

The conjoint associations of adherence to physical activity and dietary guidelines with cardiometabolic health: The Framingham Heart Study

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Keywords: physical activity, diet quality, guidelines, cardiometabolic health

Posted Date: August 2nd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-50754/v1>

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Version of Record: A version of this preprint was published at Journal of the American Heart Association on April 6th, 2021. See the published version at <https://doi.org/10.1161/JAHA.120.019800>.

Abstract

Background

The conjoint associations of adherence to the recent physical activity (PA) and dietary guidelines with the metabolic syndrome (MetS) are incompletely understood.

Methods

We evaluated 2,379 Framingham Heart Study Third Generation participants (mean age 47 years, 54.4% women) attending examination cycle 2. We examined the cross-sectional relations of adherence to the 2018 Physical Activity Guidelines for Americans (PAG, binary; moderate to vigorous PA [MVPA] \geq 150 minutes/week vs. $<$ 150 minutes/week) and 2015 Dietary Guidelines for Americans (DGA, binary; 2015 DGA adherence Index [DGAI-2015] \geq median vs. $<$ median [score 62.1/100]) with prevalence of the MetS using generalized linear models. We also related adherence to guidelines with the incidence of MetS prospectively, using Cox proportional hazards regression with discrete time intervals.

Results

Adherence to the 2018 PAG (odds ratio [OR] 0.49, 95% CI 0.40–0.60) and 2015 DGA (OR 0.67, 95% CI 0.51–0.90) were individually associated with lower odds of prevalent MetS, while conjoint adherence to both guidelines was associated with the lowest odds of MetS (OR 0.35, 95% CI 0.26–0.47) compared to the referent group (non-adherence to both guidelines). Adherence to the 2018 PAG (hazards ratio [HR] 0.66, 95% CI 0.50–0.88) and 2015 DGA (HR 0.68, 95% CI 0.51–0.90) were associated with lower risk of MetS, prospectively. Additionally, we observed a 52% lower risk of MetS in individuals who adhered to both guidelines compared to the referent group.

Conclusions

Maintaining both regular physical activity and a healthy diet in midlife may be required for optimal cardiometabolic health in later life.

Background

The metabolic syndrome (MetS) is the clustering of key cardiometabolic risk factors, such as abdominal obesity, insulin resistance, hyperglycemia, dyslipidemia, and high blood pressure [1]. The presence of MetS is a major risk factor for type 2 diabetes and cardiovascular disease (CVD) [2, 3]. However, evidence indicates that healthy lifestyle behaviors are associated with favorable cardiometabolic health [4]. Additionally, favorable cardiometabolic health in middle-adulthood has been associated with lower

disease burden later in life [5]. Thus, adherence to healthy lifestyle modifications in middle-adulthood is a feasible approach to improve cardiometabolic health later in life.

The 2018 Physical Activity Guidelines for Americans (PAG) recommend that adults (18 years and older) achieve a minimum of 150 minutes of moderate-to-vigorous physical activity (MVPA) per week to lower the burden of chronic disease [6]. Likewise, the 2015 Dietary Guidelines for Americans (DGA) suggest adhering to a high-quality healthy dietary pattern for the prevention of chronic disease [7]. Prior studies have reported that time spent in objectively-assessed MVPA [8, 9] and adherence to DGA [10, 11], quantified by the 2005 DGA Adherence Index (DGAI), are individually associated with lower odds of MetS in middle-aged adults. The independent associations of PA and diet quality with cardiometabolic health are likely due to shared biological and behavioral mechanisms. However, it is unclear whether adherence to both recent PAG and DGA (as opposed to one or the other) in midlife confers the most favorable cardiometabolic health later in life.

We hypothesized that adherence to both the 2018 PAG and the 2015 DGA will be associated with lower odds of prevalent MetS cross-sectionally, and with a lower risk of developing MetS prospectively.

Methods

Study design and sample

We evaluated participants from the Framingham Heart Study (FHS) Third Generation cohort who attended the second examination cycle (2008–2011). The study design and methods of this FHS cohort have been described elsewhere [12]. For the current investigation, we examined two analytical samples: of the 3,411 participants who attended the second examination cycle, 1,032 participants were excluded for the following reasons: refusal to wear an accelerometer or invalid PA data ($n = 866$); unavailable dietary data ($n = 150$); unavailable data on components of MetS ($n = 13$); and missing covariates ($n = 3$), resulting in a sample size of 2,379 (**Sample 1**); this sample was used to evaluate the cross-sectional associations of adherence to the 2018 PAG (MVPA ≥ 150 minutes/week vs. MVPA < 150 minutes/week) and adherence to the 2015 DGA (DGAI-2015 \geq median [score 62.1/100] vs. DGAI-2015 $<$ median) with presence of MetS cross-sectionally. Next, we excluded 817 participants from **Sample 1** because they had prevalent MetS at baseline ($n = 496$) or did not have available data on components of MetS at follow-up (third examination cycle [2016–2019, $n = 321$]), resulting in a sample size of 1,562 (**Sample 2**), which was used for evaluating the longitudinal associations of adherence to the 2018 PAG and 2015 DGA (DGAI-2015 \geq median [score 63.0/100] vs. DGAI-2015 $<$ median) with the incidence of MetS. The study was approved by the Boston University Medical Center institutional review board and all participants provided written informed consent.

