4.71	47.14±3.92	46.88±5.22	0.767
Fat (% in energy)	36.44±3.02	35.5±2.78	37.12±3.02	0.003
Fiber (g/d)	14.01±5.03	15.22±4.57	13.15±5.20	0.024
Dairy intake (serving/d)	1.20±0.54	1.42±0.53	1.04±0.49	<0.001
MVPA (min/d)	103.2±16.73	110.00±14.06	97.63±16.34	<0.001
TPA (cpm)	1192.31±252.59	1291.87±231.26	1120.79±244.29	<0.001
SBP (mm Hg)	121.89±11.39	110.86±5.66	129.82±7.01	<0.001
DBP (mm Hg)	70.35±6.24	68.57±5.57	71.63±6.42	0.007

Note: BMI, body mass index; DBP, diastolic blood pressure; HTN, hypertension; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TPA, total physical activity.

Correlation coefficients between dietary, PA, and BP measures are presented in Table 23. SBP and DBP were significantly correlated ($r = 0.25$, $p < 0.01$). SBP was negatively associated with daily consumption of fiber ($r = -0.21$, $p < 0.05$) and dairy ($r = -0.41$, $p < 0.01$), MVPA ($r = -0.37$, $p < 0.01$), and TPA ($r = -0.41$, $p < 0.01$), whereas these relationships were not significant with DBP. Daily percentage intake of fat and the score for neuroticism were significantly associated with SBP ($r = 0.27$, $p < 0.01$ for fat; $r = 0.485$, $p < 0.01$ for neuroticism) and DBP ($r = 0.26$, $p < 0.01$ for fat; $r = 0.308$, $p < 0.01$ for neuroticism). Furthermore, there was a significant relationship between MVPA and TPA ($r = 0.41$, $p < 0.01$).

Table 23: Correlation coefficients between dietary, PA, and BP measures

	Energy intake	Carbohydrate	Fat	Fiber	Dairy	MVPA	TPA	SBP	DBP
Energy intake	1.00	-	-	-	-	-	-	-	-
Carbohydrate	-0.06	1.00	-	-	-	-	-	-	-
Fat	0.14	-0.08	1.00	-	-	-	-	-	-
Fiber	0.03	-0.06	-0.11	1.00	-	-	-	-	-
Dairy	0.17	0.01	-0.10	-0.05	1.00	-	-	-	-
MVPA	0.08	-0.07	-0.07	0.14	0.17	1.00	-	-	-
TPA	0.05	-0.17	-0.04	0.04	0.21*	0.41**	1.00	-	-
SBP	0.15	-0.04	0.27**	-0.21*	-0.41**	-0.37**	-0.41**	1.00	-
DBP	0.03	0.19*	0.26**	-0.01	-0.11	-0.14	-0.12	0.25**	1.00

Note: DBP, diastolic blood pressure; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TPA, total physical activity. *, $p < 0.05$; ** $p < 0.01$.

Regression analysis after controlling for potential variables is summarized in Table 24. In Model 1 ($R^2 = 0.344$), dairy intake was significantly associated with SBP (standardized beta (b) = -0.425, $p < 0.001$). This relationship was attenuated after adding MVPA to model 1. In Model 2 ($R^2 = 0.413$), dairy intake ($b = -0.384$, $p < 0.001$) and MVPA ($b = -0.276$, $p < 0.001$) were significantly and independently associated with SBP. No interaction between dairy intake and MVPA on SBP was observed ($p = 0.209$). In Model 3 ($R^2 = 0.467$), there were significant association between dairy intake (b = -0.343, p < 0.001), MVPA (b = -0.172, p = 0.033), and TPA (b = -0.267, p = 0.001) with SBP. Dairy intake and MVPA had no interaction on SBP (p = 0.742), nor did dairy intake and TPA (p = 0.352).

Table 24: Standardized regression coefficients of dairy intake, MVPA and TPA for BP measures (without controlling for personality data).

Dependent Variable		Independent variable	Standardized beta	p value
SBP	Model 1: $R^2 = 0.344$	Dairy intake	-0.425	<0.001
	Model 2: $R^2 = 0.413$	Dairy intake	-0.384	<0.001
		MVPA	-0.276	<0.001
	Model 3: $R^2 = 0.467$	Dairy intake	-0.343	<0.001
		MVPA	-0.172	0.033
		TPA	-0.267	0.001
DBP	Model 1: $R^2 = 0.178$	Dairy intake	-0.068	0.449
	Model 2: $R^2 = 0.183$	Dairy intake	-0.056	0.535
		MVPA	-0.078	0.392
	Model 3: $R^2 = 0.184$	Dairy intake	-0.051	0.578
		MVPA	-0.066	0.509
		TPA	-0.032	0.749

Note: All models are adjusted for age, alcohol, smoking, staying up late, family history of hypertension, body mass index, total calorie intake, carbohydrate, fat intake and dietary fiber intake.
DBP, diastolic blood pressure; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TPA, total physical activity.

To eliminate the bias induced by personality, we further controlled for personality data and the results are outlined in Table 25. In Model 1, after controlling for personality data and other potential variables, dairy intake was independently associated with SBP (b = -0.342, p < 0.001), accounting for 10.2% of the variation. While this relationship was slightly attenuated (b = -0.306, p < 0.001) when MVPA was added in Model 2, which significantly increased the explained variation in SBP to 53.2% ($R^2 = 0.532$). In Model 2, MVPA was independently associated with SBP (b = -0.259, p < 0.001), explaining 5.9 % of the variance in SBP. There was no interaction between dairy and MVPA on SBP (p = 0.636). Moreover, the relationships between SBP with dairy (b = -0.275, p < 0.001) and MVPA (b = -0.167, p = 0.027) were both attenuated when TPA (b = -0.233, p = 0.002) was added in Model 3. TPA significantly further increased the explained variation in SBP with 4.0% ($R^2 = 0.572$). Dairy and MVPA had no interaction on SBP (p = 0.732), nor did dairy and TPA (p = 0.446).

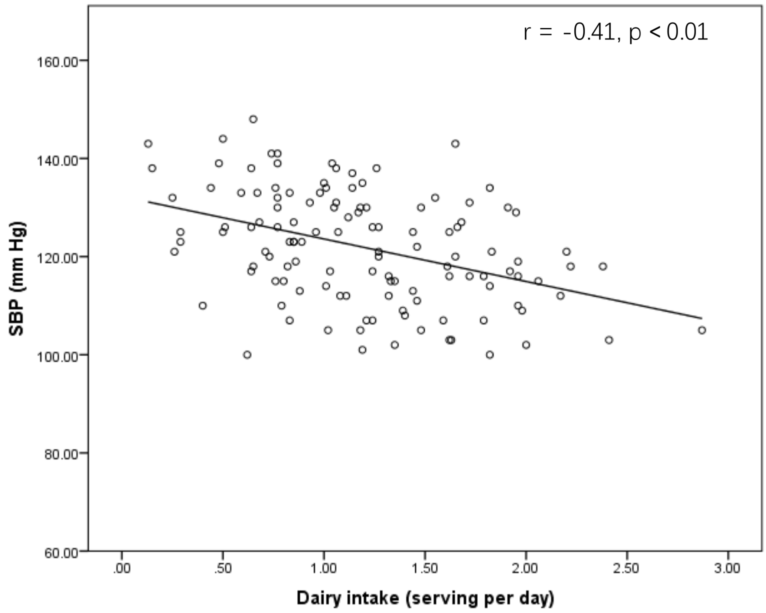
Table 25: Standardized regression coefficients of dairy intake, MVPA and TPA for BP measures (controlling for personality data).

Dependent Variable		Independent variable	Standardized beta	p value
SBP	Model 1: $R^2 = 0.473$	Dairy intake	-0.342	<0.001
	Model 2: $R^2 = 0.532$	Dairy intake	-0.306	<0.001
		MVPA	-0.259	<0.001
	Model 3: $R^2 = 0.572$	Dairy intake	-0.275	<0.001
		MVPA	-0.167	0.027
		TPA	-0.233	0.002
DBP	Model 1: $R^2 = 0.272$	Dairy intake	-0.001	0.993
	Model 2: $R^2 = 0.274$	Dairy intake	0.006	0.948
		MVPA	-0.048	0.590
	Model 3: $R^2 = 0.274$	Dairy intake	0.006	0.946
		MVPA	-0.047	0.630
		TPA	-0.002	0.980

Note: DBP, diastolic blood pressure; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TPA, total physical activity.

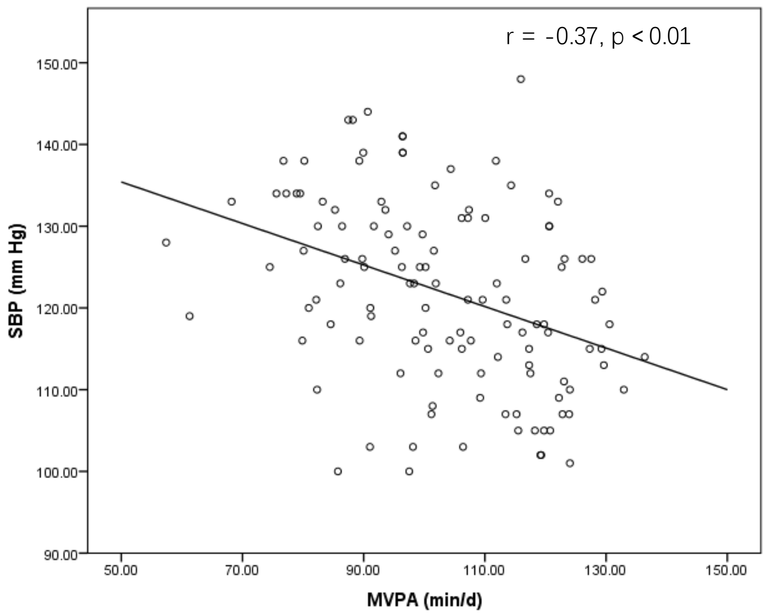
In all models, DBP was not significantly associated with dairy intake, MVPA or TPA in the total sample. There was no interaction between dairy intake with MVPA or TPA on DBP. No interactions were found between BP groups (healthy and unhealthy) and any exposures (dairy intake, MVPA and TPA) on DBP or SBP. Relationships between dairy intake, MVPA and TPA with SBP are shown in Figures 18 - 20. For the total samples, each additional serving of dairy, 10 minutes of MVPA, and 100 cpm of TPA per day, we observed a decrease of 5.82 ± 2.94, 1.13 ± 1.01, and 1.10 ± 0.60 mm Hg in SBP, respectively (Figure 18, Figure 19, Figure 20).

Figure 18: Relationship between SBP and dairy intake in total sample.



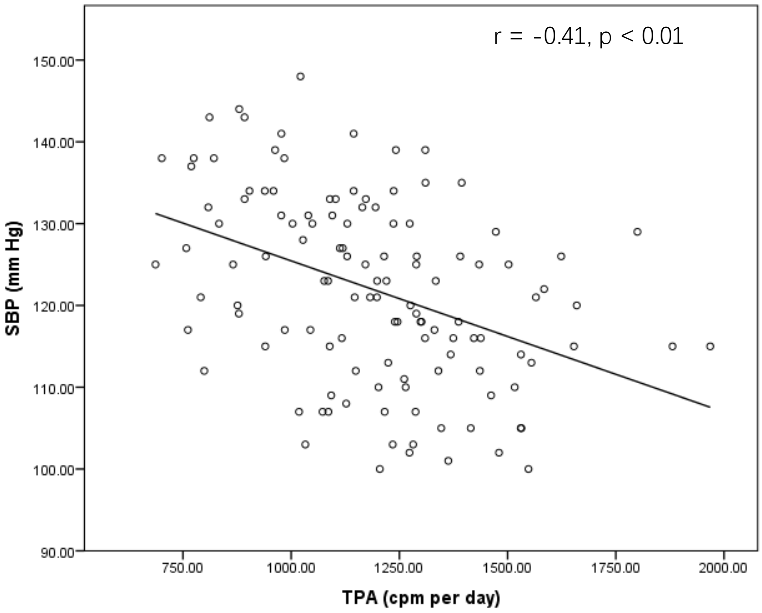
Note: SBP, systolic blood pressure.

Figure 19: Relationship between SBP and MVPA in total sample.



Note: MVPA, moderate-to-vigorous physical activity; SBP, systolic blood pressure.

Figure 20: Relationship between SBP and TPA in total sample.



Note: cpm, count per minute; SBP, systolic blood pressure; TPA, total physical activity.

4. Discussion

This study is the first to examine the relationship between dairy intake and PA in relation to BP in a sample of Chinese female university students. In our study, approximately 58.2% of female university students had unhealthy BP. Our results demonstrated that an average daily dairy serving, MVPA, and TPA were all significantly and independently associated with SBP but not with DBP in this population. However, our hypothesis that dairy intake and PA had a combined effect on BP was not supported. Overall, dairy intake explained a higher proportion of SBP variance than MVPA and TPA. It indicated that dairy consumption, the intensity, and total volume of PA play important roles in determining BP.

Emerging evidence has revealed that dairy intake is beneficial to BP because dairy products have been shown to improve nitric oxide bioavailability and decrease oxidative stress and inflammation, which have protective effects on vascular function [Ballard and Bruno, 2015]. In our study, the average daily dairy intake was 1.20 ± 0.54 per serving. Despite being below the recommended level, dairy intake was associated with a favorable SBP in Chinese female university students. This finding has been supported by previous studies. Lin et al. (2013) assessed associations between adherence to DASH and BP and reported that dairy intake was only significantly and negatively associated with the change of SBP from the year 1989 to 2002. Likewise, findings from the Guangzhou Biobank Cohort Studies show that the average SBP and DBP were 2.56 mm Hg and 1.32 mm Hg lower in adults who consumed 3 milk servings or more per week compared with those of non-consumers [Sun et al., 2014]. Similar results were reported by Zong et al. (2014) who observed that among participants with a median dairy intake of 0.89 serving per day, those who consumed more than 1 serving per day had a 3.54 mm Hg and 2.08 mm Hg lower SBP and DBP than non-consumers. However, this favorable effect was not detected with DBP in the current study. The family history of HTN and percentage daily energy intake of fat and carbohydrate yielded significant but weak associations with DBP.

In agreement with previous studies [Bravata et al., 2007; Pouliou et al., 2012; Diaz and Shimbo, 2013; Bakker et al., 2018; Barone Gibbs et al., 2021], our results demonstrated that both MVPA and TPA, measured by accelerometers, was significantly related to SBP. This was supported by a previous study in China. Analyzing data from 7140 adult women who completed at least one of the China Nutrition and Health Survey in 1997, 2000, 2004 or 2006, Chen et al. (2010) reported an inverse relationship between MVPA with SBP and DBP in women. Furthermore, we observed an additional 10 minutes of MVPA per day was associated with 1.13 ± 1.01 mm Hg lower SBP in the total sample. A previous systematic review and meta-analysis examined a 16-week exercise protocol of 120 minutes of MVPA per week [Cornelissen and Smart, 2013]. The authors reported significantly pooled reductions in SBP among normotensive, pre-hypertensive, and hypertensive subjects, with a decrease of 0.8 ± 1.4 mm Hg, 4.3 ± 3.4 mm Hg, and 8.3 ± 2.3 mm Hg in SBP, respectively. It seemed that increasing MVPA lowered SBP more in individuals with higher SBP. However, in the present study, BP status had no impact on the association between MVPA and SBP. It indicated that, for a given amount of MVPA, we did not observe lower SBP for participants with HTN than normotensive participants. This might be due the fact that MVPA was already at a high level in our samples. Conversely, some cross-sectional studies investigating young women did not find any relationship between MVPA and BP. Green et al. (2014) examined associations between accelerometer measured PA and cardiometabolic indicators in young women and found that there were no associations between MVPA with BP. Similar results were reported by Slater et al. (2021). Moreover, a previous study investigated the effects of meeting PA recommendations on CVD risk factors in young Hispanic women. The findings suggested that there were no differences in BP between women who engaged in at least 30 minutes of MVPA per day and those who did not [Vella et al., 2011]. One of the potential explanations of the inconsistent results with our study was the normal resting BP status reported in these studies, which has been suggested to influence the magnitude of BP reduction following exercise training [Pescatello et al., 2015]. In our study, the average SBP recorded was borderline (121.89 ± 11.39 mm Hg), whereas the average DBP was normal (70.35 ± 6.24 mm Hg). BP in pre-hypertensive adults benefited more in response to PA than in normotensive subjects [Fagard and Cornelissen, 2007; Pescatello et al., 2019]. This partially explains why no relationship between DBP and MVPA was detected in our study.

Although PA performed at moderate-to-vigorous intensity was evidenced and recommended to lower BP, findings from our study indicated that TPA was favorably associated with SBP, independent of MVPA. Our finding was supported by a previous meta-analysis. The authors investigated a dose-response relationship between TPA and the incidence of hypertension and reported that normotensive adults who performed 10 metabolic equivalents of task per hour per week had a 6% lower risk of hypertension [Liu et al., 2017]. Few studies have examined the relationship between BP and the device-measuring TPA. Conversely, the study by Slater et al. (2021) showed that there was no association between TPA and BP in young normotensive women, whose average daily TPA was 598 to 731 cpm. Likewise, no association between BP and TPA was reported in women in previous studies that used subjective measures to determine PA [Ohmura et al., 2002; Remsberg et al., 2007]. The significant association between TPA and SBP in the current study was mainly due to the elevated SBP and high levels of TPA in our sample. Despite the weak but significant correlation, this finding might have important implications for PA strategies to reduce BP. Compared to MVPA, accumulating more TPA appeared to be a better alternative for women who were physically inactive.

Furthermore, our results show that dairy intake, MVPA and TPA were all independently associated with SBP, with dairy intake having the strongest association and MVPA having the weakest. This was in line with the recommended lifestyle strategies aiming to delay or prevent the incidence of hypertension [Jackson et al., 2021]. These strategies included maintaining a healthy dietary pattern rich in fruits, vegetables, and low-fat dairy products, as well as increasing PA with a structured exercise protocol. However, there was no consensus on the effectiveness of dietary or PA modification in lowering BP. Consistent with our results, Fagard et al. (2005) indicated that diet was more effective than exercise in lowering blood pressure. Whereas a recent study shows a superior effect for PA on lowering BP [Barone Gibbs et al., 2021]. Although a recent review concluded that there was insufficient evidence to determine whether the frequency, intensity and duration of PA impacted its association with BP [Pescatello et al., 2019], increasing TPA might have been more advantageous in our study. Other studies suggested a combination strategy of diet and PA [Sales et al., 2012; Fraile-Bermúdez et al., 2017]. While the combined effect of dairy and PA on BP was not observed in the present study. These inconsistent conclusions might be explained by the mediating role of adiposity and cardiorespiratory fitness on the association between BP with diet and PA [Kodama et al., 2009; Green et al., 2014]. In our study, we did not find any relationship between BP and adiposity as measured by BMI in the total sample. This might be due to the exclusion of severe obese participants in our study resulting in the normal BMI value (BMI = 20.66 ± 2.58) obtained in our sample. Another explanation could be that BMI may not be a good predictor of adiposity. Previous studies revealed that women with normal BMIs and who have excess fatness had higher BPs (Marques-Vidal et al., 2010; Oliveros et al., 2014).

Additionally, our study found that personality characteristics played a role in BP, with the personality score of neuroticisms positively associated with SBP values. Neuroticism has been recognized as being composed of several negative facets such as anxiety, anger hostility, and depression and appeared to be the "disease-prone personality" [Friedman and Booth-Kewley, 1987]. Our results were in line with the study of Sutin et al. (2019) who observed that young adults with higher neuroticism had a greater risk of elevated BP. Similarly, it has been reported that high neuroticism was more likely to induce metabolic syndrome in women than in men [Montoliu et al., 2020]. Although extraversion, conscientiousness, or agreeableness was shown to be beneficial for BP in other studies, these favorable relationships between BP and other personality traits were not observed in our study. Further research should include measures of personality traits to better understand its effects on BP.

The strengths of our study included the sample of Chinese female university students who have not been investigated previously in relation to the association between dairy intake, PA, and BP. Moreover, accelerometers were used to eliminate the report bias of PA measures. Several Limitations in the current study should be noted. First, the cross-sectional design prevented the establishment of causal relationships. Although we had extensively controlled for lifestyle, personality and dietary variables, residual confounding factors such as environment, seasonality and stress were not completely ruled out. Second, the self-reported dairy assessment was subject to recall bias. Although we included the most consumed dairy products in Chinese, some increasingly popular sources of dairy were not counted such as butter, cheese, and ice cream. Moreover, calcium, vitamin D, sodium, potassium, magnesium, and other individual micronutrients were not included due to the semi-quantitative design of FFQ. Finally, results of the current study reflected an education bias. University students with relatively high education level might have more health conscious than the general young population.

5. Conclusion

The important findings of this study indicate that the higher amounts of dairy intake, MVPA, and TPA were significantly and independently associated with a lower level of SBP in Chinese female university students. Dairy intake was identified to have the strongest association with SBP, followed by TPA and MVPA, respectively. Findings from our study suggested that consuming more dairy products, engaging in more TPA and MVPA were all associated with a lower SBP in Chinese female university students. Future studies should seek a quantitative assessment tool to capture dairy intakes as well as the related nutrients to complement the evidence for a protective mechanism of dairy products.

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Chapter 9: Project JFM: The effect of a Tabata-style functional high-intensity interval training on cardiometabolic health and physical activity in female university students (Study 5: main intervention)

1. Introduction

It is well acknowledged that the process of atherosclerosis begins in childhood, and with the accumulation of cardiometabolic risk factors, its clinical manifestations are often observed in late adulthood [Andersen et al., 2004; Oliveira et al., 2010]. Even though cardiovascular disease (CVD) mortality has reduced sharply over the last few decades in middle-aged and elderly people, the reduction rate is lower in young adults [Yano, 2021]. This may be due to the accelerated aggregation of cardiovascular risk factors, which results in the increasing prevalence of metabolic syndrome (MetS) in young adults, particularly in young women [Ford et al, 2004; Regitz-Zagrosek et al., 2007; Hirode and Wong, 2020]. Substantial evidence shows that a healthy lifestyle, including maintaining a favorable body mass, engaging in high levels of leisure-time physical activity (PA), and healthy eating habits, play an important role against the risk of MetS [Dickie et al., 2014; Wu et al., 2016; Kass et al., 2017; Lv et al., 2017; Lim et al., 2021;]. In addition, a high level of cardiorespiratory fitness (CRF) tends to have a protective effect against CVDs [Rankinen et al., 2007; Kim et al., 2014] and low levels of inflammation are associated with lower risks of future CVD events [Ridker et al., 2017; Zhu et al., 2018; Arnold et al., 2021]. Unfortunately, a range of studies have found that these risk factors are not well controlled among university students, resulting in an increase of CVD risk in this population. For example, students are often observed to gain unhealthy body mass [Hovell et al., 1985; Vella-Zarb and Elgar, 2009], have low levels of leisure-time PA and prolonged sedentary time [Vella-Zarb and Elgar, 2009; Kwan et al., 2012; Kljajević et al., 2021], eat insufficient vegetables and fruits [El Ansari et al., 2012; Moreno-Gómez et al., 2012; Scarapicchia et al., 2015], and experience a downward trend in CRF [Scott et al., 2016; Lamoureux et al., 2019; Lan et al., 2022].

Although there have been multiple interventions aimed at improving university students' lifestyles [Brown et al., 2014; Soriano-Ayala et al., 2020], PA levels [Sharp and Caperchione, 2016; Chiang et al., 2019; Heeren et al., 2018], or dietary habits [Lhakhang et al., 2014; Castillo et al., 2019; Whatnall et al., 2019; Hernández-Jaña et al., 2020], their effectiveness varied widely [Plotnikoff et al., 2015]. This may be attributed to the absence of practice in most interventions. Practice is regarded as the key to the effectiveness of interventions, especially for those aimed at improving PA [Maselli et al., 2018]. However, it seems to be a challenge to enforce a practical intervention in the university setting since lack of time is the most cited barrier to PA engagement among university students [Lovell et al., 2010], and participating in a practical trial will burden students further in addition to academic work [Sweeney, 2011]. These provide a strong context for developing a novel intervention targeting modifiable risk factors associated with cardiovascular health in this population. To this end, a gender-specified strategy is necessary. Male and female students have different attitudes towards health promotion interventions [von Bothmer and Firdlund, 2005] and gender related differences in cardiovascular health risks can be observed. For example, women with insufficient PA are more likely to be obese [Vainshelboim et al., 2019]. Particularly, obese young women are associated with increased risk of preterm delivery [Cnattingius et al., 2013], as well as impaired cognitive development of their infants [Casas et al., 2013]. Given these findings, coupled with the low levels of PA [Haase et al., 2004; Grasdalsmoen et al., 2019] and the high prevalence of MetS and obesity in women [Riediger et al., 2011; Li et al., 2016; Ajlouni et al., 2020], an effective intervention to improve PA and cardiovascular health is warranted for female university students. Establishing an active lifestyle in early adulthood will contribute to long-term health [Jang and Kim, 2019].

High-intensity interval training (HIIT) has gained popularity among young people in recent years. HIIT is characterized by several short bouts of intermittent intense exercise interspersed with recovery periods of different durations [Laursen and Jenkins, 2002]. Numerous data has shown that, compared to traditional moderate-intensity continuous training (MICT), HIIT can provide similar or greater improvements in maximal oxygen uptake (VO_{2max}) with less exercise time and energy expenditure [Jelleyman et al., 2015; Milanović et al., 2015; Sultana et al., 2019]. However, its effects on cardiometabolic health outcomes are controversial. The improvements in insulin sensitivity, blood pressure (BP), and body composition using HIIT were more likely to be observed in overweight or obese individuals, especially when they continued training for 12 weeks or longer [Kessler et al., 2012; Jelleyman et al., 2015; Batacan et al., 2017].

Several studies have evaluated the efficacy and feasibility of HIIT in university settings. Foster et al. (2015) evaluated the effect of 8-weeks Tabata training with 8 intervals of 20-second cycling at 170% VO_{2max}/10-second rest on VO_{2max} and reported a significant increase of 18% in VO_{2max} [Foster et al., 2015]. Likewise, Eather et al. (2019) conducted an 8-week HIIT intervention using a frequency of 3 sessions per week. During each session, participants were required to complete a total of 8-12 minutes of training that included aerobic and strength exercises using the 30-second: 30-second work-rest ratio. After the intervention, CRF and muscular fitness were improved significantly whereas body composition had no gains [Eather et al., 2019]. On the contrary, results from the study by Hu et al. (2022) showed that, after a 4-week functional exercise based HIIT, body composition, heart rate (HR), BP and arterial stiffness were improved in female university students with normal weight obesity (NWO). Although few improvements in cardiometabolic health were observed in short term HIIT (< 12 weeks) [Batacan et al., 2017], the beneficial effects reported by Hu et al. (2022)'s study might be due in large part to the high levels of exercise intensity (90% of maximal heart rate (HR_{max})), during (3 × 9 minutes/session) and frequency (5 sessions/week) selected. Coupled with the obese participants, it was not surprising to see several improvements in cardiometabolic outcomes H following Hu et al. (2022)'s study. However, the total workout time of about 30 minutes seemed to go against the time-efficient nature of HIIT. Zhang et al. (2017) compared the fat-reducing effect of HIIT (90% of VO_{2max}) and MICT (60% of VO_{2max}) in obese female university students. After the 12-week intervention, participants in the HIIT group had similar reductions in percentage body fat (%BF) and total fat mass (FM) as those in the MICT group. Although the HIIT group had significantly shorter exercise durations than the MICT group, lasting nearly 30 minutes [Zhang et al., 2017]. Improvements on CRF were consistent after HIIT. A recent meta-analysis of randomized controlled trials reported that HIIT protocols with short-intervals (≤ 30 seconds), low-volume (≤ 5 minutes) and short-term (≤ 4 weeks) were all effective in increasing VO2max [Wen et al., 2019]. However, with respect to outcomes regarding to cardiometabolic health and body composition, the effects of HIIT appears to be more dependent on the FITT principle (frequency, intensity, times and type) as well as the baseline characteristics of participants.

Tabata training is recognized as one of the most efficient forms of HIIT. A Tabata-style HIIT protocol is characterized by its unique training procedure that comprises of 8 bouts of 20-second exercise followed by a 10-second rest [Tabata, 2019]. While the feasibility of the supramaximal intensity of 170% of VO_{2max} from its original protocol has been questioned [Gentil et al., 2016], studies have found health benefits when it is performed at an intensity of 70%-80% of HR_{max} [Menz et al., 2019; Popowczak et al., 2022]. With a total of 4 minutes, the Tabata-style HIIT protocol had been reported to significantly improve both aerobic and anerobic capacities [Tabata et al., 1996; Murawska-Cialowicz et al., 2020]. This was supported by a recent systematic review [Viana et al., 2019]. Although results from this systematic review demonstrated limited evidence on the weight-reducing effect of the Tabata protocol, some improvements on body composition were reported in the study by Murawska-Cialowicz et al. (2020) and Domaradzki et al. (2020). In addition, BP [Popowczak et al., 2022], fat oxidation [Pearson et al., 2020] and muscular performance [Menz et al., 2019; Islam et al., 2020] benefited from Tabata-style HIIT using functional exercises.

Nevertheless, there is concern that high perceived exertion and low enjoyment are associated with future PA and exercise adherence, especially in participants with a low level of CRF [Dishman, 1994; Follador et al., 2018]. Intense exercises appeared to induce a subsequent decline in non-exercise PA and an increase in sedentary time [Skovgaard et al., 2019; Joshi and Dodge, 2022]. This is thought to be a compensatory behavior, where the energy expended during exercises needs to be compensated for in other behaviors [Skovgaard et al., 2019]. The compensatory behaviors may explain in part why the intervention did not produce the results expected [King et al., 2008]. The short-term effects on compensatory movement behaviors following a Tabata-style HIIT had been investigated in our previous study and the results showed an increase in both sedentary time and moderate-to-vigorous intensity physical activity (MVPA) [Lu et al., 2022a].

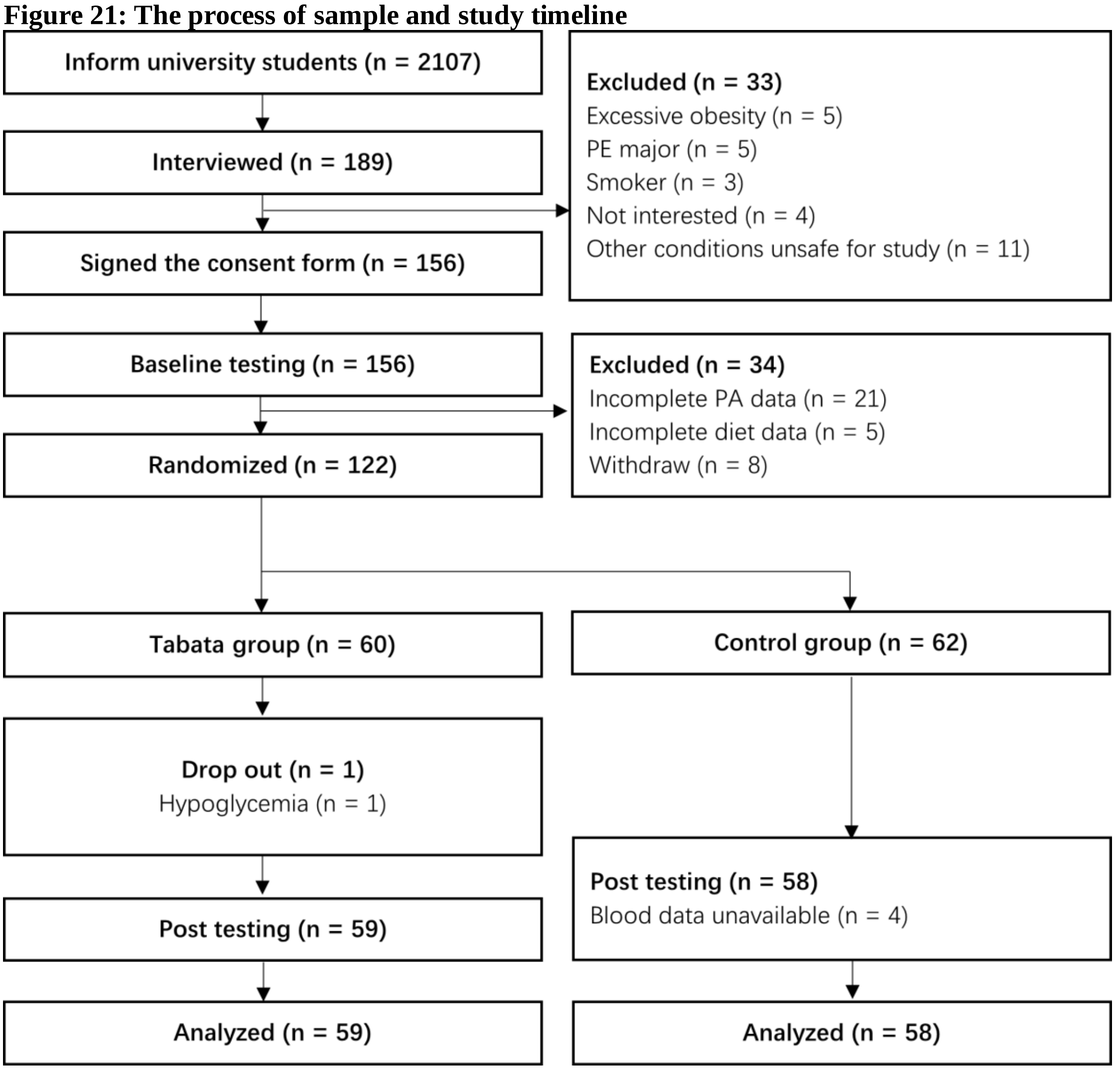
Therefore, the primary purpose of this study is to evaluate the effectiveness of a Tabata-style functional HIIT on PA and cardiometabolic health in female university students with assessments at baseline and after 12 weeks of supervised training. We hypothesize that Tabata training is effective in improving cardiometabolic health and PA. Meanwhile, within the intervention group, subgroup analysis is planned to explore whether there are differential effects between normal weight and overweight/obese participants. We hypothesize that overweight/obese participants had greater improvements compared to normal weight ones after intervention. We further examine whether changes in cardiometabolic outcomes after the intervention are associated with changes in PA. We expected to see a positive relationship between changes in cardiometabolic outcomes and changes in PA.

2. Methods

2.1 Participants

This study was approved by Ningbo University ethics committee on February 23rd, 2022 (RAGH20220166) and Cardiff Metropolitan University ethics committee on December 12nd, 2022 (PGR-6451). The participants recruitment process began in March 2022. Female students who enrolled in September 2021 from Ningbo University were invited to participate in the study via mobile messages and WeChat groups. A presentation was conducted during weekly PE classes comprised of introduction, practical demonstration, and question and answer session. The students who showed interest were then interviewed face-to-face. During the interview, participants who decided to take part in the study were instructed to sign an informed consent form and join a WeChat group. Students with symptoms of or diagnosed CVDs, diabetes, or had any other conditions that might affect PA and dietary intake were excluded. In addition, female students who were pregnant or had the likelihood of pregnancy were also excluded. Students who confirmed participation were required to complete all pre-intervention measurements by the end of March 2022. Finally, 122 female students who had complete PA, diet, laboratory, biochemical, and lifestyle data were enrolled in this study. The process of sample and study timeline were outlined in Figure 21.

Figure 21: The process of sample and study timeline



Note: PA, physical activity; PE, physical education

2.2 Study design

The study was a 12-week randomized controlled trial examining the effectiveness of a Tabata-style functional HIIT on PA and cardiometabolic health in female university students. Participants were randomly assigned to either Tabata or control groups. A complete randomization was used, and the random assignment was conducted using the RAND function in Excel. A researcher recorded the details of eligible participants in excel and assigned excel-generated random numbers to each of them. The random numbers given to the participants were ranked from the smallest to the largest, and the first 60 participants were assigned to the intervention group and the second 62 to the control group. Given our limited number of accelerometers and HR monitors, each of which was only 30, and the total of 122 participants, we decided to allocate 60 participants to the intervention group. During the following exercise sessions, 30 participants worked out in a group. The participants were then informed via phone or message. Because this was a practical exercise intervention, blinding was useless for participants. However, researchers were blinded to group assignment during the post-intervention measurement and data analysis. Participants allocated to the Tabata or the control group were invited to join a separate WeChat group. Participants in the control group were instructed to keep their routine habits during the intervention period. Participants in the intervention group were required to complete a total of 36 sessions of a Tabata-style functional HIIT with the frequency of 3 sessions per week. Each session involved a total of 19 minutes exercises (10 minutes warm-up, 4 minutes Tabata workout, and 5 minutes cool-down). Training took place in an indoor gym and was supervised by researchers. Training times were allocated on Tuesdays, Thursdays and one of the weekends, with morning and afternoon sessions from 9 to 10 AM and 3 to 4 PM, respectively. Participants chose the training session based on their time schedule and adhered to it throughout the intervention. If participants were unable to attend a scheduled session, they had to make it up the next day and be monitored by a researcher. Despite the intensity of training, the retention of participants was high, with only one participant dropping out due to the incidence of hypoglycemia during the first session. The study yielded a final analysis of 59 participants in the Tabata group. Baseline measurements were completed prior to the beginning of the 12-week intervention program and the post-training tests were conducted within the week immediately following the cessation of program. It should be noted that, due to the shortage of accelerometers, the post PA data were measured in groups. The post PA measure was conducted at intervention week 11 and 12 in the intervention group, and at the following two weeks in the control group. All measurements, except blood related ones, were completed in the laboratory of Research Academy of Grand Health from Ningbo University. Venous blood samples were collected from a superficial antecubital vein by qualified and experienced phlebotomists according to standard phlebotomy procedures in the affiliated hospital of medical school from Ningbo University. Participants were required to abstain from foods, drinks other than water, and strenuous exercises for at least 8 hours before the blood measurements.

2.3 Physical, Physiological and Body Composition Measurements

Height was measured in duplicate, using a standard stadiometer protocol. Weight, %BF, FM, fat free mass (FFM) and basal metabolic rate (BMR) were measured using bioelectrical impedance analysis (MC-180, TANITA CO., China). Participants were required to empty their bladder to minimize measurement error caused by "electrically silent" [Kushner et al., 1996]. Participants wearing normal PE clothing without any metal items were instructed to stand barefoot on the bioelectrical impedance analysis by trained researchers. Outcomes were obtained from the associated software. Body mass index (BMI) was calculated using standardized equations. Waist circumference (WC) was measured with a flexible steel tape to the nearest 0.1 cm. For WC, two measurements were taken and if the difference between two measurements was larger than 1%, a third measurement was needed. The mean value was used in the analysis if two measurements were taken, and the median value was used if three measurements were taken. The WHO recommended a BMI of 25 kg/m2 or higher as the cut-off point for overweight or obesity. Although this cut-off point is controversial for the Asian population, there is not enough evidence to indicate a clear cut-off point for Asians. Furthermore, BMI was not considered as a good predictor of CVDs and mortality. According to the optimal cut-off points for identification of the CVD risks in Chinese adults [Zhou, 2002; Yang et al., 2016], participants were classified as overweight or obesity if they met one of the following criteria: 1) BMI $\geq$ 24 kg/m2; 2) WC $\geq$ 80 cm; and 3) %BF $\geq$ 35%.

Resting HR ($HR_{resting}$), systolic BP (SBP) and diastolic BP (DBP) were measured by trained researchers using an automatic upper arm sphygmomanometer (HEM-1000, Omron, China). Prior to BP measurement, participants were required to sit and rest for at least 5 minutes. BP measurements were taken in a seated position from the left arm, with the upper section of the arm supported at the heart level. Three measurements were performed at 1-minute intervals and the average of the second and the third readings were used for analysis. If the two readings differed by more than 5 mm Hg, an additional measurement was taken. BP was classified based on the recommendation from the American Heart Association as normal (SBP < 120 mm Hg and DBP < 80 mm Hg), elevated (SBP = 120-129 mm Hg and DBP < 80 mm Hg), hypertension (HTN) stage 1 (SBP = 130-139 mm Hg or DBP = 80 - 89 mm Hg), and HTN stage 2 (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg). Participants with elevated, HTN stage 1 or stage 2 were identified as having unhealthy BP.

2.4 Cardiorespiratory fitness

Maximal oxygen uptake (VO_{2max}) was used to measure the cardiorespiratory fitness of participants. The modified YMCA submaximal cycle ergometer test was used. Details of the VO_{2max} measurement have been provided in Chapter 7.

2.5 Dietary Intake

Dietary intake was assessed by a staff-administered semi-quantitative food frequency questionnaire (FFQ). This 63-item FFQ was modified from the validated questionnaire used in the 2015 China Nutrition and Health Survey [Zhao et al., 2002]. The frequency and quantity of food intake in the past 12 months were estimated. The dietary intake was divided into 9 categories: staple food, beans, vegetables, fruits, milk, meats, eggs, snacks, and alcohol and beverages. The consumption frequency included: 1) never, 2) times per year, 3) times per month, 4) times per week, and 5) times per day and participants need to answer only one of these questions. The consumption amount for each time was recorded as gram or ml. Samples were presented to help participants more accurately record serving amount. The intake of nutrients was calculated according to the Chinese Food Composition Tables [Yang et al., 2002] and manufacturer information.

2.6 Physical Activity

Details of PA measurements had been provided in the previous chapter (chapter 7). In brief, PA was measured using a triaxial accelerometer (ActiGraph, wGT3X-BT, Pensacola, FL, USA). Participants were instructed to wear the accelerometer on the non-dominant hip for 7 consecutive days except during water-based activities [Trost et al. 2005]. A valid day was defined as not less than 75% of the wear time between 7 a.m. to 11 p.m. and participants provided at least 4 valid days including at least one weekend were included in the final analysis. The intensity of PA was classified according to the Freedson Adult algorithm. Sedentary was defined as < 100 counts per minute (cpm), light intensity physical activity (LPA) was defined as 100-1951 cpm, moderate intensity physical activity (MPA) was defined as 1952-5724 cpm, vigorous intensity physical activity (VPA) as > 5725 cpm, and moderate-to-vigorous intensity physical activity (MVPA) as > 1952 cpm. Total physical activity (TPA) was defined as the daily vector magnitude cpm.

2.7 Cardiometabolic measurements

Generally, it was recommended to use fasting blood samples for blood profiling [NCEP, 2001]. In contrast, the majority of the 24 hours were in a non-fasting state and the non-fasted lipid profile was suggested to better capture atherogenic lipoprotein levels [Nordestgaad, 2017]. Moreover, the non-fasting blood collection would help recruit and retain participants. However, considering the large sample size and the flexibility of blood collecting time, we decided to use fasting blood to control measurement bias. Fasting blood samples were collected into EDTA-treated vacutainers and analyzed using standardized procedures in the hospital laboratory (Power Processor, Beckman Coulter's complete range of clinical lab automation systems, USA). Samples will be analyzed for lipids (total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides), HbA1c, C-reactive protein (CRP), fasting glucose (FPG) and fasting insulin. HOMA-IR was calculated (from measures described above) as follows: fasting insulin (µU/mL) x fasting glucose (mmol/L)/22.5. MetS was defined as having 3 or more of the following 5 abnormalities: 1) central obesity (WC: women ≥ 80 cm); 2) elevated triglycerides (TG) (≥ 150 mg/dL (≥1.7 mmol/L)) or drug treatment; 3) low HDL (women < 50 mg/dL (< 1.3 mmol/L)) or drug treatment; 4) hypertension (systolic blood pressure ≥130 and/or diastolic ≥ 85 mm Hg) or drug treatment; 5) elevated fasting glucose (FPG) (> 100 mg/dL (>5.6 mmol/L)) or drug treatment [Alberti et al., 2009]..

2.8 Interventions

Prior to the first session, participants were instructed to perform a familiarization session, during which 4 functional movements (jumping jacks, high knees, squat jumps, and mountain climbers in sequence) and their sequence of exercise was recorded. The researchers used the "Timer Plus" App to keep time and verbally count down 3 seconds to the end of each workout and rest. During the exercise, a chest strap heart rate monitor (Polar H10, Polar, Malaysia) was used to record heart rate data per second. Monitors were placed near the heart and attached by a band to the chest using non-slip silicone dots and a buckle, which did not make participants uncomfortable and affected exercise performance. Heart rate data was processed using the Polar Flow. In this familiarization session, the age-predicted HR_{max} was used to examine the exercise intensity. According to the Tabata protocol, 90% of HR_{max} was required during the 6th bout. For example, a 20-year-old participant had to reach a 180 beats per minute (bpm) of HR. After the exercise, participants would be informed whether they performed at the target intensity. The 90% cut-off point was only used for researchers as the criterion for satisfactory delivery of Tabata training. Participants received qualitative feedbacks such as “you should go faster” or “you did a good job”. This feedback enabled them to perceive and familiarize themselves with the intensity required during the training. However, the age predicted HRmax was reported to overestimate among young adults [Gellish et al., 2007] and moreover, all participants were freshmen with few age differences. The use of age-predicted maximum HR equations appeared to result in excessive intensity for participants, especially for those with lower fitness. Therefore, during the formal intervention, the intensity of 90% HR_{max} was not compulsive. Participants would receive the feedback about their performance after each exercise session.

All exercise sessions began with a 10-min low-to-moderate warm-up. The warm-up exercises involved joints movement, static stretching, and dynamic stretching. The HR was required to reach 60% of HR_{max} during the warm-up. In the 4-minute Tabata training, 4 movements, including jumping jacks, high knees, squat jumps, and mountain climbers, were performed in sequence using participants’ own body weight. These movements were selected on the basis of the Tabata training recommendations [Tabata, 2019] and showed a good acceptance in female university students in the polit study (Chapter 7). Participants were encouraged to repeat the movement as many times as possible during the 20-second workout, then rest for 10 seconds. These 4 movements were performed in sequence and then repeated, with a total of 4 minutes exercise. There was a 5-minute cool down and stretching after the 4-minute workout.

2.9 Exercise fidelity

Participants were instructed to wear a heart rate monitor (Polar H10, Polar, Malaysia), which was able to record heart rate data at 1-second interval. The mean heart rate (HR_{mean}) and peak heart rate (HR_{peak}) of each session were recorded and presented as a percentage of the individual’s HR_{max}. Participants’ HR_{max} was estimated using the conventional age-predicted equation as 220 – age. Although this equation was limited in predicting the accurate maximal heart rate, with a high variability of 12 bpm among subjects of identical age, it was still recommended in clinical settings and published in resources by well-established organizations in the field [Fletcher et al., 2013]. Furthermore, the individualized exercise prescription was not the primary objective of the present study, the utility of age predicted HR_{max} appeared to be acceptable and reasonable. In our pilot study, the mean heart rate achieved during exercise was 82.4 ± 1.9% of age predicted HRmax. In order to reflect the high intensity, a cut-point of 80% of HR_{max} was used to evaluate the intervention fidelity [Garber et al., 2011]. Participants with a HR_{mean} below the 80% of HR_{max} over the 12-week intervention were excluded in the final analysis and would be analyzed separately.

2.10 Other variables

Other variables including demographic data, lifestyle and family history of hypertension and type 2 diabetes were identified using a standardized questionnaire. Smoking, drinking, and staying up late were classified as never, sometimes, or always. The family history of hypertension and type 2 diabetes were classified as yes or no.

2.11 Statistical analysis

All statistical analyses were performed using IBM SPSS for windows, version 23.0 (Chicago, IL, USA) and the significance level was set as $p < 0.05$.

The achieved power was estimated by G * Power (version 3.1.9.7) (Heinrich Heine University, Dusseldorf, Germany) using a post hoc, with the effect size, alpha and sample size of 0.5, 0.05 and 60, respectively. Using a t-tests marched pairs design, 60 participants in the Tabata group was able to achieve a power of 0.97.

Data normality was examined using the Kolmogorov-Smirnov and Shapiro-Wilk tests.

Logarithms were used for non-normality data. In the descriptive statistical analysis, participants were categorized into groups based on obesity status. Descriptive analyses were summarized as means with 95% confidence intervals (CI), and proportions for continuous and categorical variables, respectively. For variables that were logarithmically transformed, geometric means and geometric standard deviations were used. ANOVA and $\chi 2$ test were used to analyze differences between continuous and categorical variables, respectively. Paired t-test was used to explore any differences between pre- and post- intervention within groups. Correlations between variables were examined using the Pearson product moment correlation coefficient. Mixed linear models were used to evaluate intervention effects between the Tabata and the control group, considering the percentage change in the measurements between the posttest and pretest as outcomes. Cohen's d was used to provide a measure of effect size (mean difference on percentage change [posttest pretest] between the Tabata and the control group over the intervention divided by the pooled SD of percentage change). The effect size was classified as trivial (< 0.2), small (0.2 - 0.6), moderate (0.6 - 1.2), or large (> 1.2) [Hopkins et al., 2009]. Mixed linear models were also used to explore the moderating effect of weight status (normal weight vs. overweight/obese) with interaction terms (intervention weight status). The same statistical methods were used for subgroup analyses.

For cardiometabolic risk factors with significant changes after intervention, linear regression models were used to test the association between changes in cardiometabolic outcomes and changes in PA (MVPA and TPA). The variance inflation factor (VIF) was used to check the multicollinearity and an issue of multicollinearity was identified if VIF > 5.0. Due to the high correlation between the change of MVPA and the change of TPA, for each cardiometabolic outcome, 2 models were tested. The dependent variable was the percentage change of cardiometabolic outcome. The independent variable was the percentage change of MVPA in model 1, and the percentage change of TPA in model 2. All models controlled for age, lifestyle variables, the baseline, and the percentage change of body composition, CRF and dietary variables, the baseline value of PA data, as well as the baseline value of the cardiometabolic outcome modelled. Participants' ID numbers were used for data store and processing. Participants with less than 90% attendance were excluded in the final analysis [Heinrich et al., 2014].

3. Results

3.1 Descriptive statistics

The baseline characteristics of participants are presented in Table 26. One participant in the Tabata group dropped out the intervention due to the incidence of hypoglycemia. Four participants in the control group missed the post-test blood data. Therefore, a total of 59 participants in the Tabata groups and 58 participants in the control were included in the final analysis.

Table 26: Baseline characteristics of participants

Variables	All (n= 117)	Tabata (n=59)	Control (n=58)	p value
Age (years)	20.38 (20.14 to 20.63)	20.42 (20.03 to 20.82)	20.34 (20.03 to 20.65)	p > 0.05
Height (cm)	163.48 (162.61 to 164.35)	163.88 (162.70 to 165.07)	163.07 (161.77 to 164.37)	p > 0.05
Alcohol				p > 0.05
Never	108 (92.31%)	55 (93.22%)	53 (91.38%)	
Sometimes	9 (7.69%)	4 (6.78%)	5 (8.62%)	
Always				
Staying up late				p > 0.05
Never				
Sometimes	42 (35.90%)	20 (33.90%)	22 (37.93%)	
Always	75 (64.10%)	39 (66.10%)	36 (62.07%)	
Family history of hypertension				p > 0.05
Yes	6 (5.13%)	3 (5.08%)	3 (5.17%)	

No	111 (94.87%)	56 (94.92%)	55 (94.83%)	
Family history of diabetes				$p > 0.05$
Yes	3 (2.56%)	2 (3.39%)	1 (1.72%)	
No	114 (97.44%)	57 (96.61%)	57 (98.28%)	
Weight (kg)	56.60 (55.19 to 58.01)	56.23 (54.13 to 58.33)	56.97 (55.03 to 58.92)	$p > 0.05$
BMI (kg/m^2)	21.16 (20.69 to 21.63)	20.92 (20.22 to 21.63)	21.40 (20.76 to 22.04)	$p > 0.05$
WC (cm)	73.82 (72.91 to 74.72)	73.92 (72.59 to 75.24)	73.72 (72.45 to 74.98)	$p > 0.05$
%Body fat	27.42 (26.69 to 28.14)	27.94 (26.79 to 29.08)	26.88 (25.97 to 27.80)	$p > 0.05$
FM (kg)	15.71 (14.98 to 16.43)	15.90 (14.80 to 16.99)	15.52 (14.54 to 16.49)	$p > 0.05$
FFM (kg)	40.89 (40.07 to 41.72)	40.34 (39.06 to 41.61)	41.46 (40.39 to 42.52)	$p > 0.05$
Basal Energy expenditure (kcal)	1234.33 (1219.07 to 1249.60)	1236.17 (1212.74 to 1259.60)	1232.47 (1212.24 to 1252.70)	$p > 0.05$
VO_{2max} (mL/kg/min)	34.45 (33.72 to 35.19)	34.24 (33.21 to 35.27)	34.67 (33.59 to 35.76)	$p > 0.05$
VO_{2max} (L/min)	1.94 (1.89 to 2.00)	1.92 (1.84 to 1.99)	1.97 (1.88 to 2.06)	$p > 0.05$
Resting Heart Rate (bpm)	89.48 (87.76 to 91.20)	89.03 (86.55 to 91.52)	89.93 (87.47 to 92.39)	$p > 0.05$
SBP (mm Hg)	122.19 (120.03 to 124.29)	121.37 (118.37 to 124.38)	123.02 (120.00 to 126.04)	$p > 0.05$
DBP (mm Hg)	70.43 (69.29 to 71.56)	71.46 (69.88 to 73.04)	69.38 (67.74 to 71.01)	$p > 0.05$
HDL (mmol/L)	1.75 (1.65 to 1.84)	1.72 (1.58 to 1.85)	1.78 (1.65 to 1.91)	$p > 0.05$
LDL (mmol/L)	2.58 (2.48 to 2.69)	2.63 (2.47 to 2.78)	2.54 (2.40 to 2.68)	$p > 0.05$
TG (mmol/L)	1.10 (1.01 to 1.18)	1.09 (0.97 to 1.22)	1.10 (0.98 to 1.21)	$p > 0.05$
TC (mmol/L)	4.94 (4.81 to 5.08)	4.91 (4.70 to 5.11)	4.98 (4.80 to 5.16)	$p > 0.05$
HbA1c (%)	5.08 (5.03 to 5.14)	5.06 (4.99 to 5.14)	5.11 (5.03 to 5.18)	$p > 0.05$
FPG (mmol/L)	4.92 (4.83 to 5.01)	4.93 (4.81 to 5.04)	4.91 (4.76 to 5.05)	$p > 0.05$
Fasting insulin (μU/mL)	4.58 (4.38 to 4.79)	4.62 (4.34 to 4.90)	4.55 (4.24 to 4.85)	$p > 0.05$
HOMA-IR	1.00 (0.95 to 1.05)	1.01 (0.95 to 1.07)	0.99 (0.92 to 1.07)	$p > 0.05$
CRP (mg/L)	0.81 (0.79 to 0.83)	0.79 (0.76 to 0.82)	0.82 (0.80 to 0.85)	$p > 0.05$
MVPA (min/d)	103.68 (100.66 to 106.70)	105.14 (100.72 to 109.56)	102.20 (97.98 to 106.41)	$p > 0.05$

TPA (cpm)	1189.26 (1142.38 to 1236.13)	1167.21 (1099.78 to 1234.63)	1211.69 (1145.04 to 1278.33)	p > 0.05
Energy intake (kcal/day)	1752.56 (1661.31 to 1843.82)	1706.27 (1591.21 to 1821.32)	1799.66 (1655.01 to 1944.30)	p > 0.05
Vegetable (g/d)	263.85 (241.97 to 285.72)	249.90 (220.29 to 279.51)	278.04 (245.30 to 310.78)	p > 0.05
Fruit (g/d)	202.83 (181.28 to 224.37)	217.59 (183.39 to 251.79)	187.81 (161.27 to 214.34)	p > 0.05
Dairy (serving/d)	1.18 (1.09 to 1.28)	1.16 (1.04 to 1.29)	1.20 (1.05 to 1.37)	p > 0.05

Note: BMI, body mass index; BMR, basal metabolic rate; CRP, C-reactive protein; cpm, count per minute; DBP, diastolic blood pressure; FFM, fat-free mass; FM, fat mass; FPG, fasting glucose; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TC, total-cholesterol; TG, triglyceride; TPA, total physical activity; VO_{2max}, maximal oxygen uptake; WC, waist circumference.

At baseline, according to the definition of overweight and obesity used in this study, 27 (23.08%) participants were classified as overweight or obese. Based on the MetS definition used in this study, the prevalence of MetS was 5.13%. For individual components of MetS, high BP was the most prevalent, with 36 (30.77%) participants had a SBP ≥ 130 mm Hg. 25 (21.37%) participants had low HDL, 20 (17.09%) participants had central obesity, 13 (11.11%) had elevated TG, and 10 (8.55%) had elevated FPG. 43 (36.75%) participants had one MetS component, 22 (18.80%) participants had two MetS components and 46 (39.32%) participants had none of these. Participants showed a relatively high level of PA, with only one participant failed to meet the minimum level of MVPA recommended. The average daily PA was 103.68 (95% CI: 100.66 to 106.70) minutes for MVPA and 1189.26 (95% CI: 1142.38 to 1236.13) cpm for TPA. Based on the recommended daily vegetable (300-500g) and fruit (200-350g) intake for Chinese people [Gu et al., 2021], most participants failed to meet the minimum daily vegetable and fruit intake (64.96% for vegetable and 53.85% for fruit). The average daily vegetable, fruit and dairy intake were 263.85 (95% CI: 241.97 to 285.72) g, 202.83 (95%CI: 181.28 to 224.37) g and 1.18 (95%CI: 1.09 to 1.28) serving, respectively. Participants consumed an average of 1752.56 (95%CI: 1661.31 to 1843.82) calories per day. Alcohol and smoking were less common among female university students, with only 15 participants reporting alcohol drinking sometimes and no participants reporting smoking. Family history of hypertension and diabetes were reported by 6 and 3 participants, respectively. Staying up late was more common among participants, with 27 participants reporting staying up late sometimes and 90 reporting always. The relative and absolute cardiorespiratory fitness (VO_{2max}) was 34.45 (95% CI: 33.72 to 35.19) mL/kg/min and 1.94 (95% CI: 1.89 to 2.00) L/min, respectively. According to the CRF percentiles recommended by Kaminsky et al. (2017), 24 (20.51%) participants were below the 50th percentile VO_{2max} of women aged 20 to 29 years of 31.0 mL/kg/min. Table 26 presented the separate data for Tabata and control groups and there were no significant between-group differences in parameters between groups at baseline.

Exercise fidelity

The average HR_{max} for the total Tabata group was 199.58 ± 1.52 bpm. All participants met the minimum level of intensity, and a total of 2124 individual heart rate data were analyzed. Over the 12-week intervention, the HR_{mean} during exercise was 83.24% (95% CI: 82.75% to 83.74%) of individual HR_{max}, with a between-subject SD of 1.89%. The HR_{mean} varied between participants from 80.8% to 86.6%. The within-subject SD was 0.24%. The participants' HR_{mean} varied from 82.77% to 83.77% over 36 exercise sessions. The HR_{peak} for exercise session across the intervention was 93.32% (95% CI: 92.52% to 94.11%) of individual HR_{max}, with a between-subject SD of 3.05%. The HR_{peak} varied between participants from 89.8% to 97.3%. The within-subject SD was 0.30%. The participants' HR_{peak} varied from 92.84% to 93.91% within different exercise sessions over the intervention. There were no differences between HR_{mean} and HR_{peak} during session 1 to session 12.

Post-intervention effects

The total time spent over the 12-week intervention was 684 minutes, with 360 minutes for warming up, 144 minutes for Tabata training, and 180 minutes for cooling down and stretching. Over the intervention, participants performed a total of 96-minutes of high-intensity exercise (8 minutes per week). Only 1 participant dropped out the intervention, resulting in a satisfied exercise adherence of 98.31%. The effects of the Tabata style functional HIIT are presented in Table 27. There were significant ($p < 0.05$) interaction effects for WC ($p = 0.002$), MVPA ($p = 0.007$), TPA ($p = 0.009$), LDL ($p = 0.004$), TG ($p = 0.010$), TC ($p < 0.001$), daily energy intake ($p = 0.012$) and vegetable intake ($p = 0.001$). Therefore, within the Tabata group, we also conducted a separate analysis for participants with overweight or obesity and those with normal weight (Table 28).

Table 27: The effects of the Tabata style functional HIIT between Tabata and control groups

	Tabata (n=59)			Control (n=58)			Difference between groups		
	Preintervention mean (95% CI)	**Postintervention mean (95% CI)**	**Mean change (95% CI)**	**Preintervention mean (95% CI)**	**Postintervention mean (95% CI)**	**Mean change (95% CI)**	**Mean change (95% CI)**	**p-value**	**Cohen's d (95% CI)**
Weight (kg)	56.23 (54.13 to 58.33)	56.04 (54.24 to 57.85)	-0.06% (-0.71% to 0.58%)	56.97 (55.03 to 58.92)	57.60** (55.74 to 59.46)	1.25% (0.46% to 2.03%)	-1.31% (-2.31% to -0.31%)	**0.011**	-0.48 (-0.84 to -0.11)
BMI (kg/m^2)	20.92 (20.22 to 21.63)	20.86 (20.25 to 21.47)	-0.06% (-0.71% to 0.58%)	21.40 (20.76 to 22.04)	21.64** (21.03 to 22.25)	1.25 (0.46% to 2.03%)	-1.31% (-2.31% to -0.31%)	**0.011**	-0.48 (-0.84 to -0.11)
WC (cm)	73.92 (72.59 to 75.24)	73.78 (72.54 to 75.02)	-0.16 (-0.34% to 0.02%)	73.72 (72.45 to 74.98)	73.77 (72.53 to 75.01)	0.08 (-0.07% to 0.24%)	-0.24% (-0.48% to -0.01%)	**0.043**	-0.37 (-0.74 to -0.01)
%Body fat	27.94 (26.79 to 29.08)	27.15*** (26.08 to 28.21)	-2.57% (-4.06% to -1.09%)	26.88 (25.97 to 27.80)	27.69*** (26.83 to 28.55)	3.23% (2.10% to 4.36%)	-5.80% (-7.65% to -3.95%)	**< 0.001**	-1.15 (-1.53 to -0.75)
FM (kg)	15.90 (14.80 to 16.99)	15.34*** (14.40 to 16.27)	-2.61% (-4.36% to -0.85%)	15.52 (14.53 to 16.49)	16.12*** (15.18 to 17.06)	4.58% (2.86% to 6.30%)	-7.19% (-9.62% to 4.76%)	**< 0.001**	-1.08 (-1.46 to -0.69)
FFM (kg)	40.34 (39.06 to 41.61)	40.71* (39.53 to 41.88)	1.07% (0.37% to 1.77%)	41.46 (40.39 to 42.52)	41.48 (40.45 to 42.51)	0.13% (-0.51% to 0.77%)	0.94% (-0.00% to 1.88%)	0.051	0.37 (0.00 to 0.73)
Basal metabolic rate (kcal)	1236 (1213 to 1260)	1247** (1226 to 1268)	0.95% (0.33% to 1.56%)	1232 (1212 to 1253)	1235 (1215 to 1254)	0.20% (-0.24% to 0.64%)	0.75% (-0.00% to 1.50%)	0.050	0.37 (0.00 to 0.73)
VO_{2max} (mL/kg/min)	34.24 (33.21 to 35.27)	38.56*** (37.43 to 39.69)	12.87% (11.00% to 14.73%)	34.67 (33.59 to 35.76)	34.57 (33.51 to 35.63)	-0.27% (-0.66% to 0.13%)	13.13% (11.23% to 15.04%)	**< 0.001**	2.53 (2.03 to 3.00)
VO_{2max} (L/min)	1.92 (1.84 to 1.99)	2.15*** (2.07 to 2.24)	12.73% (11.02% to 14.44%)	1.97 (1.88 to 2.06)	1.99 (1.90 to 2.07)	0.98% (0.08% to 1.88%)	11.75% (9.82% to 13.67%)	**< 0.001**	2.24 (1.76 to 2.68)
Resting Heart Rate (bpm)	89.03 (86.55 to 91.52)	80.98*** (79.17 to 82.80)	-8.62% (-10.34% to -6.89%)	89.93 (87.47 to 92.39)	89.97 (87.55 to 92.38)	0.05% (-0.27% to 0.37%)	-8.66% (-10.42% to -6.92%)	**< 0.001**	-1.82 (-2.23 to -1.37)

SBP (mm Hg)	121.37 (118.37 to 124.38)	116.56*** (114.63 to 118.49)	-3.66% (-4.73% to -2.58%)	123.02 (119.99 to 126.04)	123.28 (120.27 to 126.28)	0.22% (-0.20% to 0.64%)	-3.88% (-5.02% to -2.73%)	**< 0.001**	-1.24 (-1.63 to -0.84)
DBP (mm Hg)	71.46 (69.88 to 73.04)	71.44 (70.01 to 72.87)	0.06% (-0.41% to 0.54%)	69.38 (67.74 to 71.01)	69.48 (67.92 to 71.05)	0.19% (-0.09% to 0.47%)	-0.13% (-0.68% to 0.42%)	0.641	-0.09 (-0.45 to 0.28)
Lipid profile									
HDL (mmol/L)	1.72 (1.58 to 1.85)	1.82*** (1.71 to 1.94)	8.54% (5.82% to 11.27%)	1.78 (1.65 to 1.91)	1.78 (1.65 to 1.91)	0.45% (-0.40% to 1.30%)	8.09% (5.25% to 10.94%)	**< 0.001**	1.04 (0.65 to 1.42)
LDL (mmol/L)	2.63 (2.47 to 2.78)	2.56* (2.42 to 2.71)	-1.95% (-3.53% to -0.38%)	2.54 (2.40 to 2.68)	2.56 (2.43 to 2.69)	1.06% (-0.11% to 2.23%)	-3.01% (-4.96% to -1.07%)	**0.003**	-0.57 (-0.93 to -0.19)
TG (mmol/L)	1.09 (0.97 to 1.22)	1.06** (0.94 to 1.18)	-1.08% (-2.85% to 0.69%)	1.10 (0.98 to 1.21)	1.10 (0.99 to 1.21)	0.83% (-0.18% to 1.83%)	-1.91% (-3.93% to 0.12%)	0.065	-0.34 (-0.71 to 0.02)
TC (mmol/L)	4.91 (4.70 to 5.11)	4.83* (4.67 to 5.00)	-1.07% (-2.00% to -0.13%)	4.98 (4.80 to 5.16)	5.02** (4.85 to 5.19)	0.90% (0.25% to 1.55%)	-1.97% (-3.10% to -0.84%)	**0.001**	-0.64 (-1.00 to -0.26)
Carbohydrate metabolism									
HbA1c (%)	5.06 (4.99 to 5.14)	5.06 (4.98 to 5.13)	-0.17% (-0.36% to 0.02%)	5.11 (5.03 to 5.18)	5.10 (5.03 to 5.17)	-0.04% (-0.16% to 0.09%)	-0.13% (-0.36% to 0.09%)	0.241	-0.23 (-0.59 to 0.14)
FPG (mmol/L)	4.93 (4.81 to 5.04)	4.90 (4.80 to 4.99)	-0.43% (-1.09% to 0.23%)	4.91 (4.76 to 5.05)	4.90 (4.76 to 5.04)	-0.05% (-0.30% to 0.20%)	-0.38% (-1.08% to 0.33%)	0.291	-0.20 (-0.56 to 0.17)
HOMA-IR	1.01 (0.95 to 1.07)	0.99** (0.94 to 1.05)	-1.24% (-2.50% to 0.03%)	0.99 (0.92 to 1.07)	1.00 (0.93 to 1.08)	0.24% (-0.07% to 0.54%)	-1.47% (-2.76% to -0.18%)	**0.026**	-0.42 (-0.78 to -0.05)
Endocrine regulators									
Fasting insulin (µU/mL)	4.62 (4.34 to 4.90)	4.56* (4.31 to 4.80)	-0.83% (-1.82% to 0.17%)	4.55 (4.24 to 4.85)	4.56 (4.25 to 4.86)	0.29% (0.00% to 0.57%)	-1.11% (-2.15% to -0.08%)	**0.035**	-0.40 (-0.76 to -0.03)
Inflammation									
CRP (mg/L)	0.79 (0.76 to 0.82)	0.80 (0.77 to 0.83)	0.46% (-0.03% to 0.96%)	0.82 (0.80 to 0.85)	0.83 (0.80 to 0.85)	0.45% (-0.03% to 0.93%)	0.01% (-0.67% to 0.70%)	0.971	0.01 (-0.36 to 0.37)

Physical activity									
MVPA (min/d)	105.14 (100.72 to 109.56)	121.08*** (116.02 to 126.13)	15.51% (13.27% to 17.74%)	102.20 (97.98 to 106.41)	98.52** (95.10 to 101.95)	-2.95% (-4.88% to -1.03%)	18.46% (15.54% to 21.38%)	**< 0.001**	2.31 (1.83 to 2.77)
TPA (cpm)	1167.21 (1099.78 to 1234.63)	1327.48*** (1263.52 to 1391.44)	14.92% (12.33% to 17.51%)	1211.69 (1145.04 to 1278.33)	1176.20*** (1121.21 to 1231.19)	-2.03% (-3.85% to -0.22%)	16.95% (13.81% to 20.09%)	**< 0.001**	1.98 (1.53 to 2.41)
Dietary intake									
Energy intake (kcal/day)	1706.27 (1591.21 to 1821.32)	1694.23 (1601.69 to 1786.77)	-0.85% (-1.36% to 3.06%)	1799.66 (1655.01 to 1944.30)	1806.37 (1663.25 to 1949.48)	0.60% (-0.19% to 1.39%)	0.26% (-2.08% to 2.59%)	0.829	0.04 (-0.32 to 0.40)
Vegetable (g/d)	249.90 (220.29 to 279.51)	249.40 (221.12 to 277.69)	-0.90% (-0.46% to 2.27%)	278.04 (245.30 to 310.78)	277.24 (244.81 to 309.68)	0.01% (-0.60% to 0.63%)	0.89% (-0.60% to 2.39%)	0.238	0.22 (-0.15 to 0.58)
Fruit (g/d)	217.59 (183.39 to 251.79)	216.09 (182.84 to 249.34)	-1.34% (-2.00% to 4.68%)	187.81 (161.27 to 214.34)	187.12 (160.67 to 213.57)	0.02% (-0.85% to 0.88%)	1.33% (-2.11% to 4.77%)	0.446	0.14 (-0.22 to 0.50)
Dairy (serving/d)	1.16 (1.04 to 1.29)	1.16 (1.04 to 1.28)	1.21% (-1.36% to 3.77%	1.20 (1.05 to 1.37)	1.20 (1.05 to 1.36)	0.34% (-0.91% to 1.58%)	-0.87% (-3.71% to 1.97%)	0.545	-0.09 (-0.45 to 0.27)

Note: BMI, body mass index; BMR, basal metabolic rate; CRP, C-reactive protein; cpm, count per minute; DBP, diastolic blood pressure; FFM, fat-free mass; FM, fat mass; FPG, fasting glucose; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TC, total-cholesterol; TG, triglyceride; TPA, total physical activity; VO_{2max}, maximal oxygen uptake; WC, waist circumference; *, difference between pre- and post- test, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Table 28: The effects of the Tabata style functional HIIT between overweight/obese and normal weight groups

	Overweight/Obese (n=10)			Normal weight (n=49)			Adjusted difference between groups		
	Preintervention mean (95% CI)	Postintervention mean (95% CI)	Mean change (95% CI)	Preintervention mean (95% CI)	Postintervention mean (95% CI)	Mean change (95% CI)	Mean change (95% CI)	p-value	Cohen's d (95% CI)
Weight (kg)	69.09 (64.67 to 73.51)	66.62*** (62.51 to 70.73)	-3.54% (-4.63% to -2.45%)	53.61 (52.04 to 55.18)	53.89 (52.48 to 55.29)	0.65% (0.08% to 1.21%)	-4.18% (-5.51% to -2.86%)	**< 0.001**	-2.19 (-2.95 to -1.38)
BMI (kg/m2)	25.21 (24.29 to 26.14)	24.31*** (23.50 to 25.12)	-3.54% (-4.63% to -2.45%)	20.05 (19.47 to 20.62)	20.16 (19.63 to 20.68)	0.65% (0.08% to 1.21%)	-4.18% (-5.51% to -2.86%)	**< 0.001**	-2.19 (-2.95 to -1.38)
WC (cm)	82.66 (81.38 to 83.94)	81.63* (80.31 to 82.95)	-1.24% (-2.13% to -0.35%)	72.13 (71.16 to 73.11)	72.18** (71.21 to 73.14)	0.06% (0.02% to 0.10%)	-1.30% (-1.66% to -0.95%)	**< 0.001**	-2.56 (-3.35 to -1.71)
%Body fat	32.79 (29.58 to 36.00)	30.99** (28.13 to 33.85)	-5.28% (-8.04% to -2.52%)	26.95 (25.89 to 28.01)	26.36** (25.31 to 27.41)	-2.02% (-3.71% to -0.33%)	-3.26% (-7.16% to 0.64%)	0.100	-0.58 (-1.26 to 0.12)
FM (kg)	22.67 (20.02 to 25.31)	20.66*** (18.30 to 23.03)	-8.61% (-11.85% to -5.37%)	14.51 (13.73 to 15.30)	14.25* (13.53 to 14.97)	-1.38% (-3.24% to 0.48%)	-7.23% (-11.54% to -2.93%)	**0.001**	-1.17 (-1.86 to -0.44)
FFM (kg)	46.43 (42.91 to 49.94)	45.96 (42.75 to 49.17)	-0.91% (-2.31% to 0.49%)	39.10 (37.98 to 40.21)	39.64*** (38.57 to 40.70)	1.47% (0.71% to 2.23%)	-2.37% (-4.15% to -0.60%)	**0.010**	-0.93 (-1.62 to -0.22)
Basal metabolic rate (kcal)	1334 (1247 to 1420)	1331 (1246 to 1415)	-0.19% (-0.84% to 0.45)	1216 (1197 to 1236)	1230** (1213 to 1247)	1.18% (0.46% to 1.90)	-1.37% (-2.99% to 0.24%)	0.094	-0.59 (-1.27 to 0.10)
VO_{2max} (mL/kg/min)	31.73 (28.88 to 34.58)	37.11*** (33.52 to 40.70)	16.98% (12.68% to 21.28%)	34.75 (33.66 to 35.84)	38.85*** (37.65 to 40.06)	12.03% (9.98% to 14.08%)	4.96% (0.11% to 9.80%)	**0.045**	0.71 (0.01 to 1.39)
VO_{2max} (L/min)	2.20 (1.93 to 2.47)	2.47*** (2.18 to 2.77)	12.82% (8.90% to 16.74%)	1.86 (1.79 to 1.93)	2.09*** (2.01 to 2.17)	12.71% (10.75% to 14.67%)	0.11% (-4.50% to 4.71%)	0.963	0.02 (-0.66 to 0.70)
Resting Heart Rate (bpm)	91 (83 to 98)	82* (76 to 88)	-9.13% (-15.94% to -2.31%)	89 (86 to 91)	81*** (79 to 83)	-8.51% (-10.23% to -6.80%)	-0.61% (-5.24% to 4.02%)	0.792	-0.09 (-0.77 to 0.59)
SBP (mm Hg)	121 (115 to 127)	117* (113 to 121)	-3.35% (-6.12% to -0.57%)	121 (118 to 125)	117*** (114 to 119)	-3.72% (-4.92% to -2.51%)	0.37% (-2.52% to 3.26%)	0.798	0.09 (-0.59 to 0.77)

DBP (mm Hg)	71 (68 to 74)	71 (68 to 73)	0.07% (-1.22% to 1.36%)	72 (70 to 73)	72 (70 to 73)	0.06% (-0.47% to 0.59%)	0.01% (-1.27% to 1.28%)	0.991	0.01 (-0.67 to 0.69)
Lipid profile									
HDL (mmol/L)	1.69 (1.28 to 2.11)	1.88*** (1.51 to 2.26)	13.65% (6.73% to 20.57%)	1.72 (1.58 to 1.87)	1.81*** (1.69 to 1.93)	7.50% (4.52% to 10.48%)	6.15% (-0.99% to 13.28%)	0.090	0.60 (-0.10 to 1.28)
LDL (mmol/L)	3.07 (2.74 to 3.41)	2.81* (2.43 to 3.18)	-8.59% (-15.09% to - 2.10%)	2.53 (2.37 to 2.70)	2.51 (2.36 to 2.67)	-0.60% (-1.81% to 0.61%)	-8.00% (-11.67% to 4.32%)	**< 0.001**	-1.51 (-2.22 to - 0.76)
TG (mmol/L)	1.57 (1.41 to 1.73)	1.47** (1.33 to 1.61)	-6.30% (-9.23% to - 3.37%)	1.00 (0.86 to 1.13)	0.98 (0.85 to 1.11)	-0.02% (-1.96% to 1.93%)	-6.28% (-10.75% to - 1.82%)	**0.007**	-0.98 (-1.67 to - 0.26)
TC (mmol/L)	5.67 (5.27 to 6.06)	5.38** (5.14 to 5.61)	-4.83% (-7.31% to - 2.35%)	4.75 (4.54 to 4.96)	4.72 (4.54 to 4.91)	-0.30% (-1.20% to 0.60%)	-4.53% (-6.74% to - 2.31%)	**< 0.001**	-1.42 (-2.12 to - 0.67)
Carbohydrate metabolism									
HbA1c (%)	5.39 (5.28 to 5.51)	5.35 (5.26 to 5.45)	-0.73% (-1.48% to 0.03%)	5.00 (4.92 to 5.08)	4.99 (4.92 to 5.07)	-0.06% (-0.23% to 0.12%)	-0.67% (-1.15% to - 0.19%)	**0.008**	-0.97 (-1.66 to - 0.25)
FPG (mmol/L)	4.91 (4.58 to 5.23)	4.83* (4.56 to 5.10)	-1.50% (-2.92% to - 0.09%)	4.93 (4.80 to 5.06)	4.91 (4.81 to 5.02)	-0.21% (-0.95% to 0.54%)	-1.30% (-3.04% to 0.45%)	0.142	-0.52 (-1.19 to 0.18)
HOMA-IR	1.21 (1.04 to 1.38)	1.16** (1.02 to 1.30)	-3.84% (-6.11% to - 1.57%)	0.97 (0.90 to 1.04)	0.96 (0.90 to 1.01)	-0.70% (-2.13% to 0.72)	-3.13% (-6.42% to 0.15%)	0.061	-0.66 (-1.34 to 0.04)
Endocrine regulators									
Fasting insulin (μU/mL)	5.58 (4.73 to 6.42)	5.42* (4.70 to 6.14)	-2.36% (-4.52% to - 0.19%)	4.43 (4.15 to 4.70)	4.38 (4.14 to 4.62)	-0.51% (-1.64% to 0.61%)	-1.84% (-4.48% to 0.79%)	0.166	-0.49 (-1.17 to 0.20)
Inflammation									
CRP (mg/L)	0.92 (0.87 to 0.96)	0.92 (0.88 to 0.97)	0.36% (-0.49% to 1.21%)	0.77 (0.73 to 0.80)	0.77 (0.74 to 0.80)	0.49% (-0.10% to 1.07%)	-0.13% (-1.46% to 1.20%)	0.848	-0.07 (-0.75 to 0.61)
Physical activity									

MVPA (min/d)	102.22 (86.04 to 118.41)	124.80*** (105.30 to 144.30)	22.50% (17.76% to 27.24%)	105.74 (101.20 to 110.27)	120.32*** (115.24 to 125.39)	14.08% (11.71% to 16.45%)	8.42% (2.85% to 14.00%)	**0.004**	1.05 (0.33 to 1.74)
TPA (cpm)	1178.83 (1047.84 to 1309.81)	1439.70*** (1307.90 to 1571.49)	22.84% (17.07% to 28.60%)	1164.84 (1086.40 to 1243.27)	1304.58*** (1232.33 to 1376.83)	13.30% (10.56% to 16.04%)	9.54% (3.05% to 16.02%)	**0.005**	1.02 (0.30 to 1.71)
Dietary intake									
Energy intake (kcal/day)	2148.36 (1872.15 to 2424.56)	2008.19* (1789.30 to 2227.08)	-5.78% (-11.31% to -0.24%)	1616.05 (1501.67 to 1730.42)	1630.16 (1534.86 to 1725.46)	2.21% (-0.11% to 4.52%)	-7.98% (-13.54% to -2.42%)	**0.006**	-1.00 (-1.69 to -0.28)
Vegetable (g/d)	211.42 (135.71 to 287.13)	220.30* (145.48 to 295.12)	5.37% (0.49% to 10.25%)	257.75 (224.85 to 290.66)	255.34 (223.92 to 286.77)	-0.01% (-1.28% to 1.26%)	5.38% (1.99% to 8.77%)	**0.002**	1.10 (0.38 to 1.80)
Fruit (g/d)	115.71 (79.04 to 152.37)	117.59 (81.37 to 153.81)	2.28% (-0.92% to 5.48%)	238.38 (200.15 to 276.61)	236.19* (199.01 to 273.37)	1.15% (-2.85% to 5.16%)	1.13% (-7.85% to 10.11%)	0.803	0.09 (-0.59 to 0.77)
Dairy (serving/d)	1.11 (0.87 to 1.35)	1.06 (0.86 to 1.25)	-2.90% (-10.06% to 4.25%)	1.17 (1.03 to 1.32)	1.18 (1.04 to 1.32)	2.05% (-0.74% to 4.83%)	-4.95% (-11.72% to 1.83%)	0.149	-0.13 (-0.80 to 0.56)

Differences between groups were adjusted for training groups (morning or afternoon).

Note: BMI, body mass index; BMR, basal metabolic rate; CRP, C-reactive protein; cpm, count per minute; DBP, diastolic blood pressure; FFM, fat-free mass; FM, fat mass; FPG, fasting glucose; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TC, total-cholesterol; TG, triglyceride; TPA, total physical activity; VO_{2max}, maximal oxygen uptake; WC, waist circumference; *, difference between pre- and post- test, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Body composition

Body mass and BMI were unchanged in the Tabata group after intervention, while they increased in the control group (1.25%, 95% CI: 0.46% to 2.03%), with statistically significant differences on percentage changes between Tabata group and control group ($p = 0.011$, $d = -0.48$, 95% CI: -0.84 to -0.11). Both effects were small in magnitude. There was no statistically significant change in WC for both groups while a statistically significant differences on percentage changes was observed ($p = 0.043$, $d = -0.37$, 95% CI: -0.74 to -0.01). The intervention effect was small on WC. There were significant decreases in %BF (-2.57%, 95%CI: -4.06% to -1.09%) and FM (-2.61%, 95% CI: -4.36% to -0.85%) for the Tabata group, with moderate intervention effects between the Tabata group and control group ($p < 0.001$, $d = -1.15$, 95% CI: -1.53 to -0.75 for %BF; $p < 0.001$, $d = -1.08$, 95% CI: -1.46 to -0.69 for FM). FFM and metabolic basal rate (MBR) were improved significantly in the Tabata group (1.07%, 95% CI: 0.37% to 1.77% for FFM; 0.95%, 95% CI: 0.33% to 1.56% for MBR) and no significant intervention effects were observed between two groups ($p = 0.051$ and $p = 0.050$ for FFM and BMR, respectively).

Subgroup analysis showed that weight and BMI significantly decreased in participants with overweight or obesity only (-3.54%, 95% CI: -4.63% to -2.45%). There were significant differences on percentage changes on weight and BMI between the overweight/obese group and the normal weight group after adjusting for the training group (morning/afternoon group). ($p < 0.001$, $d = -2.19$, 95% CI: -2.95 to -1.38). The effects were large in magnitude. Although WC was not improved after intervention in the pooled sample in Tabata group, a significant decrease on WC was observed in participants with overweight or obesity (-1.24%, 95% CI: -2.13% to -0.35%). Even though %BF and FM decreased significantly in both normal weight and elevated weight participants; we observed significant differences on percentage changes on FM between groups ($p = 0.001$, $d = -1.17$, 95% CI: -1.86 to -0.44). Among overweight or obesity participants, we observed a decrease of 5.28% (95% CI: 2.52% to 8.04%) for %BF and 8.61% (95% CI: 5.37% to 11.85%) for FM. There was a decline of 2.02% (95% CI: -0.33% to -3.71%) for %BF and 1.38% (95% CI: -0.48% to 3.24%) for FM in normal-weight participants. Only participants with normal weight had an increase in FFM and RBR after intervention (1.47%, 95% CI: 0.71% to 2.23%). There was a significant difference on percentage change on FFM between groups ($p = 0.010$, $d = -0.93$, 95% CI: -1.62 to -0.22).

Cardiorespiratory fitness

After 12-week intervention, VO_{2max} was significantly improved in the Tabata group (12.87%, 95% CI: 11.00% to 14.73% for relative VO_{2max}; 12.73%, 95% CI: 11.02% to 14.44% for absolute VO_{2max}), with a large intervention effect between groups ($p < 0.001$, $d = 2.53$, 95% CI: 2.03 to 3.00 for relative VO_{2max}; $p < 0.001$, $d = 2.24$, 95% CI: 1.76 to 2.68 for absolute VO2max). Neither relative nor absolute VO2max increased in the control. We found a significant decrease in $HR_{resting}$ in Tabata group only (-8.62%, 95% CI: -10.34% to -6.89%), with a significant between-group difference ($p < 0.001$, $d = -1.82$, 95% CI: -2.23 to -1.37). The intervention effect was large.

Subgroup analysis showed that there was a significant difference on percentage change on relative VO_{2max} between the overweight/obese participants and the normal weight counterparts ($p = 0.045$, $d = 0.71$, 95% CI: 0.01 to 1.39). The effect was moderate. After the intervention, participants with overweight or obesity had a greater improvement in relative VO_{2max} of 16.98% (95% CI: 12.68% to 21.28%) compared with those with normal weight (12.03%, 95% CI: 9.98% to 14.08%). However, no between-group differences were observed on absolute VO_{2max} ($p = 0.963$) or $HR_{resting}$ ($p = 0.792$).

Blood pressure

For BP data, only SBP decreased significantly in the Tabata group (-3.66%, 95% CI: -4.73% to -2.58%), with a large intervention effect ($p < 0.001$, $d = -1.24$, 95% CI: -1.63 to -0.84). DBP was unchanged after intervention in both groups. Among the Tabata group, there was no difference on percentage change on SBP ($p = 0.798$) or DBP ($p = 0.991$) between participants with overweight or obesity and those with normal weight.

Lipid profiles

HDL significantly increased in the Tabata group (8.54%, 95% CI: 5.82% to 11.27%), with a moderate intervention effect between groups ($p < 0.001$, $d = 1.04$, 95% CI: 0.65% to 1.42%). Tabata group showed significant decreases in LDL (-1.95%, 95% CI: -3.53% to -0.38%), TG (-1.08%, 95% CI: -2.85% to 0.69%) and TC (-1.07%, 95% CI: -2.00% to -0.13%), whereas control group demonstrated no changes in LDL and TG and a significant increase in TC (0.90%, 95% CI: 0.25% to 1.55%). A small intervention effect on LDL ($p = 0.003$, $d = -0.57$, 95% CI: -0.93 to -0.19) and a moderate effect on TC ($p = 0.001$, $d = -0.64$, 95% CI: -1.00 to -0.26) were observed.

Subgroup analysis showed significant differences in LDL (p < 0.001, d = -1.51, 95% CI: -2.22 to -0.76), TG (p = 0.007, d = -0.98, 95% CI: -1.67 to -0.26) and TC (p < 0.001, d = -1.42, 95%CI: -2.12 to -0.67) between overweight/obese participants and their normal weight counterparts. The effects were large in LDL and TC, and the effect was moderate in TG. Significant improvements in LDL, TG and TC were only observed in overweight/obese participants9, with a decrease of 8.59% (95% CI: 2.10% to 15.09%), 6.30% (95% CI: 3.37% to 9.23%) and 4.83% (95% CI: 2.35% to 7.31%) for LDL, TG and TC, respectively. Both overweight/obese participants (13.65%, 95% CI: 6.73% to 20.57%, p p < 0.001) and their normal weight counterparts had a significant improvement in HDL (7.50%, 95% CI: 4.52% to 10.48%, p < 0.001). However, there was no statistically significant difference on the percentage change on HDL between groups (p = 0.090).

Carbohydrate metabolism and endocrine regulators

There were no significant changes in FPG and HbA1c for both groups, with no intervention effect. HOMA-IR improved significantly in the Tabata group (-1.24%, 95% CI: -2.50% to 0.03%) after intervention. There was a small intervention effect on HOMA-IR between groups (p = 0.026, d = -0.42, 95% CI: -0.78 to -0.05). Similarly, a small intervention effect was observed on fasting insulin (p = 0.035, d = -0.40, 95% CI: -0.76 to -0.03). There was a 0.83% (95% CI: -0.17% to 1.82%) decrease in fasting insulin from preintervention to postintervention for those in the Tabata group (p = 0.018).

Although FPG was not improved in the overall sample in the Tabata group, in the subgroup analysis it significantly decreased in overweight or obese participants (-1.50%, 95% CI: -2.92% to -0.09%, p = 0.034). There was a significant difference in percentage change in HbA1c between the overweight/obese group and the normal weight group (p = 0.008, d = -0.97, 95% CI: -1.66 to -0.25). The effect was moderate. HOMA-IR and fasting insulin were improved only in the overweight or obesity group (-3.84%, 95% CI: -6.11% to -1.57%, p = 0.009 for HOMA-IR; -2.36%, 95% CI: -4.52% to -0.19%, p = 0.042), while no effects on weight status was observed (p = 0.061 for HOMR-IR; p = 0.166 for fasting insulin).

Inflammation markers

There was no statistically significant change in CRP for both groups after the intervention, with no statistically significant intervention effect (p = 0.971). Subgroup analysis showed no significant improvement in CRP in either the overweight/obese or the normal weight group.

Metabolic syndrome

Following 12-week intervention, the prevalence of MetS decreased significantly in Tabata group from 5.08% to 0.00%, whereas it did not change significantly in the control group (5.17% vs. 5.17%). Among Tabata group, 27 (79.41%) participants improved at least 1 component of MetS after training. Among the remaining 7 participants, 2 of them had insufficient improvement of SBP, 2 participants had insufficient improvement of WC, 1 participant had insufficient improvement of TG and 1 participant had insufficient improvement of HDL. For the remaining 1 participant, both WC and HDL were not improved sufficiently to below cut points.

Physical activity

MVPA and TPA significantly increased in the Tabata group (15.51%, 95% CI: 13.27% to 17.74%, p < 0.001 for MVPA; 14.92%, 95% CI: 12.23% to 17.51% for TPA), whereas both MVPA and TPA decreased in the control group (-2.95%, 95% CI: -4.88% to -1.03%, p =0.001 for MVPA; -2.03%, 95% CI: -3.85% to 0.22%, p < 0.001 for TPA), with a large intervention effect between groups (p < 0.001, d = 2.31, 95% CI: 1.83 to 2.77).

Subgroup analysis showed that there were significant differences in percentage change on MVPA (p = 0.004, d = 1.05, 95% CI: 0.33 to 1.74) and TPA (p = 0.005, d = 1.02, 95% CI: 0.30 to 1.71) between overweight/obese and normal weight groups after the intervention. Both effects were moderate. MVPA significantly increased by 22.50% (95% CI: 17.76% to 27.24%) and 14.08% (95% CI: 11.71% to 16.45%) for participants with overweight/obesity and normal weight, respectively (p < 0.001). TPA significantly increased by 22.84% (95% CI: 17.07% to 28.60%) and 13.30% (95% CI: 10.56% to 16.04%) for participants with overweight/obesity and normal weight, respectively (p < 0.001).

Dietary data

After intervention, both the Tabata group and control group showed slightly but not significant increases in dietary intake including energy intake, vegetable, fruit, and dairy intake. There were no intervention effects. While in the sub-group analysis, overweight/obese participants significantly decreased daily energy intake by 5.78% (95% CI: 0.24% to 11.31%) and increased vegetable intake by 5.37% (95% CI: 0.49% to 10.25%). There were significant differences on daily energy intake (p = 0.006, d = -1.00, 95% CI: -1.69 to -0.28) and vegetable intake (p = 0.002, d = 1.10, 95% CI: 0.38 to 1.80) between the overweight/obese participants and the normal weight ones. Both effects were large. For daily fruit intake, only normal weight participants showed a significant increase (1.15%, 95% CI: -2.85% to 5.16%, p = 0.022), with weight status effect (p = 0.803). There was no difference on dairy intake between groups (p > 0.05).

Correlation data

At baseline, body composition parameters including BMI, WC, %BF, and FM, were significantly and positively associated with BMR, LDL, TG, TC, HbA1c, fasting insulin, HOMA-IR, CRP. VO_{2max} was significantly associated with weight (r = -0.221), BMI (r = 0.209), FFM (r = 0.228), MVPA (r = 0.398) and $HR_{resting}$ (r = -0.339). Body composition variables were highly correlated with each other. Regarding to PA data, MVPA was significantly associated with TPA (r = 0.406), $HR_{resting}$ (r = -0.186), SBP (r = -0.295), HDL (r = 0.630), LDL (r = 0.210), and TC (r = 0.203). While TPA was significantly associated with HDL (r = 0.391) and dairy intake (r = 0.198). For dietary data, daily energy intake was significantly associated with weight (r = 0.382), BMI (r = 0.458), WC (r = 0.511), %BF (r = 0.273), FM (r = 0.369), FFM (r = 328), BMR (r = 0.222), DBP (r = -0.199), LDL (r = 0.314), TG (r = 0.220), TC (r = 0.328), HbA1c (r = 0.252), fasting insulin (r = 0.209), HOMA-IR (r = 0.212) and CRP (r = 0.235). Vegetable intake was significantly associated with SBP (r = -0.337) and HDL (r = 0.188). Dairy intake was significantly associated with SBP (r = -0.431) and HDL (r = 0.210). Dairy intake was associated with vegetable intake (r = 0.216). There were significant and negative association between fruit intake and CRP (r = -0.211). It should be noted that there was a strong correlation between the percentage change of MVPA and the percentage of TPA (r = 0.936, p < 0.001).

Correlation data was used to determine the highly collinear variables, which were removed from the regression model to avoid potential multicollinearity.

Regression analysis

According to the literature review, age, body composition (weight, BMI, %BF, FM, and FFM), cardiorespiratory fitness (VO_{2max}), PA (MVPA and TPA), and dietary intake (daily energy intake, daily vegetable, fruit, and dairy intake) were all included in the regression model. Additionally, to evaluate the effect of intervention, both the baseline value and the percentage change of covariables were included in the model. We also adjusted for the baseline value of cardiometabolic outcomes.

Regression analysis for cardiometabolic indicators were outlined in Table 28. In Model 1, after controlling for potential variables, neither the baseline value of MVPA nor TPA were associated with the percentage change of SBP (ΔSBP), HDL (ΔHDL), LDL (ΔLDL), TG (ΔTG), or TC (ΔTC). The baseline value of MVPA was significantly associated with the percentage change of fasting insulin (Δfasting insulin) (b = 278, p = 0.049) and HOMA-IR (ΔHOMA-IR) (b = 0.287, p = 0.020).

In Model 2, adding the percentage change of TPA (ΔTPA) significantly increased the explained variation in ΔHDL to 69.2% (Adjusted R^2 = 0.692). ΔTPA was independently associated with ΔHDL (b = 0.480, p = 0.001), accounting for 7.4% of the variation. For every 1% increase in TPA, HDL improved by 0.5%. The baseline value of MVPA was significantly associated with ΔLDL (b = 0.336, p=0.048), Δfasting insulin (b = 0.302, p = 0.037), and ΔHOMA-IR (b = 0.316, p = 0.013) in Model 2. While ΔTPA was not associated with ΔSBP, ΔLDL, ΔTG, or ΔTC.

In Model 3, the percentage change of MVPA (ΔMVPA), significantly increased the explained variation in ΔHDL to 64.5% (Adjusted R^2 = 0.645). ΔMVPA was independently associated with ΔHDL (b = 0.326, p = 0.015), accounting for 3.9% of the variation. For every 1% increase in MVPA, HDL improved by 0.398%. The baseline value of TPA was significantly associated with ΔTC (b = 0.298, p = 0.049) in model 3. Furthermore, the baseline level of MVPA was significantly associated with Δfasting insulin (b = 0.326, p = 0.015) and ΔHOMA-IR (b = 0.302, p = 0.015).

Table 29: Regression data

Dependent Variable		Independent variable	Standardized beta	p value	Δ R^2
	Model 1: adjusted R^2 = 0.601	TPA	-0.171	0.112	
		MVPA	0.018	0.900	
	Model 2: adjusted R^2 = 0.692	TPA	0.121	0.323	
		MVPA	-0.040	0.751	
Δ HDL		Δ TPA	0.480	0.001	0.074
	Model 3: adjusted R^2 = 0.645	TPA	0.014	0.912	
		MVPA	-0.052	0.704	
		Δ MVPA	0.326	0.015	0.039
Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, HDL					
	Model 1: adjusted R^2 = 0.228	TPA	0.060	0.683	
		MVPA	0.296	0.080	
	Model 2: adjusted R^2 = 0.251	TPA	0.127	0.503	
		MVPA	0.336	0.048	
Δ LDL		Δ TPA	-0.309	0.131	0.031
	Model 3: adjusted R^2 = 0.219	TPA	-0.021	0.911	
		MVPA	0.307	0.073	
		Δ MVPA	-0.309	0.131	0.007
Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, LDL					
	Model 1: adjusted R^2 = 0.254	TPA	0.094	0.542	
		MVPA	0.087	0.546	
	Model 2: adjusted R^2 = 0.241	TPA	0.021	0.912	
		MVPA	0.109	0.490	
Δ TG		Δ TPA	-0.116	0.604	0.004
	Model 3: adjusted R^2 = 0.237	TPA	0.106	0.566	
		MVPA	0.092	0.556	
		Δ MVPA	0.033	0.869	0.000
Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, TG					

	Model 1: adjusted R^2 = 0.499	TPA	0.208	0.083	
		MVPA	0.051	0.702	
	Model 2: adjusted R^2 = 0.488	TPA	0.178	0.255	
		MVPA	0.059	0.669	
ΔTC		Δ TPA	-0.049	0.767	0.001
	Model 3: adjusted R^2 = 0.499	TPA	0.298	0.049	
		MVPA	0.036	0.79	
		Δ MVPA	0.154	0.312	0.009
Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, TC					
	Model 1: adjusted R^2 = 0.780	TPA	0.003	0.965	
		MVPA	0.033	0.697	
	Model 2: adjusted R^2 = 0.788	TPA	0.110	0.281	
		MVPA	-0.001	0.993	
Δ SBP		Δ TPA	0.174	0.111	0.010
	Model 3: adjusted R^2 = 0.779	TPA	0.054	0.581	
		MVPA	0.024	0.777	
		Δ MVPA	0.087	0.392	0.003
Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, SBP					
	Model 1: adjusted R^2 = 0.391	TPA	-0.139	0.287	
		MVPA	0.278	0.049	
	Model 2: adjusted R^2 = 0.388	TPA	-0.239	0.171	
		MVPA	0.302	0.037	
Δ fasting insulin		Δ TPA	-0.170	0.381	0.008
	Model 3: adjusted R^2 = 0.400	TPA	-0.263	0.110	
		MVPA	0.295	0.037	
		Δ MVPA	-0.213	0.212	0.017
Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, fasting insulin					
Δ HOMA-IR	Model 1: adjusted R^2 = 0.539	TPA	-0.105	0.358	
		MVPA	0.287	0.020	

Model 2: adjusted R^2 = 0.543	TPA	-0.217	0.150	
	MVPA	0.316	0.013	
	Δ TPA	-0.197	0.251	0.011
Model 3: adjusted R^2 = 0.544	TPA	-0.207	0.147	
	MVPA	0.302	0.015	
	Δ MVPA	-0.178	0.23	0.012

Model 1: adjusted for age, BMI, ΔBMI, VO_{2max}, ΔVO_{2max}, energy intake, Δ energy intake, vegetable, Δ vegetable, fruit, Δ fruit, dairy, Δ dairy, HOMA-IR

Note: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; MVPA, moderate-to-vigorous intensity physical activity; SBP, systolic blood pressure; TC, total-cholesterol; TG, triglyceride; TPA, total physical activity; VO_{2max}, maximal oxygen uptake.

4. Discussion

Even though there is accumulating evidence for the health benefits of HIIT in adults, the most consistent benefits had been seen in improving cardiorespiratory fitness. The benefits of HIIT on cardiometabolic health remain controversial. Particularly, there was limited data on the effects of HIIT on habitual PA. Since PA was found to be associated with cardiometabolic risk factors, it remains unknown whether PA played a mediating role on the effectiveness of HIIT. Furthermore, the effectiveness of a Tabata-style functional HIIT utilizing very short intervals and the exercise modality other than running or cycling on favorable changes in health has not been fully explored. The primary aim of the present study, therefore, was to examine the effects of a 12-week Tabata-style functional HIIT program on cardiometabolic risk factors and PA levels in female university students. The Tabata-style functional HIIT involved 8 bouts of 20-second "all-out" functional exercises, intermitted by 10-second rest between each bout. In terms of exercise adherence, only 1 student dropped out due to the hypoglycemia during the first session. There was a satisfied adherence that 98.33% of participants attended all sessions. The fidelity of the intervention, which was evaluated by heart rate responses during exercises, was largely upheld since a high intensity was delivered to all of the participants (between-subject SD), consistently throughout the 12-week intervention (within-subject SD). The variation in both HR_{mean} and HR_{peak} across different exercise sessions were small (0.24% for HR_{mean} and 0.30% for HR_{peak}), indicating that the exercise remained relatively consistent across the sessions. Furthermore, we did not find any difference on both HR measures between sessions. This might have been due to the familiarization session prior to the intervention.

After the 12-week intervention, compared to the control group, favorable intervention effects were observed in the Tabata group on cardiorespiratory fitness, most variables of body composition, some outcomes of cardiometabolic risk factors, and daily MVPA and TPA. These findings extended beneficial effects reported by previous studies and moreover, they were of particular importance from a perspective of health promotion in emerging adults, since the increasing prevalence of MetS and physical inactivity were observed in this population [Ford et al., 2004; Hirode et al., 2020; Tcymbal et al., 2020]. Collectively, the Tabata-style functional HIIT provided a feasible and effective strategy to improving young women's cardiometabolic health and habitual PA in the university setting.

4.1 Cardiorespiratory fitness effect

The improvement in cardiorespiratory fitness measured by VO_{2max} after HIIT were consistently reported by previous studies [Batacan et al., 2017; Jelleyman et al., 2015; Kessler et al., 2012]. It was supported by our finding that VO_{2max} increased by 12.87±7.16% in the Tabata group after intervention. Likewise, previous studies based on young adults showed similar improvements. De Revere et al. (2021) investigated the effect of a 3-week cycling-based HIIT protocol in non-obese and inactive women. Participants were required to complete 8-10 sets of 1-minute workout followed by 75-second recovery. After a total of 9 sessions, VO_{2max} increased about 10%. In the study by Menz et al. (2019), following a 4-week Tabata-style HIIT protocol with a total of 14 sessions, participants (5 females and 2males) improved their VO_{2max} by 11±7% [Menz et al., 2019]. However, compared with our protocol, the exercise volume was higher in De Revere et al. (2021) and Menz et al (2019)'s protocols, which was about 16 minutes per session. With a higher training volume, it was not surprising that participants were able to benefit from the HIIT program with short duration. Indeed, evidence from a previous systematic review showed that the improvement in VO_{2max} can be achieved following two weeks of HIIT with few exercise sessions [Kessler et al., 2012]. Although the longer intervention duration appeared to contribute to additional increases in VO_{2max} [Milanović et al., 2015], it was not true in the present study. One of the potential explanations were the low training volume of each session. In our protocol, the total workout duration per session was just 4 minutes, which was only a quarter of Menz et al (2019)'s and one fifth of De Revere et al. (2021)'s protocol. Moreover, Rosenblat et al. (2022) suggested that although the improvement in VO_{2max} seemed similar between protocols with different interval types, those with shorter intervals (2s-60s) were more likely to increase skeletal capillary density and mitochondrial respiration. This might facilitate the ultimate improvements in whole body exercise capacity and endurance in untrained people [Jacobs et al., 2013]. A greater improvement of 18% was reported by Foster et al. (2015) after an 8-week (24 sessions) cycling-based Tabata. The original exercise intensity for Tabata training of 170% VO_{2max} was used. Although an additional increase in VO_{2max} were obtained under the high intensity stimulation, it resulted in a negative affective response in the participants [Foster et al., 2015]. It was the fact that the feasibility of the original intensity of 170% VO_{2max} was questioned in the real-world setting. The result of this study revealed that Tabata protocol utilizing a modified lower intensity (83.24% of HR_{max}) was an alternative to effectively improve cardiorespiratory fitness in untrained individuals.

In contrast, in the work by Islam er al. (2020), participants completed a conventional 4-minute Tabata training 4 times a week for 4 weeks. The exercise modality was whole body functional exercises including burpee push-ups, mountain climber push-ups, jumping jacks and squat and thrusts. After intervention, no significant improvement on VO_{2max} was observed [Islam et al., 2020]. This might be due to the short duration of the intervention, as well as the better cardiorespiratory fitness of participants at baseline. Baseline cardiorespiratory fitness and initial training status were found to be associated with the training effects [Milanović et al., 2015; Støren et al., 2017].

Several studies examined the effects on cardiorespiratory fitness in overweight and obese individuals. After a 5-week HIIT intervention with a total of 20 sessions, VO_{2max} increased by 7.9% in obese young women [Kong et al., 2016b]. In Kong et al. (2016b)'s protocol, each session lasted 20 minutes and comprised of 60 repeats of 8-second cycling followed by 12-second rest. The HRmean over the intervention was 164 ± 8 bpm (81% of age predicted HRmax). In the study by Hu et al. (2021), a high volume of HIIT protocol was used. Each session involved 4 minutes of cycling at 90% of VO_{2max} followed by 3 minutes rest for a total of 60 minutes, with a frequency of 3 times a week. Following 36 training sessions, the obese participants had a significant increase of 20% in VO_{2max} [Hu et al., 2021]. The study be Sun et al. (2019) reported a greater improvement of 25% in VO_{2max} in overweight young females following a 12-week HIIT protocol with a frequency of 3 times per week. During each session, participants were required to complete 9 sets of 4-minute cycling (90% of VO_{2max}) followed by 3-minute rest [Sun et al., 2019]. Despite the low volume in the present study, in line with previous studies, findings from our sub-group analysis revealed that overweight and obese participants had a significant increase in VO_{2max} after the intervention (16.98 ± 6.01%). Furthermore, we found that the percentage increase in relative VO_{2max} differed statistically significantly between elevated- and normal-weight participants. However, absolute VO_{2max} showed no differences between groups. This might be due to the larger decrease on weight in the overweight/obese group. There was limited data on the direct comparison of the effects on cardiorespiratory fitness between normal weight adults and overweight or obese adults. Findings from a systematic review and meta-analysis showed that short-term HIIT (< 12 weeks) had a large effect on improving VO_{2max} in normal weight adults, while a medium effect in overweight or obese adults. Meta-analysis was also available for the effect of long-term HIIT (≥ 12 weeks) in overweight or obese adults and the pooled result showed a large effect in overweight or obese adults [Batacan et al., 2017]. It suggested that the duration of intervention was positively associated with the effectiveness, at least for overweight or obese populations. When studying the mechanism associated with the improvements on VO_{2max}, central factors and peripheral factors should be considered. After HIIT, plasma volume, lest ventricular mass, maximal stroke volume, and maximal cardiac output were increased. In addition to central adaptations, capillary density, maximal citrate synthase activity and mitochondrial respiration were increased [Rosenblat et al., 2022]. These physiological adaptations were responsible for the improvements on VO_{2max}.

4.2 Body composition effect

Despite the increasing popularity of HIIT for weight and fat loss, its effectiveness remains controversial. Our results demonstrated that a 12-week Tabata-style functional HIIT was effective on reducing %BF and FM and increasing FFM. There were no changes in weight, BMI, or WC. The results from the current study indicated that HIIT was effective for fat loss but not for weight loss. It was in line with previous studies [Macpherson et al., 2011; Zhang et al., 2021]. Macpherson et al. (2011) used a typical running-based HIIT that involved 4 to 6 sets of 30-second sprint followed by 4-minute recovery. After 6 week's intervention (3 times per week), %BF and FM decreased significantly and FFM increased significantly, but body mass was unchanged [Macpherson et al., 2011]. The fat-reducing effect was also supported by Zhang et al. (2021)'s study, in which the reductions in whole-body and regional FM were reported after 12-week's HIIT intervention in obese young women [Zhang et al., 2021]. This was in line with a previous systematic review and meta-analysis that HIIT were able to significantly reduce total, abdominal and visceral fat mass [Maillard et al., 2018]. However, the authors indicated that the reduction in abdominal fat mass could only be detected by computed tomography scan or magnetic resonance imaging. This might account for the absence of significant change in WC in the present study. Furthermore, only the HIIT protocol utilizing the exercise modality of running or cycling were included, and our results expanded the knowledge of the efficacy of HIIT in reducing fat. Nonetheless, there was controversy over whether HIIT was effective in lowering fat. Proponents argued that HIIT increased both aerobic and anaerobic capacity, reduced insulin resistance, and thus increased fat oxidation [Boutcher, 2011]. On the contrary, the counterargument was that when exercises were performed at an intensity of 85% of VO2max or greater, fat had little to do with energy, and metabolic energy comes almost exclusively from the breakdown of sugars in the body [Achten and Jeukendrup, 2004; Venables et al., 2005]. From the perspective of energy balance, we believed that without controlling total energy expenditure and intake, it was hard to determine whether the fat-lowering effect of HIIT was caused by training itself or by dietary intake or habitual physical activity. Well-controlled studies are expected in the future.

However, the simultaneous loss of weight and body fat after HIIT training has been reported in several studies. Trapp et al. (2008) investigated the effects of a 15-week cycling-based HIIT on fat loss in young normal weight women. Participants performed 8-second sprinting followed by 12-second recovery for 60 repeats. After a total of 45 session (20 minutes each session), the body mass, fat mass, and %BF were significantly reduced [Trapp et al., 2008]. In the study by Tjønna et al. (2008), participants completed a total of 48 sessions of HIIT (90% of HRmax) with the frequency of 3 sessions a week. After 16 weeks' intervention, body mass and fat were significantly reduced [Tjønna et al., 2008]. Given the fact that there was no change in energy intake between pre- and post- tests, the absence of reduction on body mass might be due to the following reasons: 1) the low exercise volume resulted in low energy expenditure, which was not sufficient to induce energy deficit and further reducing weight; 2) participants were normal weight at baseline and most favorable effects on body mass were observed in participants with overweight or obese [Tjønna et al., 2008; Martins et al., 2016; D'Amuri et al., 2021]. It was supported by findings from our subgroup analysis that body mass, BMI and WC significantly decreased in overweight/obese participants after intervention whereas these variables did not change in normal weight participants. Although the weight-lowering effect of the Tabata-style functional HIIT was not significant in the present study, it appeared to be a time-efficient way to prevent the abnormal weight gain among freshmen. Moreover, results from the present study demonstrated that overweight/obesity had an effect on weight change but did not affect the association between Tabata training and weight change. The greater weight-lowering effect observed in overweight/obese participants might be attributed to their larger increase in PA and decrease in energy intake compared to normal weight counterparts. This was further reinforced by acknowledging that the role of exercise training in the maintenance or improvement of weight was predominantly influenced by the cumulative effect of energy deficit during the daily life [LaForgia et al., 2006].

On the contrary, a systematic review and meta-analysis evaluated the effect of low-volume HIIT on body composition and reported that improvements on body composition outcomes such as FM, %BF or FFM were hardly observed following low-volume HIIT [Sultana et al., 2019]. In the present study, the favorable effects observed on some body composition measures might be partially explained by the increased daily MVPA and TPA. According to the meta-analytical findings from our previous study, there was a moderate correlation between TPA and %BF [Lu et al., 2022b]. The study also indicated that the improvement on adiposity could be seen when PA performed at moderate or higher intensity. On the other hand, the adaptations of fat in response to low-volume HIIT suggested a different underlying mechanism for fat reduction with MICT. The fat reduction after low-volume HIIT was not likely dependent on the amount of energy expended during exercise sessions. This might be attributed to the larger improvement on the metabolic rate and fat expenditure post intervention, because the magnitude and duration of excess post-exercise oxygen consumption was greater after HIIT [LaForgia et al., 2006] and lipolytic hormones, such as catecholamines and growth hormone, have been reported to increase with exercise intensity [McMurray et al., 1987]. Moreover, HIIT was found to elicit a larger elevation of plasma catecholamines compared with steady-state exercise. This potentially facilitated fat reduction after HIIT [Zouhal et al., 2008].

4.3 Cardiometabolic indicators

Blood pressure

Aerobic exercise was well documented to reduce resting BP and was recommended in the primary and secondary prevention of CVDs [Cornelissen and Smart, 2013; Johnson et al., 2014]. While there was emerging evidence from intervention studies that HIIT was effective on improving resting SBP [Nybo et al., 2010; Holloway et al., 2018; Aghaei Bahmanbeglou et al., 2019; de Oliveira et al., 2020] or both SBP and DBP [Ciolac et al., 2010; Hu et al., 2022]. Results from the present study showed that only SBP was significantly decreased after 12-week intervention. This agreed with several previous studies.

In the work by Aghaei Bahmanbeglou et al. (2019), participants with stage 1 hypertension completed either short interval HIIT (work rest ratio: 30-second/30-second at 80-100% of VO2max) or long interval HIIT (work rest ratio: 4-minute/4-minute at 75-90% of VO2max) for a total of 8 weeks. After the intervention, SBP was significantly decreased in both short interval HIIT and long interval HIIT, suggesting that the SBP-lowing effect of HIIT was irrespective of the intensity and exercise interval [Aghaei Bahmanbeglou et al., 2019]. Similarly, de Oliveira et al. (2020) also reported a significant decrease in SBP but not in DBP after an 8-week's HIIT intervention in young obese women with elevated BP at baseline. The training protocol involved 4 bouts of 4-minute high-intensity running at 85-95% of HRmax, followed by 3-minute active recovery at 65-75 of HRmax [de Oliveira et al., 2020]. It seemed that HIIT was effective in improving SBP in young and middle-aged individuals with abnormal SBP. It was supported by a recent systematic review and meta-analysis by Costa Lêdo et al. (2018). The authors reported that HIIT was equally effective in reducing BP compared to MICT in participants with pre- and established hypertension [Costa Lêdo et al., 2018]. Nevertheless, inconsistent with our results, this systematic review suggested that DBP could also be improved by HIIT. The baseline value of DBP might explain the inconsistence because higher baseline values were more likely to be improved by exercises [Bravata et al., 2007].

In the subgroup analysis, we observed significant decreases in both overweight/obese group and normal weight group and there was no between-group difference. Most studies evaluated the effectiveness of HIIT in overweight or obese participants. A systematic review and meta-analysis examined the effect of HIIT in overweight/obese and normal weight population [Batacan et al., 2017]. The results indicated the difference in the effect of HIIT on BP between participants with different BMI. The BP-lowing effect of HIIT was only observed in overweight/obese participants. However, our results showed that normal weight participants with elevated SBP could also benefit from HIIT. This was confirmed by previous studies that the degree of BP reduction was related to its baseline value [Pescatello et al., 2004; Bravata et al., 2007]. A greater reduction on BP were found in participants with higher baseline BP readings.

However, a recent study provided opposite results that functional HIIT was not effective in reducing BP [Nunes et al., 2022]. In Nunes et al. (2022)'s protocol, participants were required to complete 10 sets of 60-second of functional exercise followed by 60-second active recovery. After 12 weeks' intervention (36 sessions), neither SBP nor DBP were improved significantly. The lack of a significant reduction in BP might be explained by the age of participants. In Nunes et al. (2022)'s study, participants were postmenopausal women with the mean age of 61.5 years, whereas participants in our study were young females with the age of 20.42 years. On one hand, SBP and DBP increased with age [Landahl et al., 1986]. On the other hand, postmenopausal women were at high risk of hypertension due to the decline in estrogen [Saeed et al., 2017]. Collectively, it seemed reasonable that post-intervention BP was not improved in older women after low-volume HIIT.

In general, BP improvements were more likely to be observed in aerobic, resistance and concurrent training (moderate-intensity aerobic exercise and high intensity resistance exercise) with a volume of 150 minutes per week [Sabbahi et al., 2016; Corso et al., 2016; Son et al., 2017]. Our finding supported the favorable effect on SBP following low-volume HIIT. This favorable change might be due to the high intensity achieved during exercises [Eicher et al., 2010]. Higher intensity was reported to be associated with greater acute reduction on BP following exercises, which contributed to chronic BP lowing responses [Liu et al., 2012]. From a physiological perspective, several mechanisms had been proposed for BP reduction after aerobic training, such as improved vascular function, lowered inflammation, and oxidative stress. The work by Sawyer et al. (2016) suggested different vascular adaptations between HIIT and MICT [Sawyer et al., 2016]. HIIT was found to increase brachial artery flow-mediated dilation [Tjønna et al., 2008] while MICT increased resting artery diameter and low flow-mediated constriction. These vascular adaptations could occur without improvements in body composition, which further supported our findings. Although only an improvement in SBP was detected after the intervention, it had important implications for CVD risk factors management, as a 10 mm Hg increase in SBP during young adulthood was found to be associated with a 14% increased risk of CVD mortality over a 41-year follow-up [McCarron et al., 2000]. However, whether such HIIT protocol could be used in the clinical setting to improve the BP in participants with established hypertension need further investigations.

Lipid profiles

Our findings suggested favorable effects on HDL, LDL, and TC after intervention, while all these improvements were observed in participants with overweight and obesity. We also found intervention weight status interaction effects for LDL, TC and TG. This might be due to the higher pre-test value involved in the overweight/obese group. Our findings were in line with a previous study by Tjønna et al. (2008), in which HDL increased significantly after a 16-week (48 sessions) HIIT with an exercise intensity of 90% of HRmax in overweight/obese participants [Tjønna et al., 2008]. Our findings were partly supported by a systematic review and meta-analysis that neither short-term nor long-term HIIT had significant effects on cardiometabolic risk factors in normal weight participants [Batacan et al., 2017]. However, the authors indicated that the lipid profile was not improved in overweight/obese participants neither. Findings from another systematic review reported the same results that TC, TG, HDL, or LDL were not improvement after HIIT [Kessler et al., 2012].

Few studies examined effects on lipid biomarkers after HIIT in normal weight participants. Nevertheless, normal weight obesity had gained increasing attention in recent years and a study by Hu et al. (2022) investigated the effects of HIIT in this population. The HIIT protocol used in Hu et al. (2022)'s study involved 3 sets of 9-minute workout at 90% of HRmax followed by 1-minute rest, with a high frequency of 5 days per week. After 4 weeks' training, TC, TG, LDL and HDL were significantly improved in young women with NOW [Hu et al., 2022]. Although the intervention duration was only 4 weeks, which was one third of that in the present study, its training volume was as high as 1350 MET-min/week. This volume was sufficient to see a meaningful amelioration in lipid levels [Mann et al., 2014].

Most beneficial effects of HIIT on lipid profiles were reported among overweight/obese men. In the work by Fisher et al. (2015), after 6 weeks' intervention, TC, TG, LDL, and HDL were improved in young men with overweight or obesity [Fisher et al., 2015]. A previous study reported similar results that HDL increased after an 8-week HIIT program in untrained young men. However, TC was unchanged. It was believed that HDL was the most easily improved lipid profile component from exercise [Mann et al., 2014]. This was supported by evidence from the study by Nybo et al. (2010). The authors indicated that TC/HDL ratio was the only index that improved significantly after 150 minutes of MICT weekly at 65% of VO2max for 12 weeks in untrained young men. Additionally, the authors compared the MICT with HIIT (40 minutes workout at 95% HRmax weekly) and there were no improvements in lipid profiles after HIIT [Nybo et al., 2010]. This suggests that the volume of exercise, rather than the intensity of exercise, was the key to improving blood lipids and a relationship between body composition (body mass and %BF decreased only in MICT) and blood lipids was proposed. Similar findings were reported by Ho et al. (2012) that only combination exercise, after which weight, %BF, and FM decreased, had a beneficial effect on lipid profiles including TG, TC, HDL, and LDL [Ho et al., 2012]. This was supported by a previous systematic review that weight loss provided significant favorable changes on blood lipid [Aucott et al., 2011]. Therefore, despite the low training volume, the favorable effects on blood lipid observed in our study might be due to the reduction on body mass and fat.

Carbohydrate metabolism and fasting insulin

Findings from the current study revealed that FPG and HbA1c were not significantly decreased after the Tabata-style functional HIIT, but HOMA-IR and fasting insulin decreased significantly. The improvements on fasting insulin and HOMA-IR observed in the present study were supported by a previous systematic review and meta-analysis [Jelleyman et al., 2015]. Jelleyman et al. (2015) evaluated the effects of HIIT on biomarkers of glucose regulation and insulin resistance and meta-analytical findings demonstrated that compared to the control and MICT, insulin resistance significantly reduced following HIIT. The significant reduction on FPG only occurred in participants with elevated FPG value or diagnosed type 2 diabetes. This may help to explain the lack of advancement of FPG reduction in the present study as the baseline FPG value was normal in our samples. In contrast to our finding, HbA1c decreased significantly following HIIT compared to control. Another systematic review and meta-analysis provided similar finding related to insulin resistance, but FPG was not improved after HIIT [Kessler et al., 2012]. These results appeared to be more consistent with the amelioration of insulin resistance following HIIT. Particularly, a previous study by Babraj et al. (2009) indicated that insulin sensitivity was improved following as short as 2 weeks of HIIT in normal weight adults. Unfortunately, this conclusion was based on males exclusively [Babraj et al., 2009]. Contrast to the present study, Arad et al. (2015) reported that insulin sensitivity was not changed significantly after a 14-week HIIT in overweight/obese women [Arad et al., 2015]. This discrepancy might be due to fact that neither weight nor fat were reduced in participants from Arad et al. (2015)'s study. It was evidenced by other studies that exercise training did not increase insulin sensitivity without weight and fat loss, whether that weight and fat loss is exercise-induced or diet-related [Ross et al., 2000; Gillen et al., 2013]. However, a recent study indicated that both exercise training and weight loss (diet-induced) interventions improved insulin sensitivity. Body weight and fat mass were not significantly changed in participants in the exercise training group [Ryan et al., 2021]. The authors also suggested that there were differential effects on signaling pathways in skeletal muscle between the exercise training and the diet-predominated weight loss intervention. It was supposed that exercise had an independent mechanism for improving insulin sensitivity and, in addition, might increase insulin sensitivity by losing weight. The latter might be explained from the perspective of energy expenditure, as evidence from previous studies suggests that total energy expenditure rather than exercise intensity is key to stimulating insulin sensitivity [Mayer-Davis et al., 1998]. Previous studies studied physiological and molecular responses to a low-volume HIIT. Results from the Parolin et al. (1999)'s study showed that, during 3 x 30s all-out cycling, glycogen phosphorylase is predominantly activated during the first 15s of the first bout [Parolin et al., 1999]. The study by Metcalfe et al. (2015) substantiated that the glycogen degradation with HIIT incorporating 20s all-out sprint was similar to that observed with those involving prolonged intervals [Metcalfe et al., 2015]. The glycogen degradation was associated with the activation of AMPK [McBride and Hardie, 2009], which further contributed to the increase in peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) and glucose transporter 4 (GLUT 4) gene expressions [Gibala et al., 2009]. As such, it remained unclear whether the improvement in insulin sensitivity was induced by the intervention. On the one hand, the intervention effect observed in our study did not control for changes of body weight. On the other hand, we did not control the timing of the post-test, which could occur 1-7 days after the last session. Since a previous study showed no difference on insulin sensitivity between pre-training and 4 days after 12 weeks of training [Ryan et al., 2020], early post-intervention measurement might contribute to a higher level of insulin sensitivity. In line with our subgroup's finding in relation to FPG, Tjønna et al. (2008) reported that after 16-week HIIT (48 sessions), overweight/obese participants had improved FPG, but insulin was not changed significantly [Tjønna et al., 2008]. While it should be noted that the overweight/obese participants recruited by Tjønna et al. (2008) had elevated FPG, which was not the case for our participants. Another study based on overweight/obese participants with normal FPG reported that FPG decreased after 5-week HIIT (20 sessions) in young women [Kong et al., 2016]. In was consistent with findings from a previous systematic review and meta-analysis that FPG improved significantly after HIIT in overweight/obese participants [Kessler et al., 2012]. The change on FPG after training appeared to be independent of the pre-training value, but rather related to overweight/obesity. Results from our study suggested that low-volume HIIT was effective in improving FPG for overweight/obese young women with normal FPG value. This finding was important as MHO was an instable and transient phenotype and individuals with MHO were more likely to develop CVD events in the future [Eckel et al., 2016].

4.4 Inflammation

It is well known that exercise could mitigate the deleterious effects of aging, not only by improving adiposity and mitochondrial function, the key to oxidative stress and inflammation, but also by enhancing the antioxidant and anti-inflammatory capacities [Sallam and Laher, 2016]. Some researchers claimed that exercise performed at high intensities increased inflammation and oxidative stress rather than reduced them [Davies et al., 1982; Bergholm et al., 1999; Goto et al., 2003], while others suggested that acute bouts of exercise induced oxidative stress and inflammatory responses [Moldoveanu et al., 2001; Farias-Junior et al., 2019]. Our results revealed that inflammation, measured by pro-inflammatory production of CRP, was not significantly changed following a 12-week Tabata-style functional HIIT. Likewise, in the work by Allen et al. (2017), participants completed a 9-week cycling-based HIIT with a frequency of 3 times per week. There were no significant changes on inflammatory biomarkers including TNF-α and CRP after intervention [Allen et al., 2017]. These were not surprising because on one hand, intense exercise induced oxidative stress was normally recovered within 24 hours according to our previous systematic review [Lu et al., 2021]; on the other hand, 12 weeks was not sufficient long to exert the long-term anti-oxidative and anti-inflammatory effects of exercise training. Long-term HIIT (12 months), accompanied by high levels of habitual PA was recommended to establish a significant anti-inflammatory effect [Balducci et al., 2010]. Additionally, Balducci et al. (2010) claimed that exercise induced anti-inflammatory effect was independent of weight loss. This was further confirmed by the present study that although weight and fat reduced significantly among overweight/obese participants, their CRP did not change following intervention.

4.5 Physical activity

There was limited data on the effect of HIIT on habitual PA. According to previous study, short-term Tabata-style functional HIIT was able to increase MVPA and TPA [Lu et al., 2022a]. The present study examined the long-term effect on PA and similar results were observed. This suggested that long-term low-volume HIIT did not induce compensatory movement behaviors such as decreasing habitual PA among young women. It might be due to the low energy expenditure during the exercises. Compared to the control group, whose daily PA was significantly decreased over 12 weeks, the Tabata-style functional HIIT seemed to be a time-efficient way to promote habitual PA in the university setting. Furthermore, we also found a high correlation between the increase in MVPA and TPA, suggesting that the majority of TPA increased over 12 weeks was accumulated from the increase in MVPA. Although all participants in our study met the PA recommendation for health maintenance, MVPA that higher than 300 minutes weekly could provide additional health benefits [Bull et al., 2020]. Surprisingly, we found intervention × weight status interactions for MVPA and TPA. There were greater increases on MVPA and TPA in overweight/obese participants compared to normal weight counterparts. It was hard to explain. This might be explained by several psychological changes. The intervention might have a greater effect on the autonomous motivation and exercise in overweight/obese women, facilitating the internalization of exercise behavioral regulation [Silva et al., 2011]. Comparative studies were warranted in the future.

Moreover, to our knowledge, this was the first study to examine the association between changes in PA and in cardiometabolic outcomes. Our hypothesis that there was a positive relationship between changes in cardiometabolic outcomes and changes in PA was partially confirmed. Results from the regression analysis showed that increasing TPA and MVPA were both independently associated with improvements on HDL. However, other cardiometabolic indicators showed no associations with improvements in MVPA or TPA. Surprisingly, we found a positive association between the baseline value of MVPA and the percentage of fasting insulin and HOMA-IR, indicating that participants with higher level of daily MVPA had greater increase in fasting insulin and HOMA-IR. It was hard to explain and might be due to the statistical error. Evidence from cross-sectional studies revealed that MVPA was negatively associated with fasting insulin and HOMA-IR values [Green et al., 2014]. Therefore, the lower baseline value of fasting insulin and HOMA-IR had the potential to result larger percentage change, and the slight increase in post-test values were induced by the measurement errors. We also found a positive relationship between the baseline value of TPA and ΔTC. It might be related to the dietary pattern which was not examined in the present study.

5. Limitations

This was the first study to evaluate the effects of a Tabata-style functional HIIT on multiple cardiometabolic outcomes and physical activity in university female students. The strengths of our study included the randomized controlled design with a relatively large sample, supervised exercise training and robust measures of cardiometabolic biomarkers in a clinical setting. There were several limitations that should be noted. Firstly, it was noted that there was associations between dietary intake and multiple investigated cardiometabolic measures, however, the nature of these associations was not fully investigated and well controlled in this study. Secondly, the present study was conducted based on a population who were more likely to gain weight during their first year of university. Such weight gain was not only associated with lifestyle changes, but also with several psychological factors such as perceived stress [Economos et al., 2008; Hootman et al., 2018] and the influence of peers [Smith-Jackson and Reel, 2012]. Therefore, future studies aimed at weight management, psychological factors should be taken into consideration. Furthermore, the inter-individual variability for exercise fidelity was not further investigated and might have limited the ability to evaluate the intervention effects. Finally, although long-term HIIT (≥12 weeks) were recommended to evaluate the effects of HIIT, the duration of 12 weeks was still too short to evaluate clinical changes and sustainability in certain physiological and cardiometabolic health outcomes.

Particularly, due to the lack of follow-up, we were unable to determine whether participants were willing or able to commit to such low-volume HIIT for a long period of time. Future research needs to be rigorously designed to include follow-up measures that will confidently assist policy makers in recommending the Tabata-style functional HIIT to promote health in the university setting.

6. Conclusion

The findings of the present study demonstrated that a 12-week Tabata-style functional exercises based HIIT intervention improved the cardiorespiratory fitness, body composition, some cardiometabolic biomarkers (SBP, HDL, LDL, TC, fasting insulin, and HOMA-IR), as well as daily habitual PA (MVPA and TPA) in female freshmen. Most health benefits in relation to body composition and cardiometabolic risk factors were observed in overweight/obese individuals. Furthermore, this study extends the current knowledge, by showing that increases in habitual PA following intervention were associated with a greater improvement on HDL post intervention. However, further randomized controlled trials with a long duration (at least 6 months) and follow-up measures are needed to confirm the magnitude and persistence of health gains.

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Chapter 10: Overall conclusion and future direction

The studies presented in this thesis showed the background, development, implementation and assessment of the Project JFM (Just Four Minutes). The main aim of this program was to develop a practical, feasible and acceptable high-intensity interval training (HIIT) protocol in the university setting and to evaluate its effectiveness on improving cardiometabolic health and physical activity (PA) in female university students. The second aim was to explore the effect of changes in PA on the cardiometabolic health related intervention effects. This program was developed based on the Medical Research Council's framework for developing and evaluating complex interventions. There were a total of 5 studies and each study was summarized as follows.

Study 1:

The purpose of Study 1 was to qualitatively synthesize and quantitatively assess the evidence for the relationship between objectively determined volumes of PA with adiposity and cardiometabolic health in women. Four databases (PubMed, Web of Science, Scopus, and the Cochrane library) were searched for eligible studies. Adiposity measures and cardiometabolic health were assessed separately. For meta-analysis of adiposity, 35 studies were included (25 observational and 10 interventional studies), with a total of 9176 women from 20 countries included. The overall pooled correlation for random effects model ($n = 1$ intervention and $n = 15$ cross-sectional studies) revealed that the total volume of physical activity (TPA) was moderately associated with percentage body fat (%BF) ($r = -0.59$; 95% CI: -1.11 to -0.24; $p = 0.003$). There was a weak but significant association between moderate-to-vigorous physical activity (MVPA) with body mass index (BMI), waist circumference (WC), and visceral adiposity. Daily steps were significantly associated with BMI, %BF, WC, and fat mass (FM), showing the strongest association with %BF ($r = -0.41$; 95% CI: -0.66 to -0.19; $p < 0.001$). Walking programs resulting in increasing daily steps only had a significant effect on WC (SMD = -0.35; 95% CI: -0.65 to -0.05; $p = 0.02$). Overall, objectively determined PA in terms of steps, TPA and MVPA were favorably associated with adiposity outcomes. The improvement in adiposity can be achieved by simply accumulating more PA than previously and adiposity is more likely to be benefited by PA performed at higher intensity. Nonetheless, these results should be interpreted with caution as there were a small number of studies included in the meta-analysis and the majority of studies included utilized cross-sectional designs.

For meta-analysis of cardiometabolic health indicators, 24 eligible studies were included, with a total of 2105 women from 8 countries. Correlational meta-analysis showed that MVPA was favorably associated with high density lipoprotein (HDL) ($r = 0.16$; 95% CI: 0.06 to 0.25; $p = 0.002$), however, there was limited evidence for the effects of most of the other cardiometabolic biomarkers recorded from steps, TPA, light- and moderate- intensity PA and MVPA. It was most compelling and consistent that being more physically active was beneficial to the metabolic syndrome. Overall, PA level was low in adult women, suggesting that increasing TPA was more important than emphasizing the intensity and duration of PA. Findings also indicated that, according to the confounding effects of body composition and cardiorespiratory fitness (CRF), meeting the minimal level of 150 minutes of moderate intensity physical activity recommended was not enough for significant improvement on cardiometabolic indicators. Nonetheless, the high heterogeneity between studies inhibited robust conclusions.

Study 2:

The primary purpose of Study 2 was to examine the efficacy of a 12-week functional HIIT (HIIT-F) for female univerisy students and compared its efficacy to running based HIIT (HIIT-R) in terms of body composition and CRF. The second objective was to compared physiological and phychological responses between two HIIT protocols. The participants' perspectives towards HIIT-F were also generated by the post-intervention focus group to refine the HIIT-F protocol. Twenty healthy, untrained female university students (20.5 ± 0.7 years old) were randomly assigned to a 12-week HIIT-R ($n = 10$) or HIIT-F ($n = 10$) intervention. HIIT-R group involved 30-second maximal shuttle run with a 30-second recovery period, whereas HIIT-F involved multiple functional exercises with 2:1 work-recovery ratio. Body composition and maximal oxygen uptake (VO_{2max}) were measured pre- and post-intervention. Heart rate (HR) data was recorded objectively during exercises. Perceived exercise exertion and exercise enjoyment were subjective meansured. A post-intervention focus group was conducted to explore participants' experience of HIIT-F. As a result, HIIT-R and HIIT-F stimulated similar improvements in VO_{2max} (17.1% ± 5.6% and 12.7% ± 6.7% respectively, $p > 0.05$). %BF decreased (17.1% ± 7.4% and 12.6% ± 5.1% respectively, $p < 0.05$) in both HIIT-R and HIIT-F with no between-group differences. We concluded that HIIT-F was equally effective in promoting body composition and CRF compared to HIIT-R. Moreover, similar HR responses during sessions were observed between two protocols, whereas HIIT-F reported lower exercise exertion and higher exercise enjoyment. Focus group data showed the satisfaction and acceptance of HIIT-F for univeristy female students. Accordingly, the HIIT-F protocol was improved by eliminating 8 different movements to 4 and rep

Study 3:

The primary purpose of Study 3 was to examine if the refined HIIT-F was associated with changes in 24-h movement behaviors in the short term. The second objective was to examine the HR responses and perceived exercise exertion. A quasi-experimental study design was used. We collected accelerometry data from 21 eligible participants who consistently wore an ActiGraph for a period of two-weeks. Differences in behaviors were analyzed using a paired t-test and repeated measures analysis of variance. Regression analysis was used to explore relationships with factors that impacted changes. The results indicated a compensatory increase in sedentary time (ST) (4.4 ± 6.0%, $p < 0.01$) and a decrease in light-intensity physical activity (LPA) (-7.3 ± 16.7%, $p < 0.05$). Meanwhile, moderate-intensity physical activity (MPA), vigorous-intensity physical activity (VPA), and TPA increased following exercise ($p < 0.001$). Sleep duration and prolonged ST were reduced ($p < 0.05$). Exercise intensity and CRF were associated with changes in ST. The results from the study indicated that participating in a low-volume HIIT-F encouraged participants who were previously inactive to become more active. The observations of increases in ST might have displaced a prolonged sitting time. The decrease in sleeping time observed might be reflecting an increased sleep quality in connection with increased higher-intensity PA. HR data showed that the refined HIIT-F protocol used was able to be performed at a satisfied high intensity by university female students. Overall, short-term HIIT-F had an impact on PA among unversity female students, while its long term effects on PA was unclear. Given that PA was associated with health outcomes, findings from Study 3 supported the inclusion of changes in PA when evaluating the main intervention effect.

Study 4:

The prevalence of hypertension (HTN) has been increasing in young adults. The elevated BP was the most prevalent individual component of the metabolic syndrome in our sample. A healthy dietary pattern and increasing PA are commonly recommended as the lifestyle modifications needed to manage blood pressure (BP). However, little is known about the relationship between dairy intake, PA, and BP in Chinese young women. The objective of this cross-sectional study was to examine whether BP was associated with dairy intake, MVPA and TPA in a sample of university female students. A total of 122 women (20.4 ± 1.4 years old) who had complete data sets were included in this cross-sectional analysis. Data related to dairy intake and PA was collected using a food frequency questionnaire and an accelerometer. BP was measured following standardized procedures. The association between BP with dairy intake and PA was examined using linear regression models. After controlling for potential covariables, we observed a significant and independent relationship only between systolic BP with dairy intake ($r = -0.275$, $p < 0.001$), MVPA ($r = -0.167$, $p = 0.027$), and TPA ($r = -0.233$, $p = 0.002$). Furthermore, we found a decrease of 5.82 ± 2.94, 1.13 ± 1.01, and 1.10 ± 0.60 mm Hg in systolic BP for daily additional servings of dairy, 10 minutes of MVPA, and 100 counts per minute of TPA, respectively. Our results support the protective effect of increasing dairy consumption and PA in Chinese young women on BP. Our findings also indicate that dairy intake was a contributer to cardiometabolic health independent of exercises. Dairy intakes should be included as covariables to evaluate the main intervention effect in this population.

Study 5:

The increasing prevalence of metabolic syndrome and physical inactivity enhances exposure to cardiometabolic risk factors in university students. HIIT improved cardiometabolic health in clinical adults but the evidence in the university setting is limited. Furthermore, few studies examined the effect of low-volume HIIT on habitual (PA). Therefore, the primary objective of this study was to evaluate the efficacy of a 12-week Tabata-style functional HIIT for improving multiple cardiometabolic health outcomes and habitual PA. We also investigated whether changes in habitual PA over the intervention period had an impact on exercise-induced health outcomes. 122 female freshmen were randomized into the Tabata group (n=60) and the control (n=62). The Tabata training protocol involved 8 × 20s maximal repeated functional exercises followed by 10 s rest with a frequency of 3 times per week for 12 weeks. Body composition, VO_{2max}, BP, blood lipids, fasting glucose and insulin, C-reactive protein and PA were objectively measured using standardized methods. Dietary intake was measured using a valid food frequency questionnaire. All variables were measured pre- and post- intervention. Mixed linear modelling results showed that there were large intervention effects on VO_{2max} ($p < 0.001$, d = 2.53, 95% CI: 2.03 to 3.00 for relative VO_{2max}; $p < 0.001$, d = 2.24, 95% CI: 1.76 to 2.68 for absolute VO_{2max}), resting heart rate ($p < 0.001$, d = -1.82, 95% CI: -2.23 to -1.37), systolic BP ($p < 0.001$, d = -1.24, 95% CI: -1.63 to -0.84), MVPA ($p < 0.001$, d = 2.31, 95% CI: 1.83 to 2.77), TPA ($p < 0.001$, d = 1.98, 95% CI: 1.53 to 2.41); moderate effects on %BF ($p < 0.001$, d = -1.15, 95% CI: -1.53 to -0.75), FM ($p < 0.001$, d = -1.08, 95% CI: -1.46 to -0.69), HDL ($p < 0.001$, d = 1.04, 95% CI: 0.65 to 1.42), total cholesterol (p = 0.001, d = -0.64, 95% CI: -1.00 to -0.26); small effects on BMI (p = 0.011, d = -0.48, 95% CI: -0.84 to 0.11), WC (p = 0.043, d = -0.37, 95% CI: -0.74 to -0.01), low-density lipoprotein (p = 0.003, d = -0.57, 95% CI: -0.93 to -0.19), HOMA-IR (p = 0.026, d = -0.42, 95% CI: -0.78 to -0.05) and fasting insulin (p = 0.035, d = -0.40, 95% CI: -0.76 to -0.03). Regression analysis showed that only the percentage change of HDL was associated with the change of MVPA (b = 0.326, p = 0.015) and TPA (b = 0.480, p = 0.001). From the findings of the study we can concluded that 12-weeks low-volume Tabata-style functional HIIT was highly effective for university female students to improve CRF, body fat, some cardiometabolic health outcomes and habitual PA.

Overall summary and future directions

The studies presented in this thesis show that the Tabata-style functional exercise based HIIT is a practical and effective strategy to improve CRF, some body composition variables and most cardiometabolic outcomes in female university students. Moreover, it has been shown that this Tabata-style functional HIIT is effective in increasing daily MVPA and TPA in both short-term and long-term. The increases in MVPA and TPA is associated with the improvement on HDL. These results, to some extent, confirm our meta-analytical findings that the exercise duration can be compensated with exercise intensity. PA performed at higher intensity is more effective on improving adiposity measures and some cardiometabolic biomarkers. Additionally, we find that a healthy dietary habit such as consuming more dairy products is associated with better BP.

Although findings from the main intervention do not provide an explanation for physiological mechanisms under favorable changes, this is not the objective of this project. Rather, the aim of this project is to extend findings from previous studies based on HIIT. The HIIT protocol used in this thesis is a very low-volume functional exercises based model, which is not fully investigated before.

However, there remains unanswered questions. Firstly, the present thesis can not answer whether HIIT can replace traditional moderate-to-vigorous aerobic exercise to maintain and promote health. To answer this question, further studies need to include a comparator group of moderate intensity training and furthermore, dose-response relationships for HIIT should be quantified. More importantly, whether individuals are willing to maintain a high exercise fidelity and make it a part of lifestyles is unknown. More HIIT programs utilizing the long-term designs (at least 6 months) are need in the future. Therefore the sustainability of the Project JFM is still unknown. Future studies should also explore the use of HIIT in the university setting, such as including it as a session in physical education classes, which requires the full support and participation from universities. Most importantly, due to the low frequency of adverse events reported in HIIT based studies, its safety and universality for individuals with multiple health status is unclear. These are all exciting directions for future HIIT research investigations.

Supplementary Table

Supplementary Table A: Search strategies for study 1 part 1

Database		PubMed (n=2954)
Date		January 1, 1990-January 31, 2022
Search Terms	#1	(Accelerometry[Mesh] OR Accelero*[TIAB] OR Actigraphy[MAJR] OR actigra* [TIAB]) Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#2	(objectively[TIAB] AND assessed[TIAB] AND physical[TIAB] AND activity[TIAB]) Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#3	(objectively[TIAB] AND measured[TIAB] AND physical[TIAB] AND activity[TIAB]) Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#4	pedometer[TIAB] Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#5	"Body Composition"[Mesh] OR BMI OR “body mass index” OR fat OR overweight OR obes* OR adipos* OR waist OR “fat mass” OR “fat free mass” OR “body fat” Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
		#1 OR #2 OR #3 OR #4 AND #5
		(((((Accelerometry[Mesh] OR Accelero*[TIAB] OR Actigraphy[Mesh] OR actigra* [TIAB]) AND (adult[Filter] OR middleaged[Filter] OR youngadult[Filter])) OR ((objectively[TIAB] AND assessed[TIAB] AND physical[TIAB] AND activity[TIAB]) AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter]))) OR ((objectively[TIAB] AND measured[TIAB] AND physical[TIAB] AND activity[TIAB]) AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter]))) OR (pedometer[TIAB] AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter]))) AND ("Body Composition"[Mesh] OR BMI OR "body mass index" OR fat OR overweight OR obes* OR adipos* OR waist OR "fat mass" OR "fat free mass" OR "body fat" AND ((female[Filter]) AND (english[Filter]) AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter])))
Database		SCOPUS (n=921)
Date		January 1, 1990-January 31, 2022
	#1	TITLE-ABS-KEY (accelerometry OR accelero* OR actigra* OR actigraphy)
	#2	TITLE-ABS-KEY ((objectively AND measured AND physical AND activity))
	#3	TITLE-ABS-KEY ((objectively AND assessed AND physical AND activity))
	#4	TITLE-ABS-KEY (pedometer)
	#5	"Body Composition" OR BMI OR “body mass index” OR fat OR overweight OR obes* OR adipos* OR waist OR “fat mass” OR “fat free mass” OR “body fat”
		#1 OR #2 OR #3 OR #4 AND #5
		(TITLE-ABS-KEY(accelerometry OR accelero* OR actigra* OR actigraphy) OR TITLE-ABS-KEY(objectively AND measured AND physical AND activity) OR TITLE-ABS-KEY(objectively AND assessed AND physical AND activity) OR TITLE-ABS-KEY(pedometer)) AND (TITLE-ABS-KEY ("Body Composition" OR bmi OR "body mass index" OR fat OR overweight OR obes* OR adipos* OR waist OR "fat mass" OR "fat free mass" OR "body fat")) AND NOT ((child*) OR (old*) OR (eld*) OR (pregnan*) OR (disable*) OR (athlete)) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE , "English"))
Database		Web of Science (n=4666)
Date		January 1, 1990-January 31, 2022
	#1	TS=(accelerometry OR accelero* OR actigra* OR actigraphy)
	#2	TS=(objectively AND measured AND physical AND activity)
	#3	TS=(objectively AND assessed AND physical AND activity)
	#4	TS=(pedometer)
	#5	TS=(“Body Composition” OR BMI OR “body mass index” OR fat OR overweight OR obes* OR adipos* OR waist OR “fat mass” OR “fat free mass” OR “body fat”)
		(((((#1) OR #2) OR #3) OR #4) AND #5) NOT ALL=(((child*) OR (old*) OR (eld*) OR (pregnan*) OR (disable*) OR (athlete)))
Database		The Cochrane library (n=1636)
Date		January 1, 1990-January 31, 2022
	#1	MeSH descriptor: [Accelerometry] this term only
	#2	accelero* OR actigra* OR actigraphy
	#3	#1 OR #2

	#4	objectively AND measured AND physical AND activity:ti,ab,kw
	#5	objectively AND assessed AND physical AND activity:ti,ab,kw
	#6	pedometer
	#7	#3 OR #4 OR #5 OR #6
	#8	"Body Composition" OR BMI OR “body mass index” OR fat OR overweight OR obes* OR adipos* OR waist OR “fat mass” OR “fat free mass” OR “body fat”
	#9	MeSH descriptor: [Chronic Disease] this term only
	#10	#8 OR #9
	#11	(child*) OR (old*) OR (eld*) OR (pregnan*) OR (disable*) OR (athlete)
	#12	#7 AND #10 NOT #11

Supplementary Table B: methodological quality of studies for study 1 part 1

Supplementary Table B.1 Assessment of methodological quality of nonrandomized studies (Newcastle Ottawa Scale)

Study	Selection				Comparability	Outcome			Total	Quality
	Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study	Adjusted for age and other important covariates	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow up		
Ayabe et al. 2013	-	*	*	*	**	*	n/a	n/a	6	High
Bailey et al. 2015	-	*	*	*	**	*	n/a	n/a	6	High
Bailey et al. 2014	-	*	*	*	**	*	n/a	n/a	6	High
Bailey et al. 2007	*	*	-	*	**	*	*	-	7	High
de Hoed et al. 2008	-	*	-	*	-	*	n/a	n/a	3	Low
Diniz et al. 2015	-	*	*	*	*	*	n/a	n/a	5	High
Graff et al. 2012	-	*	-	*	-	*	n/a	n/a	3	Low
Green et al. 2014	*	*	*	*	-	*	n/a	n/a	5	High
Hasan et al. 2018	-	*	*	*	-	*	-	*	5	High
Hornbuckle et al. 2005	*	*	*	*	**	*	n/a	n/a	7	High
Koniak-Griffin et al. 2014	*	*	-	*	-	*	n/a	n/a	4	High
Musto et al. 2010	-	*	-	*	-	*	-	*	4	Low
Panton et al. 2007	-	*	-	*	-	*	n/a	n/a	3	Low
Park et al. 2011	-	*	-	*	-	*	n/a	n/a	3	Low
Pelclová et al. 2012	-	*	*	*	-	*	n/a	n/a	4	Low
Phelan et al. 2007	-	-	*	*	-	*	n/a	n/a	3	Low
Slater et al. 2021	*	*	*	*	**	*	n/a	n/a	7	High
Smith et al. 2013	*	*	*	*	**	*	n/a	n/a	7	High
Sternfeld et al. 2005	*	*	*	*	**	*	n/a	n/a	7	High
Strath et al. 2008	*	*	*	*	**	*	n/a	n/a	7	High
Swartz et al. 2003	-	*	-	*	-	*	-	*	4	Low
Thompson et al. 2004	-	*	-	*	*	*	n/a	n/a	4	High
Tolonen et al. 2018	*	*	*	*	**	*	n/a	n/a	7	High

Tucker et al. 2003	-	*	*	*	-	*	n/a	n/a	4	Low
Tudor-Locke et al. 2009	*	*	*	*	-	*	n/a	n/a	5	High
Vella et al. 2011	*	*	*	*	-	*	n/a	n/a	5	High
Vella et al. 2009	*	*	*	*	**	*	n/a	n/a	7	High
Van Dyck et al. 2015	*	*	*	*	**	*	n/a	n/a	7	High

Notes: Representativeness of the exposed cohort: One star = truly/somewhat representative of general female adults; Selection of the non-exposed cohort: One star = drawn from the same community as the exposed cohort; Comparability: One star = study controls for age, 2nd star = study controls for other confounders; Follow-up long enough for outcomes to occur: One star = ≥12 months; Adequacy of follow up: Complete follow up/all groups had similar loss to follow-up/less than 5% of total lost to follow-up
n/a: not applicable

Supplementary Table B.2 Assessment of methodological quality of randomized studies (the Cochrane Collaboration's tool)

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Overall Quality
Bailey et al. 2019	L	L	L	L	L	L	L	High
Cayir et al. 2015	L	U	L	L	L	L	L	U
Holliday et al. 2018	L	L	L	L	L	L	L	High
Hornbuckle et al. 2012	L	L	L	L	L	L	L	High
Moreau et al. 2001	U	L	L	L	L	L	L	U
Pal et al. 2011	U	L	L	L	L	L	L	U
Sugawara et al. 2006	U	L	L	L	L	L	L	U

Note: L, low risk; H, high risk, U, unclear.

Supplementary Table B.3 GRADE assessment for study 1 part 1

PA measures	No. of participants (#studies)	Study design	Quality Assessment					Absolute effect	Quality
			Risk of bias[1]	Inconsistency[2]	Indirectness[3]	Inprecision[4]	Publication bias[5]		
Steps	1970(11)	cross-sectional	no serious	no serious	no serious	no serious	no serious	BMI: favorable (9/10); null (1/10); %BF: favorable (5/5); WC: favorable (4/7); null (3/7); FM: favorable (2/2); VAT: favorable (1/1).	Low
	272(5)	RTs	no serious	serious	no serious	serious	not applicable	BMI: favorable (1/4); null (3/4); %BF: favorable (1/4); null (3/4); WC: favorable (1/3); null (2/3); FM: null (2/2); VAT: null (1/1).	Low
	147(3)	NRTs	no serious	serious	no serious	serious	not applicable	BMI: favorable (2/3); null (1/3); %BF: favorable (1/2); null (1/2); WC: favorable (2/3); null (1/3); FM: favorable (1/1); VAT: favorable (1/1).	Very low
TPA	4158(7)	cross-sectional	no serious	no serious	no serious	no serious	not applicable	BMI: favorable (1/2); null (1/2); %BF: favorable (3/4); null (1/4); WC: favorable (2/2); VAT: favorable (2/1).	Low
LPA	931(5)	cross-sectional	no serious	no serious	no serious	no serious	not applicable	BMI: null (2/2); %BF: null (2/2); WC: null (1/1); FM: null (1/1); VAT: null (1/1).	Low
	228(1)	Longitudinal	no serious	no serious	no serious	serious	not applicable	%BF:null (1/1).	Very low
MPA	1095(5)	cross-sectional	serious	serious	no serious	no serious	not applicable	BMI: favorable (2/3); null (1/3); %BF: favorable (1/2); null (1/2); WC: favorable (2/3); null (1/3); FM: favorable (1/1); VAT: favorable (1/1).	Very low
	228(1)	Longitudinal	no serious	no serious	no serious	serious	not applicable	%BF: null (1/1).	

	75(2)	RTs	no serious	no serious	no serious	serious	not applicable	BMI: null (1/1); WC: null (1/1); FM: null (1/1); VAT: null (1/1).	Moderate
MVPA	5745(10)	cross-sectional	no serious	serious	no serious	serious	no serious	BMI: favorable (2/5); null (3/5); %BF: favorable (2/3); null (1/3); WC: favorable (2/4); null (2/4); FM: null (1/1); VAT: favorable (1/3); null (2/3).	Very low
VPA	970(5)	cross-sectional	serious	no serious	no serious	no serious	not applicable	BMI: favorable (2/2); %BF: favorable (3/3); WC: favorable (1/1); FM: favorable (1/1); VAT: favorable (1/1).	Very low
	228(1)	Longitudinal	no serious	no serious	no serious	serious	not applicable	%BF: favorable (1/1).	Low
	17(1)	RTs	no serious	no serious	no serious	serious	not applicable	BMI: favorable effect (1/1).	Moderate
10min PA bout	1854(3)	cross-sectional	no serious	serious	no serious	no serious	not applicable	BMI: favorable (1/2); null (1/2); WC: favorable (1/3); null (2/3);	Very low

Note:

1. We downgraded one level if 50% to 75% of studies were at low quality and two levels if more than 75% of studies low quality.
2. We downgraded one level if findings were highly inconsistent.
3. We downgraded one level for indirectness if studies provided indirect evidence or made indirect comparisons.
4. We downgraded one level for imprecision if the number of participants was less than 400.
5. Publication bias test was not applicable when n<10.

BMI, body mass index; FM, fat mass; LPA, low intensity physical activity; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; PA, physical activity; RTs, random trials; TPA, total physical activity; VAT, visceral adipose tissue; VPA, vigorous physical activity; WC, waist circumference; %BF, percentage body fat.

Supplementary Table C: Characteristics of participants for study 1 part 1

Reference	Country	Race	Sample size	Age	BMI	Menstrual status	Diet	Education	Lifestyle	Socio-economic level	Tobacco
Ayabe et al. 2013	Japan	Asian	42	50±6	22.3±3.2	n/r	n/r	n/r	physically inactive	part-time	n/r
Bailey et al. 2007	USA	Caucasian (96%)	228	40.0±3.0	23.8±3.4	premenopausal	n/r	college or more (57%)	n/r	n/r	non-smoker
Bailey et al. 2014	USA	Caucasian (90%)	186	23.0±1.7	22.5±3.0	n/r	no affected medications	n/r	n/r	collage student	n/r
Bailey et al. 2015	USA	Caucasian (88%)	343	20.2±1.6	22.5±2.9	n/r	no affected medications	n/r	n/r	n/r	non-smoker
Bailey et al. 2019	USA	n/r	92	18.1±0.3	23.1±2.5	n/r	no affected medications	college	physically inactive	collage student	n/r
Cayir et al. 2015 Pedometer	Turkey	n/r	45	41.1±9.3	35.9±4.5	n/r	n/r	n/r	n/r	employed (43%)	n/r
Cayir et al. 2015 Control	Turkey	n/r	39	38.8±11.2	34.3±2.8	n/r	n/r	n/r	n/r	employed (33%)	n/r
de Hoed et al. 2008	Netherlands	n/r	80	21.0±2.0	21.8±2.5	n/r	no affected medications	n/r	n/r	collage student	n/r
Diniz et al. 2015 Active	Brazil	n/r	25	55.8±7.2	26.9±5.1	postmenopausal	no affected medications	n/r	physically active	n/r	n/r
Diniz et al. 2015 Sedentary	Brazil	n/r	24	61.6±6.2	29.1±9.0	postmenopausal	no affected medications	n/r	physically inactive	n/r	n/r
Graff et al. 2012	Brazil	Caucasian (73%)	68	28.0±6.0	28.0±6.0	premenopausal	no affected medications	n/r	n/r	n/r	n/r
Green et al. 2014	USA	Caucasian (92%)	50	24.0±4.8	27.0±4.8	premenopausal	no affected medications	collage student (84%)	n/r	collage student (84%)	no smoke for 6 months
Hasan et al. 2018	UAE	n/r	52	21.43±4.8	27.5±5.6	n/r	no affected medications	college	n/r	college student	n/r
Holliday et al. 2018	UK	n/r	58	41.0±2.0	29.2±3.4	n/r	no affected medications	n/r	physically inactive	n/r	non-smoker
Hornbuckle et al. 2005	USA	African American	69	51.4±5.4	30.9±6.8	n/r	n/r	n/r	n/r	n/r	non-smoker
Hornbuckle et al. 2012	USA	African American	44	49.0±5.5	34.7±6.4	n/r	n/r	n/r	physically inactive	n/r	no smoke for 6 months
Koniak-Griffin et al. 2014	USA	Latina	210	44.6±7.9	32.6±5.7	n/r	n/r	n/r	n/r	low income	n/r
Moreau et al. 2001	USA	n/r	24	54.0±1.0	n/r	postmenopausal	n/r	n/r	physically inactive	n/r	non-smoker

Musto et al. 2010 Active	USA	n/r	43	46.3±10.4	30.4±5.5	n/r	n/r	n/r	physically inactive	n/r	n/r
Musto et al. 2010 Control	USA	n/r	34	45.7±9.5	29.5±5.0	n/r	n/r	n/r	physically inactive	n/r	n/r
Pal et al. 2011 10000 steps	Australia	n/r	13	41.4±2.7	28.9±1.2	n/r	no affected medications	n/r	physically inactive	n/r	non-smoker
Pal et al. 2011 30 minutes	Australia	n/r	15	45.3±2.2	29.7±1.1	n/r	no affected medications	n/r	physically inactive	n/r	non-smoker
Panton et al. 2007	USA	African American	35	48±8	42.3±9.8	n/r	no affected medications	n/r	n/r	low income	non-smoker (83%)
Park et al. 2011	Japan	Asian	100	51.8±11.2	23.5±4.4	n/r	n/r	n/r	n/r	n/r	n/r
Pelclová et al. 2012 Czech Republic	Czech Republic	n/r	45	64.2±3.8	26.1±3.6	n/r	n/r	n/r	n/r	the Third Age University student	n/r
Pelclová et al. 2012 Slovakia	Slovakia	n/r	51	61.8±5.0	27.5±4.2	n/r	n/r	n/r	n/r	the Third Age University student	n/r
Pelclová et al. 2012 Poland	Poland	n/r	71	62.5±5.2	27.9±4.5	n/r	n/r	n/r	n/r	the Third Age University student	n/r
Phelan et al. 2007 weight-loss maintainers	USA	Caucasian (93%)	135	49.1±11.3	22.0±1.6	n/r	n/r	college or more (76%)	n/r	n/r	n/r
Phelan et al. 2007 always normal weight	USA	Caucasian (95%)	102	48.6±11.2	21.1±1.3	n/r	n/r	college or more (80%)	n/r	n/r	n/r
Slater et al. 2021 Pacific normal weight	New Zealand	Pacific	61	25.0±7.0	25.9±3.9	premenopausal	n/r	n/r	n/r	low income	n/r
Slater et al. 2021 Pacific obesity	New Zealand	Pacific	55	26.0±.0	35.6±6.1	premenopausal	n/r	n/r	n/r	more deprived	n/r
Slater et al. 2021 European normal weight	New Zealand	European	85	22.5±2.1	22.5±2.1	premenopausal	n/r	n/r	n/r	less deprived	n/r
Slater et al. 2021 European obesity	New Zealand	European	74	33.7±3.8	33.7±3.8	premenopausal	n/r	n/r	n/r	less deprived	n/r
Smith et al. 2013	USA	Caucasian (81%)	183	38.2±5.8	32.6±4.0	n/r	n/r	college or more (71%)	physically inactive	n/r	n/r
Sternfeld et al. 2005 Chinese premenopausal	USA	Asian	78	49.7±2.1	n/r	premenopausal	n/r	n/r	n/r	n/r	n/r
Sternfeld et al. 2005 Chinese postmenopausal	USA	Asian	79	52.3±2.4	n/r	postmenopausal	n/r	n/r	n/r	n/r	n/r
Sternfeld et al. 2005 Caucasian premenopausal	USA	Caucasian	45	49.4±1.9	n/r	premenopausal	n/r	n/r	n/r	n/r	n/r
Sternfeld et al. 2005 Caucasian postmenopausal	USA	Caucasian	46	52.7±2.8	n/r	postmenopausal	n/r	n/r	n/r	n/r	n/r

Strath et al. 2008	USA	Caucasian (75%)	1594	48.1±17.1	28.4±6.8	n/r	n/r	n/r	n/r	n/r	non-smoker(80%)
Sugiura et al. 2002 intervention	Japan	Asian	14	48.6±4.2	22.3±1.6	n/r	no affected medications	n/r	physically inactive	n/r	n/r
Sugiura et al. 2002 control	Japan	Asian	13	48.0±3.6	22.6±1.9	n/r	no affected medications	n/r	physically inactive	n/r	n/r
Swartz et al. 2003	USA	n/r	18	53.3±7.0	35.0±5.1	n/r	n/r	n/r	physically inactive	n/r	non-smoker
Thompson et al. 2004	USA	n/r	80	50.3±6.8	26.0±5.1	n/r	n/r	n/r	n/r	n/r	n/r
Tolonen et al. 2018	Finland	n/r	837	31-46	24.7-26.1	n/r	n/r	n/r	n/r	n/r	n/r
Tucker et al. 2003	USA	Caucasian (90%)	278	40.1±3.0	23.9±3.3	premenopausal	n/r	college or more (37%)	n/r	n/r	non-smoker
Tudor-Locke et al. 2009	Australia	n/r	158	56.4±1.4	26.9±5.4	n/r	n/r	college or more (46%)	n/r	employed (63%)	n/r
Van Dyck et al. 2015	multi-country	n/r	3027	18-65	22.6-28.0	n/r	n/r	n/r	n/r	n/r	n/r
Vella et al. 2009	USA	Hispanic	60	24.9±0.7	23.6±0.5	n/r	no affected medications	n/r	n/r	n/r	no smoke for 6 months
Vella et al. 2011 no meet PA Guideline	USA	Hispanic	42	25.2±5.6	23.8±4.0	n/r	no affected medications	n/r	n/r	n/r	no smoke for 6 months
Vella et al. 2011 meet PA Guideline	USA	Hispanic	18	24.4±4.9	23.0±4.6	n/r	no affected medications	n/r	n/r	n/r	no smoke for 6 months

Note: n/r, not report; PA, physical activity

Supplementary Table D: Ascertainment and measurement characteristics of objectively measured PA for study 1 part 1

Reference	Divice name	Wearing position	Frequency/Epoch	Required time	Valid time	Reported measure, Cut-off ponits/definitions
Ayabe et al. 2013	A: Lifecorder-Ex,uniaxial	left waist	32Hz/4s	10d/wake	10h/7d	MVPA min/d, 4-9METs; VPA min/d, 7-9METs; TPA min/d, 1-9METs
Bailey et al. 2007	A: ActiGraphs, uniaxial	left hip	10 min	7d/day exp. w	/	LPA group, less than 30,000 counts per epoch; MPA, 30000-50000 counts per epoch; VPA, ≥ 50000 counts per epoch
Bailey et al. 2014	P: Omeron HJ-720-ITC	right-waist/blinded	/	7d/day exp. w	80% time(7a.m.-11p.m.)/7d	Aerobic steps n/d, 60 steps per minute for a minimum of 10 minutes
Bailey et al. 2015	A: ActiGraph GT3x, triaxial	right hip	60s	7d/day exp. w	75% (7a.m.-11p.m.)	LPA min/d, 250-2019 cpm; MPA min/d, 2020-5999 cpm; VPA min/d, ≥ 6000 cpm; MVPA min/d, ≥ 2020 cpm
Bailey et al. 2019	A: ActiGraph GT3x, triaxial; P: Omeron HJ-720-IT	hip	60s	4d (2weekday, 2weekend)/day exp. W; 24w/day exp. W	75% (7a.m.-11p.m.)	LPA min/d, 100-2019 cpm; MVPA min/d, ≥ 2020 cpm
Cayir et al. 2015	P: Voit 3d	/	/	/	/	/
de Hoed et al. 2008	A: Tracmor IV, triaxial	/	/	14d/wake exp. w	/	TPA, megacounts/day
Diniz et al. 2015	A: ActiGraph GT3x, triaxial	waist	60s	7d/wake exp. w	10h/5d	LPA, <1952 cpm; MPA, 1952-5724 cpm; VPA, 5725-9498 cpm; VVPA, >9499 cpm
Graff et al. 2012	P: BP 148	/	/	6d/day exp. w	/	inactive, <6000 step/d; active, ≥ 6000 step/d
Green et al. 2014	A: ActiGraph GT3X+, triaxial	right hip	60s	7d/day exp. w	10h/4d(1 weekend)	LPA, 150-2689 cpm; MVPA, ≥2690 cpm

Hasan et al. 2018	P: KenzLifeCoder e-step	waist	/	9w/wake exp. w	/	sedentary, <5000 steps/d; low active, 5000-7499 steps/d; somewhat active, 7500-9999 steps/d; active, 10000-12499 steps/d; highly active, ≥12500 steps/d
Holliday et al. 2018	A: ActiGraph GT3X+, triaxial	right hip	15s	3d/wake	10h/3d	MPA min/d, 2020-5999 cpm; VPA min/d, ≥ 6000 cpm; MVPA min/d, ≥ 2020 cpm
Hornbuckle et al. 2005	P: New Lifestyles Digi-Walker SW-200	hip	/	7d/wake	7d	sedentary, <5000 steps/d; low active, 5000-7499 steps/d; somewhat active, 7500-9999 steps/d; active, ≥10000 steps/d
Hornbuckle et al. 2012	P: New Lifestyles Digi-Walker SW-200	hip	/	/	/	/
Koniak-Griffin et al. 2014	A: Kenz Lifecorder Plus, uniaxial		4s	7d/wake exp. w	8h/4d	MVPA, ≥3METS
Moreau et al. 2001	P: Yamax SW200 pedometer	waist	/	1-2w/wake	/	/
Musto et al. 2010	P: Sportline 330	/	/	7d/wake	/	/
Pal et al. 2011	P: Yamax Digi-Walker SW-200	waist	/	/	/	/
Panton et al. 2007	P: Yamax Digi-Walker SW-200, sealed	waist	/	2w/wake exp. w	/	Sedentary, <5000 steps/d; Active, ≥5000 steps/d
Park et al. 2011	A: Lifecorder EX, uniaxial	left waist	/	/	/	LPA, <3 METs; MPA, 3-6 METs; VPA, ≥6 METs
Pelclová et al. 2012	A: ActiGraph GT1M, uniaxial	right hip	60s	8d/wake exp. w	10h/7d	LPA, <1952 cpm; MPA, 1952-5724 cpm; VPA, >5724 cpm
Phelan et al. 2007	A: RT3, triaxial	waist	60s	wake	2h/4d	LPA, ≥2METs; MPA, ≥3METs; VPA, ≥5METs

Slater et al. 2021	A: Actigraph w-GT3X, triaxial; A: Acti-Watch	non-dominant hip; non-dominant wrist	60s	8d/day exp. w	12h/4d	sedentary, 0-99 cpm; LPA, 100-2019 cpm; MPA, 2020-5998 cpm; VPA, ≥5999 cpm; MVPA, ≥2020 cpm
Smith et al. 2013	A: Actigraph AM7164, uniaxial	dominant hip	60s	7d/wake	10h/4d	LPA, 100-1951 cpm; MPA, 1952-5724 cpm; VPA, ≥5725 cpm; TPA, ≥100 cpm; sedentary, 0-99 cpm
Sternfeld et al. 2005	A: CSA; uniaxial	waist	/	7d/wake exp. w	/	TPA, mean cpm MPA, 1000-4999 cpm VPA, ≥5000 cpm
Strath et al. 2008	A: AM-7164; uniaxial	right hip	60s	7d	10h/4d	MVPA, ≥760 cpm
Sugawara et al. 2006	A: Lifecorder, uniaxial	hip	32Hz/4s	14d	7d	LPA, <4METs; MPA, 4-6 METs; VPA, >6 METs
Swartz et al. 2003	P: Yamax Digi-Walker SW-200,	/	/	12w	/	/
Thompson et al. 2004	P: Yamax Digi-Walker SW-200	right waist	/	7d/wake exp. w	7d	inactive, < 6000 steps; somewhat active, 6000-9999 steps; regularly active, ≥10000 steps
Tolonen et al. 2018	P: Walking style One, HJ-152R-E	waist	/	7d/day exp. w	8h/4d	/
Tucker et al. 2003	A: CSA; uniaxial TPA (counts) (min/w) Intensity of PA (counts/10min)	left hip	10 min	7d/day exp. w	/	TPA, counts 10000-19999 counts, -2.7 METs 20000 to 49999 counts, -4.2 METs 50000 and more, -8.5+ METs
Tudor-Locke et al. 2009	P: Yamax Digiwalker SW700	waist	/	7d/day exp. w	/	/
Van Dyck et al. 2015	A: ActiGraph 7164/71256, GT1M, ActiTrainer, GT3X; uniaxial&triaxial	right hip	60s	7d/wake exp. w	/	LPA, 100-1952 cpm; MPA, 1952-5724 cpm; VPA, >5725

Vella et al. 2009	A: Actigraph GT1M, uniaxial	right hip	60s	4d(3weekday, 1weekend)/wake exp. w	12h/4d	/
Vella et al. 2011	A: Actigraph GT1M, uniaxial	right hip	60s	4d(3weekday, 1weekend)/wake exp. w	12h/4d	LPA, 100-1951 cpm; MPA, 1952-5724 cpm; VPA, ≥5725 cpm

Note: A, accelerometer; cpm, counts per minute; d, day; exp, expect; h, hour; LPA, light intensity physical activity; METs, metabolic equivalents; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; P, pedometer; VPA, vigorous intensity physical activity; W, water activities

Supplementary Table E: Search strategies for study 1 part 2

Database		PubMed (n=1265)
Date		January 1, 1990-January 31, 2022
Search Terms	#1	(Accelerometry[Mesh] OR Accelero*[TIAB] OR Actigraphy[MAJR] OR actigra* [TIAB]) Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#2	(objectively[TIAB] AND assessed[TIAB] AND physical[TIAB] AND activity[TIAB]) Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#3	(objectively[TIAB] AND measured[TIAB] AND physical[TIAB] AND activity[TIAB]) Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#4	pedometer[TIAB] Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
	#5	"blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR triglyceride OR TG OR "high density lipoprotein" OR HDL OR "low density lipoprotein" OR LDL OR "total cholesterol" OR TC OR insulin OR HOMA OR glucose OR HbA1c OR "glycosylated hemoglobin" OR "glycated hemoglobin" OR CRP OR "C-reactive protein" OR IL-6 OR interleukin-6 OR TNF-alpha OR TNF-α OR "Cardiometabolic Risk Factors"[Mesh] OR "Metabolic Syndrome"[Mesh] Filters: Young Adult: 19-24 years, Adult: 19-44 years, Middle Aged: 45-64 years, Female
		#1 OR #2 OR #3 OR #4 AND #5
		(((((Accelerometry[Mesh] OR Accelero*[TIAB] OR Actigraphy[Mesh] OR actigra* [TIAB]) AND (adult[Filter] OR middleaged[Filter] OR youngadult[Filter])) OR ((objectively[TIAB] AND assessed[TIAB] AND physical[TIAB] AND activity[TIAB]) AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter]))) OR ((objectively[TIAB] AND measured[TIAB] AND physical[TIAB] AND activity[TIAB]) AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter]))) OR (pedometer[TIAB] AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter]))) AND ("blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR triglyceride OR TG OR "high density lipoprotein" OR HDL OR "low density lipoprotein" OR LDL OR "total cholesterol" OR TC OR insulin OR HOMA OR glucose OR HbA1c OR "glycosylated hemoglobin" OR "glycated hemoglobin" OR CRP OR "C-reactive protein" OR IL-6 OR interleukin-6 OR TNF-alpha OR TNF-α OR "Cardiometabolic Risk Factors"[Mesh] OR "Metabolic Syndrome"[Mesh] AND ((female[Filter]) AND (english[Filter]) AND (youngadult[Filter] OR adult[Filter] OR middleaged[Filter])))
Database		SCOPUS (n=619)
Date		January 1, 1990-January 31, 2022
	#1	TITLE-ABS-KEY (accelerometry OR accelero* OR actigra* OR actigraphy)
	#2	TITLE-ABS-KEY ((objectively AND measured AND physical AND activity))
	#3	TITLE-ABS-KEY ((objectively AND assessed AND physical AND activity))
	#4	TITLE-ABS-KEY (pedometer)
	#5	"blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR triglyceride OR TG OR "high density lipoprotein" OR HDL OR "low density lipoprotein" OR LDL OR "total cholesterol" OR TC OR insulin OR HOMA OR glucose OR HbA1c OR "glycosylated hemoglobin" OR "glycated hemoglobin" OR CRP OR "C-reactive protein" OR IL-6 OR interleukin-6 OR TNF-alpha OR TNF-α OR "Cardiometabolic Risk Factors" OR "Metabolic Syndrome"

		#1 OR #2 OR #3 OR #4 AND #5
		(TITLE-ABS-KEY(accelerometry OR accelero* OR actigra* OR actigraphy) OR TITLE-ABS-KEY(objectively AND measured AND physical AND activity) OR TITLE-ABS-KEY(objectively AND assessed AND physical AND activity) OR TITLE-ABS-KEY(pedometer)) AND (TITLE-ABS-KEY ("blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR triglyceride OR tg OR "high density lipoprotein" OR hdl OR "low density lipoprotein" OR ldl OR "total cholesterol" OR tc OR insulin OR homa OR glucose OR hba1c OR "glycosylated hemoglobin" OR "glycated hemoglobin" OR crp OR "C-reactive protein" OR il-6 OR interleukin-6 OR tnf-alpha OR tnf-α OR "Cardiometabolic Risk Factors" OR "Metabolic Syndrome")) AND NOT ((child*) OR (old*) OR (eld*) OR (pregnan*) OR (disable*) OR (athlete)) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "English"))
Database		Web of Science (n=2067)
Date		January 1, 1990-January 31, 2022
	#1	TS=(accelerometry OR accelero* OR actigra* OR actigraphy)
	#2	TS=(objectively AND measured AND physical AND activity)
	#3	TS=(objectively AND assessed AND physical AND activity)
	#4	TS=(pedometer)
	#5	TS=("blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR triglyceride OR TG OR "high density lipoprotein" OR HDL OR "low density lipoprotein" OR LDL OR "total cholesterol" OR TC OR insulin OR HOMA OR glucose OR HbA1c OR "glycosylated hemoglobin" OR "glycated hemoglobin" OR CRP OR "C-reactive protein" OR IL-6 OR interleukin-6 OR TNF-alpha OR TNF-α OR "Cardiometabolic Risk Factors" OR "Metabolic Syndrome")
		(((((#1) OR #2) OR #3) OR #4) AND #5) NOT TS=(((child*) OR (old*) OR (eld*) OR (pregnan*) OR (disable*) OR (athlete)))
Database		The Cochrane library (n=1154)
Date		January 1, 1990-January 31, 2022
	#1	MeSH descriptor: [Accelerometry] this term only
	#2	accelero* OR actigra* OR actigraphy
	#3	#1 OR #2
	#4	objectively AND measured AND physical AND activity:ti,ab,kw
	#5	objectively AND assessed AND physical AND activity:ti,ab,kw
	#6	pedometer
	#7	#3 OR #4 OR #5 OR #6
	#8	"blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR triglyceride OR TG OR "high density lipoprotein" OR HDL OR "low density lipoprotein" OR LDL OR "total cholesterol" OR TC OR insulin OR HOMA OR glucose OR HbA1c OR "glycosylated hemoglobin" OR "glycated hemoglobin" OR CRP OR "C-reactive protein" OR IL-6 OR interleukin-6 OR TNF-alpha OR TNF-α
	#9	MeSH descriptor: [Cardiometabolic Risk Factors] this term only
	#10	#8 OR #9
	#11	MeSH descriptor: [Metabolic Syndrome] this term only

	#12	#10 OR #11
	#13	(child*) OR (old*) OR (eld*) OR (pregnan*) OR (disable*) OR (athlete)
	#14	#7 AND #12 NOT #13

Supplementary Table F: methodological quality of studies for study 1 part 2

Supplementary Table F.1 Assessment of methodological quality of nonrandomized studies (Newcastle Ottawa Scale)

Study	Selection				Comparability	Outcome			Total	Quality
	Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome does not present at start of study	Adjusted for age and other important covariates	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow up		
Camhi et al. 2015	-	*	*	*	**	*	n/a	n/a	6	High
Diniz et al. 2015	-	*	*	*	*	*	n/a	n/a	5	High
Graff et al. 2012	-	*	-	*	-	*	n/a	n/a	3	Low
Green et al. 2014	*	*	*	*	-	*	n/a	n/a	5	High
Hasan et al. 2018	-	*	*	*	-	*	-	*	5	High
Koniak-Griffin et al. 2014	*	*	-	*	-	*	n/a	n/a	4	High
Lecheminant et al. 2011	*	*	*	*	**	*	n/a	n/a	7	High
Loprinzi et al. 2012	*	*	-	*	**	*	n/a	n/a	6	High
Macena et al. 2021	-	*	*	*	**	*	n/a	n/a	6	High
Musto et al. 2010	-	*	-	*	-	*	-	*	4	Low
Panton et al. 2007	-	*	-	*	-	*	n/a	n/a	3	Low
Rodriguez-Hernandez et al. 2018	-	*	*	*	-	*	n/a	n/a	4	Low
Slater et al. 2021	*	*	*	*	**	*	n/a	n/a	7	High
Swartz et al. 2003	-	*	-	*	-	*	-	*	4	Low
Tabozzi et al. 2020	-	*	*	*	*	*	n/a	n/a	5	High
Vella et al. 2011	*	*	*	*	-	*	n/a	n/a	5	High
Vella et al. 2009	*	*	*	*	**	*	n/a	n/a	7	High
Zając-Gawlak et al. 2017	-	*	*	*	-	*	n/a	n/a	4	High

Notes: Representativeness of the exposed cohort: One star = truly/somewhat representative of general female adults; Selection of the non-exposed cohort: One star = drawn from the same community as the exposed cohort; Comparability: One star = study controls for age, 2nd star = study controls for other confounders; Follow-up long enough for outcomes to occur: One star = ≥12 months; Adequacy of follow up: Complete follow up/all groups had similar loss to follow-up/less than 5% of total lost to follow-up

n/a: not applicable

Supplementary Table F.2 Assessment of methodological quality of randomized studies (the Cochrane Collaboration’s tool)

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Overall Quality
Hornbuckle et al. 2012	L	L	L	L	L	L	L	High
Moreau et al. 2001	U	L	L	L	L	L	L	U
Pal et al. 2011	U	L	L	L	L	L	L	U
Sugawara et al. 2006	U	L	L	L	L	L	L	U
Sugiura et al. 2002	U	U	L	L	L	L	L	U

Note: L, low risk; H, high risk, U, unclear.

Supplementary Table F.3 GRADE assessment

			Quality Assessment					
	No. of participants (#studies)	**study design**	**Risk of bias[1]**	**Inconsistency[2]**	**Indirectness[3]**	**Imprecision[4]**	**Publication bias[5]**	**Absolute effect**
Blood pressure	113(4)	RCTs	no serious	no serious	serious	serious	not applicable	2/4 reported increased steps/d had no effect on SBP and DBP [Hornbuckle et al., 2012; Pal et al., 2011] 1/4 reported increased steps/d had favorable effect on SBP, and no effect on DBP [Moreau et al., 2001] 1/4 reported increased PA intensity with no effect on SBP or DBP [Sugawara et al., 2006]
	147(3)	NRTs	no serious	no serious	no serious	serious	not applicable	1/3 reported increased steps/d had no effects on SBP or DBP [Hasan et al., 2018] 1/3 reported increased steps/d had favorable effect on SBP and DBP [Swartz et al., 2003] 1/3 reported increased steps/d had favorable effect on SBP, but no effect on DBP [Musto et al., 2010]
	690(6)	Cross-sectional	no serious	no serious	no serious	no serious	not applicable	**Steps:** no association with SBP or DBP (3/3 Koniak-Griffin et al., 2014; Panton et al., 2007; Vella et al., 2009); **TPA:** no association with SBP or DBP (1/1 Slater et al., 2021); **LPA:** no association with SBP or DBP (1/1 Green et al. 2014); **MVPA:** no association with SBP or DBP (3/3 Green et al., 2014; Koniak-Griffin et al., 2014; Slater et al., 2021); **MVPA bouts (10min):** no association with SBP or DBP (2/2 Green et al., 2014; Koniak-Griffin et al., 2014) **Meeting PA guideline (≥150 min/w MVPA):** no association with SBP or DBP (1/1 Vella et al., 2011)
Lipid profile	71(2)	RCTs	no serious	no serious	no serious	serious	not applicable	1/2 reported inceased steps/d had no effects on HDL, TG, or T-Chol [Hornbuckle et al., 2012] 1/2 reported increased steps/d had favorable effects on HDL and T-Chol, had no effects on TG or LDL [Sugiura et al., 2002].
	129(2)	NRTs	serious	no serious	no serious	serious	not applicable	1/2 reported increased steps/d had favorable effects on LDL [Hasan et al. 2018]; 2/2 reported increased steps/d had no effects on T-Chol, TG, or HDL [Hasan et al., 2018; Musto et al., 2010]

	800(8)	Cross-sectional	no serious	serious	no serious	no serious	not applicable	**Steps:** *LDL:* no association [2/3 Graff et al., 2012; Koniak-Griffin et al., 2014]; unfavorable association [1/3 Panton et al., 2007]; *HDL:* no association [3/4 Graff et al., 2012; Koniak-Griffin et al., 2014; Panton et al., 2007]; favorable association [1/4 Vella et al., 2009]; *T-Chol:* no association [2/3 Graff et al., 2012; Koniak-Griffin et al., 2014]; unfavorable association [1/3 Panton et al., 2007]; *TG:* favorable association [2/4 Koniak-Griffin et al., 2014; Vella et al,. 2009]; no association [2/4 Graff et al., 2012; Panton et al., 2007]; **TPA:** no association with LDL, HDL, TG, or T-Chol [Slater et al. 2021]; **LPA:** favourable association with TG and T-chol; no association with HDL or LDL [Green et al., 2014]; **MVPA:** *LDL:* no association [3/3 Slater et al., 2021; Green et al., 2014; Koniak-Griffin et al., 2014]; *HDL:* favorable association [2/3 Slater et al., 2021; Koniak-Griffin et al., 2014); no association [Green et al., 2014]; *T-Chol:* no association [2/3 Slater et al., 2021; Green et al., 2014]; unfavorable association [1/3 Koniak-Griffin et al., 2014]; *TG:* no association [3/3 Slater et al., 2021; Green et al., 2014; Koniak-Griffin et al., 2014] **MVPA bouts (10min):** no association with LDL, HDL, TG, or T-Chol [2/2 Green et al., 2014; Koniak-Griffin et al., 2014] **Meeting PA guideline (≥150 min/w MVPA):** favorable association with TG and T-Chol; no association with LDL or HDL [Vella et al. 2011].
Carbohydrate metabolism	68(2)	RCTs	serious	no serious	no serious	serious	not applicable	1/2 reported increased steps/d had no effects on HbA1c [Hornbuckle et al., 2012]; 1/2 reported increased steps/d had no effects on FGLC or HOMA-IR [Moreau et al., 2001];
	157(4)	NRTs	serious	no serious	no serious	serious	not applicable	**Increased steps:** FGLC: favorable association [1/3 Musto et al. 2010]; no association [2/3 Hasan et al., 2018; Swartz et al., 2003] PGLC: favorable association with 2h-PGLC [1/1 Swartz et al. 2003]; HOMA-IR: no association [Hasan et al., 2018] 2h-AUCglc: favorable association [1/1 Swartz et al. 2003] **Increased %MVPA:** favorable association with 4h-PGLC, 2h-AUCglc; no association with peak PGCL [1/1 Rodriguez-Hernandez et al., 2018];

								Increased %LPA: no association with PGLC, or 2h-AUCgle [1/1 Rodriguez-Hernandez et al., 2018].
	1135(11)	Cross-sectional	no serious	no serious	no serious	no serious	no serious	**Steps:** *FGLC:* no association [4/4 Graff et al., 2012; Koniak-Griffin et al., 2014; Tabozzi et al., 2020; Vella et al., 2009]; *PGLC:* no association [2/2 Graff et al., 2012; Tabozzi et al., 2020]; *HbA1c:* no association [1/1 Panton et al., 2007] *HOMA-IR:* favorable association [1/2 Graff et al., 2012]; no association [1/2 Macena et al., 2021] **TPA: no association with FGLC, HbA1c, or HOMA-IR [1/1 Slater et al., 2021]** **LPA:** *HOMA-IR:* no association [2/2 Macena et al. 2021; Green et al. 2014]; *FGLC:* no association [1/1 Green et al. 2014] **%LPA:** no association with FGLC or PGLC [1/1 Tabozzi et al., 2020] **MPA:** no association with HOMA-IR [2/2 Lecheminant et al., 2011; Macena et al., 2021]; **%MPA and %VPA:** no association with FGLC, favorable association with PGLC [1/1 Tabozzi et al., 2020]; **MVPA:** *FGLC:* no association [4/4 Green et al., 2014; Koniak-Griffin et al., 2014; Slater et al., 2021; Tabozzi et al., 2020] *PGLC:* favorable association with peak PGLC [1/1 Tabozzi et al., 2020] *HbA1c:* no association [1/1 Slater et al., 2021] **MVPA bouts (10min):** no association with FGLC [2/2 Green et al., 2014; Koniak-Griffin et al., 2014]; favorable association with HOMA-IR [1/1 Green et al., 2014] **Meeting PA guideline (≥150 min/w MVPA):** *FGLC:* no association [1/1 Vella et al., 2011]; *HOMA-IR: no association [*3/3 Lecheminant et al., 2011; Diniz et al., 2015; Vella et al., 2011]
Endocrine regulators	24(1)	RCTs	serious	no serious	no serious	serious	not applicable	Increased steps had no effect on fasting insulin [Moreau et al., 2001]

	70(2)	NRTs	serious	no serious	no serious	serious	not applicable	2/2 reported increased steps had no effect fasting insulin or postprandial insulin [Hasan et al., 2018; Swartz et al., 2003]
	502(5)	Cross-sectional	no serious	serious	no serious	no serious	not applicable	**Steps/d:** favorable association with fasting insulin and postprandial insulin [1/1 Graff et al., 2012]; **TPA:** favorable association with fasting insulin [1/1 Slater et al., 2021]; **LPA:** no association with fasting insulin [1/1 Green et al., 2014]; **MVPA:** no association with fasting insulin [2/2 Green et al., 2014; Slater et al., 2021] **MVPA bouts (10min):** favorable association with fasting insulin [1/1 Green et al., 2014] **Meeting PA guideline (≥150 min/w MVPA):** no association with fasting insulin [2/2 Diniz et al., 2015; Vella et al., 2011]
Inflammation marker	44(1)	RCTs	no serious	no serious	no serious	serious	not applicable	1/1 reported increased steps/d had no effect on CRP [Hornbuckle et al., 2012]
	409(4)	Cross-sectional	no serious	serious	no serious	no serious	not applicable	**Steps:** no association with CRP [1/1 Panton et al., 2007] **TPA:** favorable with CRP [1/1 Slater et al., 2021] **LPA:** no association with TNF-a, CRP, or IL-6 [1/1 Green et al., 2014] **MVPA:** favorable association with TNF-a and CRP, no association with IL-6 (1/1 Green et al. 2014); unfavorable with CRP [1/1 Slater et al., 2021] **MVPA bouts (10min):** favorable association with CRP, no association with IL-6 or TNF-a [1/1 Green et al., 2014] **Meeting PA guideline (≥150 min/w MVPA):** no association with TNF-a [1/1 Diniz et al., 2015)
MetS	52(1)	NRTs	no serious	no serious	no serious	serious	not applicable	1/1 reported increased steps/d had favourable effect on MetS score (Hasan et al. 2018)
	708(4)	Cross-sectional	no serious	no serious	no serious	no serious	not applicable	**Steps:** favorable association [1/2 Zając-Gawlak et al., 2017]; no association [1/2 Camhi et al., 2015]; **LPA:** favorable association [Camhi et al., 2015]; **MPA, VPA, MVPA bouts (10min) and TPA:** no association [Camhi et al., 2015]; **MVPA:** favorable association [1/1 Loprinzi et al., 2012]; no association [Camhi et al., 2015].

Note:
1. We downgraded one level if 50% to 75% of studies were low quality and two levels if more than 75% of studies were low quality.
2. We downgraded one level for inconsistency of findings were highly inconsistence
3. We downgraded one level for indirectness if studies examined various types of PA intervention and provided indirect evidence or made indirect comparisons.
4. We downgraded one level for imprecision if the number of participants was less than 400.
5. Publication bias test was not applicable when n<10.

CRP, C-reactive protein; DBP, diastolic blood pressure; FGLC, fasting glucose; HbA1c, glycosylated hemoglobin; HDL, high density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; IL-6, interleukin-6; LDL, low density lipoprotein; LPA, low intensity physical activity; MPA, moderate intensity physical activity; MetS, metabolic syndrome; MVPA, moderate to vigorous intensity physical activity; PGLC, postprandial glucose; SBP, systolic blood pressure; T-Chol, total cholesterol; TG, triglyceride; TNF-a, tumor necrosis factor-a; TPA, total physical activity; VPA, vigorous physical activity.

Supplementary Table G: Characteristics of participants for included studies for study 1 part 2

Reference	country	race	sample size	age	BMI	menstrual status	diet	education	lifestyle	socio-economic level	tobacco
Camhi et al. 2015	USA	African American (61%)	46	26.7±4.7	31.1±3.7	/	no affected medications and dietary supplements	/	/	/	non-smoker (80%)
Diniz et al. 2015 meet PA guideline	Brazil	/	25	55.8±7.2	26.9±5.1	postmenopausal	no affected medications	/	physically active	/	/
Diniz et al. 2015 not meet PA guideline	Brazil	/	24	61.6±6.2	29.1±9.0	postmenopausal	no affected medications	/	physically inactive	/	/
Graff et al. 2012	Brazil	Caucasian (73%)	68	28.0±6.0	28.0±6.0	premenopausal	no affected medications	/	/	/	/
Green et al. 2014	USA	Caucasian (92%)	50	24.0±4.8	27.0±4.8	premenopausal	no affected medications	collage (84%)	/	college student (84%)	no smoke for 6 months
Koniak-Griffin et al. 2014	USA	Latina	210	44.6±7.9	32.6±5.7	/	/	college or more (4%)	/	low income	/
Lecheminant et al. 2011	USA	Caucasian (90%)	264	40.1±3.0	31.7±6.9	premenopausal	/	college or more (50%)	/	/	non-smoker
Loprinzi et al. 2012	USA	Caucasian (73%)	535	49.3±0.9	28.8±0.3	/	/	/	/	/	non-smoker (60%)
Macena et al. 2021	Brazil	/	58	31.0±7.0	33.3±4.1	premenopausal	no affected medications	/	/	low income	/
Panton et al. 2007	USA	African American	35	48±8	42.3±9.8	/	no affected medications	/	/	low income	non-smoker (83%)
Slater et al. 2021 Pacific normal	New zealand	Pacific	61	25.0±7.0	25.9±3.9	premenopausal	/	/	/	low income	/
Slater et al. 2021 Pacific obesity	New zealand	Pacific	55	26.0±.0	35.6±6.1	premenopausal	/	/	/	low income	/
Slater et al. 2021 European normal	New zealand	European	85	22.5±2.1	22.5±2.1	premenopausal	/	/	/	less deprived	/
Slater et al. 2021 European obesity	New zealand	European	74	33.7±3.8	33.7±3.8	premenopausal	/	/	/	less deprived	/
Tabozzi et al. 2020	Italy	/	13	32.5±16.1	24.0±3.3	/	no affected medications	/	physically inactive	university nurse students/research staff	/
Vella et al. 2011 no meet PA Guideline	USA	Hispanic	42	25.2±5.6	23.8±4.0	/	no affected medications	/	/	/	no smoke for 6 months

Vella et al. 2011 meet PA Guideline	USA	Hispanic	18	24.4±4.9	23.0±4.6	/	no affected medications	/	/	/	no smoke for 6 months
Vella et al. 2009	USA	Mexican and Mexican American	60	24.9±0.7	23.6±0.5	/	no affected medications	/	/	/	no smoke for 6 months
Zając-Gawlak et al. 2017	Poland	/	85	62.8±5.9	27.6±4.5	postmenopausal	/	/	physically active	the Third Age University student	/
Hasan et al. 2018	UAE	/	52	21.4±4.8	27.5±5.6	/	no affected medications	college	/	college student	/
Hornbuckle et al. 2012	USA	African American	44	49.0±5.5	34.7±6.4	/	/	/	physically inactive	/	no smoke for 6 months
Moreau et al. 2001	USA	/	24	54.0±1.0	/	postmenopausal	/	/	physically inactive	/	non-smoker
Musto et al. 2010 Control	USA	/	34	45.7±9.5	29.5±5.0	/	/	/	physically inactive	/	/
Musto et al. 2010 Active	USA	/	43	46.3±10.4	30.4±5.5	/	/	/	physically inactive	/	/
Pal et al. 2011 10000 steps	Australia	/	13	41.4±2.7	28.9±1.2	/	no affected medications	/	physically inactive	/	non-smoker
Pal et al. 2011 30min walking	Australia	/	15	45.3±2.2	29.7±1.1	/	no affected medications	/	physically inactive	/	non-smoker
Rodriguez-Hernandez et al. 2018	USA	/	10	36.0±5.0	38.0±1.6	/	no affected medications	/	physically inactive	/	/
Sugawara et al. 2006 moderate intensity training	Japan	Asian	8	58.0±4.0	25.5±3.6	postmenopausal	/	/	physically inactive	/	non-smoker
Sugawara et al. 2006 vigorou intensity training	Japan	Asian	9	59.0±6.0	24.2±3.0	/	/	/	/	/	/
Sugiura et al. 2002 intervention	Japan	Asian	14	48.6±4.2	22.3±1.6	both	no affected medications	/	physically inactive	/	/
Sugiura et al. 2002 control	Japan	Asian	13	48.0±3.6	22.6±1.9	both	no affected medications	/	physically inactive	/	/
Swartz et al. 2003	USA	/	18	53.3±7.0	35.0±5.1	both	/	/	physically inactive	/	non-smoker

Supplementary Table H: Ascertainment and measurement characteristics of objectively measured PA for study 1 part 2

Reference	Device	Wear position	Frequency/Epoch	Required time	Valid time	Reported measure, Cut-off/definition
Camhi et al. 2015	A: ActiGraph GT3X+, triaxial	waist	/	7d/wake exp. w	8h/3d	LPA min/d, 100-759 cpm; MPA min/d, 760-5998 cpm; VPA min/d, ≥ 5999 cpm; MVPA bouts n/d, a minimum of 10 minutes with allowance for a 2-minute interruption with a minimum of 760 cpm
Diniz et al. 2015	A: ActiGraph GT3x, triaxial	waist	60s	7d/wake exp. w	10h/5d	LPA, <1952 cpm; MPA, 1952-5724 cpm; VPA, 5725-9498 cpm; VVPA, >9499 cpm
Graff et al. 2012	P: BP 148	/	/	6d/day exp. w	/	inactive, <6000 step/d; active, ≥ 6000 step/d
Green et al. 2014	A: ActiGraph GT3X+, triaxial	right hip	60s	7d/day exp. w	10h/4d (1 weekend)	LPA, 150-2689 cpm; MVPA, ≥2690 cpm
Hasan et al. 2018	P: KenzLifeCoder e-step	waist	/	9w/wake exp. w	/	sedentary, <5000 steps/d; low active, 5000-7499 steps/d; somewhat active, 7500-9999 steps/d; active, 10000-12499 steps/d; highly active, ≥12500 steps/d
Hornbuckle et al. 2012	P: New Lifestyles Digi-Walker SW-200	hip	/	/	/	/
Koniak-Griffin et al. 2014	A: Kenz Lifecorder Plus, uniaxial		4s	7d/wake exp. w	8h/4d	/
Lecheminant et al. 2011	A: Actigraph, uniaxial	left hip	10 min	7d/day exp. w	/	MPA, 30000-49999 counts/10min; VPA, ≥ 50000 counts/10min
Loprinzi et al. 2012	/	right hip	/	7d/wake	10h/4d	MPA min/d, 2020-5999 cpm; VPA min/d, ≥ 6000 cpm; MVPA min/d, ≥ 2020 cpm
Macena et al. 2021	A: ActivPAL, triaxial	right hip	10s	3d/day exp. w	3d	Sitting/lying down h/d, 1.25MET; Standing h/d, 1.40MET; Walking, 120 steps/min 4MET

Moreau et al. 2001	P: Yamax SW200 pedometer	waist	/	1-2w/wake	/	/
Musto et al. 2010	P: Sportline 330	/	/	7d/wake	/	/
Pal et al. 2011	P: Yamax Digi-Walker SW-200	waist	/	/	/	/
Panton et al. 2007	P: Yamax Digi-Walker SW-200, sealed	waist	/	2w/wake exp. w	/	Sedentary, <5000 steps/d; Active, ≥5000 steps/d
Rodriguez-Hernandez et al. 2018	A: ActiGraph GT3X, triaxial	right hip	30Hz/60s	wake exp. w	10h/3d	sedentary, <100 cpm; LPA, 500-2019 cpm; MPA, 2020-5999 cpm; VPA, >5999 cpm
Slater et al. 2021	A: Actigraph w-GT3X, triaxial; A: Acti-Watch	non-dominant hip; non-dominant wrist	60s	8d/day exp. w	12h/4d	sedentary, 0-99 cpm; LPA, 100-2019 cpm; MPA, 2020-5998 cpm; VPA, ≥5999 cpm; MVPA, ≥2020 cpm
Sugawara et al. 2006	A: Lifecorder, uniaxial	hip	32Hz/4s	14d	7d	LPA, <4METs; MPA, 4-6 METs; VPA, >6 METs
Sugiua et al. 2002	P: n/r	/	/	/	/	/
Swartz et al. 2003	P: Yamax Digi-Walker SW-200,	/	/	12w	/	/
Tabozzi et al. 2020	A: ActiGraph GT3X + BT, triaxial	waist	/	7d/wake exp. w	8h	sedentary, ≤ 1.5METs; LPA, 1.5-4 METs; MPA, 4-7 METs; VPA, >7METs; MVPA, >4

Vella et al. 2011	A: Actigraph GT1M, uniaxial	right hip	60s	4d (3weekday, 1weekend)/wake exp. w	12h/4d	LPA, 100-1951 cpm; MPA, 1952-5724 cpm; VPA, ≥5725 cpm
Vella et al. 2009	A: ActiGraph GT1M, uniaxial	right hip	60s	4d (3weekday, 1weekend)/wake exp. w	12h/4d	/
Zając-Gawlak et al. 2017	A: ActiGraph GT1M, uniaxial	right hip	60s	8d/wake exp. w	12h/8d	active, 10000-12499 steps/d; highly active, ≥12500 steps/d

Note: A, accelerometer; cpm, count per minute; d, day, exp., expect; h, hour; LPA, light intensity physical activity; METs, metabolic equivalents; MPA, moderate intensity physical activity; MVPA, moderate to vigorous intensity physical activity; P, pedometer; s, second; w, water activity.