Objective assessment of physical activity

At the second examination cycle, participants were asked to wear an omnidirectional accelerometer (Actical model no. 198-0200-00; Philips Respironics, Murrysville, PA, USA) on the hip for eight days, 24

hours per day (except when bathing or involved in water activity). This accelerometer records signals within 0.5–3 Hz and accelerations/decelerations within 0.05–2 g. Recorded signals were grouped into ‘counts’ during 30-second intervals and stored on the device. Data were analyzed using customized software (Kinesoft, version 3.3.63, Saskatchewan, Canada) and a pre-defined protocol for quality control. Measures from the first day of wear were excluded from the analysis. Accelerometer data were considered valid if the device was worn for ≥ 10 hours per day for at least 4 out of 7 days. Non-wear time was defined as 60 consecutive minutes of zero counts, allowing for 2-minute interruption periods. Non-wear bouts were removed during data processing. Each minute of wear time was classified using previously established cut-points [13–15]. For the current investigation, MVPA was defined as ≥ 743 counts per 30-second epoch. We defined adherence to the 2018 PAG as MVPA ≥ 150 minutes/week in accordance with the 2018 PAG Advisory Committee Scientific Report [6]. For participants with < 7 days, but ≥ 4 days of valid wear time, we averaged the measured time spent in MVPA over the valid days and extrapolated it to estimate MVPA over 7 days.

Dietary assessment

Dietary intake was measured using data from the Harvard semi-quantitative food frequency questionnaire (FFQ) administered at the second examination cycle. The Harvard FFQ measures the typical frequency and consumption of 150 food items over the past year [16]. The validity of the Harvard FFQ was previously assessed using seven-day dietary records [16–17]. We only used FFQs that were considered valid (< 13 blank items and estimated daily caloric intake ≥ 600 kcal/d and $< 4,000/4,200$ kcal/d for women/men) [18].

2015 Dietary Guidelines Adherence Index (DGAI-2015)

The DGAI-2015 is designed to measure adherence to the 2015 DGA [7]. Details of the DGAI-2015 have previously been described [19]. The DGAI is composed of two sub-scores: food intake and healthy choice. The food intake sub-score measures intake of 14 food groups (fruit; dark green vegetables; orange and red vegetables; starchy vegetables; other vegetables; grains; dairy; meat, proteins, and eggs; seafood; nuts, seeds, and soy; legumes; empty calories, variety in protein choices; and variety of fruits and vegetables). The healthy choice sub-score measures adherence to 10 consumption recommendations regarding intake levels of food groups and nutrients (amounts of total fat, saturated fat, trans fat, sodium, fiber, alcohol; percentage of protein that is lean, dairy that is low-fat, grains that are whole grain, and fruits that are whole fruits). Adherence to dietary recommendations for each sub-score component is scored as a proportion on a continuous scale of 0–1 (food intake maximum = 14 and healthy choice maximum = 10). The final DGAI-2015 score consists of summed component scores that are standardized to a range of 0–100; $\left(\frac{\text{total food intake score} + \text{total healthy choice score}}{24} \right) \times 100 = \text{final DGAI-2015 score}$. The maximum DGAI-2015 score is 100, with a higher score indicating higher diet quality. For the present investigation, we dichotomized DGAI-2015 based on the median and used both binary (DGAI-2015 \geq median vs. DGAI-2015 $<$ median) and the continuous DGAI-2015 variable (ranging from 0 to 100).

Metabolic syndrome (MetS)

Participants who met at least three of the following criteria were considered as having the MetS according to the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) guidelines [4]: (1) waist circumference $\geq 40/35$ inches (men/women); (2) systolic/diastolic blood pressure $\geq 130/85$ mm Hg or use of antihypertensive medication; (3) fasting glucose ≥ 100 mg/dL or use of anti-diabetic medication; (4) serum triglycerides ≥ 150 mg/dL or use of lipid-lowering medication; and (5) HDL-C $\leq 40/50$ mg/dL (men/women).

Covariates

All covariates were collected from routine medical history, physical examination, and laboratory assessment at the second examination cycle. In the current investigation, we included the following covariates: age, sex, accelerometer wear time, number of cigarettes smoked per day, total daily calorie intake, and the prevalence of CVD. Accelerometer wear time was determined by subtracting the non-wear time from a 24-hour period. Total daily calorie intake was derived from the aforementioned 150-item FFQ. Prior history of CVD, including fatal or nonfatal myocardial infarction, unstable angina (the prolonged ischemic episode with documented reversible ST-segment changes), peripheral vascular disease (intermittent claudication), cerebrovascular disease (ischemic or hemorrhagic stroke or transient ischemic attack), or heart failure was collected by medical history questionnaire, physical examination, and hospitalization records. All events were adjudicated by a panel of FHS physicians based on previously reported criteria [20].

Statistical analysis

Age- and sex-adjusted linear regression models were used to evaluate the association between adherence to the 2018 PAG (MVPA ≥ 150 minutes/week or MVPA < 150 minutes/week, independent variable) and the continuous DGAI-2015 (dependent variable). Participants were cross-classified by using the binary DGAI-2015 \geq median vs. DGAI-2015 $<$ median and MVPA ≥ 150 minutes/week vs. MVPA < 150 minutes/week variables. We used multivariable-adjusted generalized linear models (SAS PROC GENMOD) to evaluate the individual associations of adherence to the 2018 PAG and 2015 DGA (independent variables, separate model for each) with the prevalence of MetS (dependent variable), accounting for familial relatedness. To examine the longitudinal associations of adherence to the 2018 PAG and 2015 DGA with the incident MetS. We modeled MVPA as a binary variable (MVPA ≥ 150 minutes/week vs. MVPA < 150 minutes/week [referent]) and as a continuous variable. Adherence to the 2015 DGA was also modeled as a binary variable (DGAI-2015 \geq median vs. DGAI-2015 $<$ median), and a continuous variable. We used Cox proportional hazards regression models with discrete time intervals to evaluate the individual associations of adherence to the 2018 PAG and 2015 DGA (independent variables, separate model for each) with risk of MetS, adjusting for the same covariates at baseline. We confirmed the proportional hazards assumption by including an interaction term between log-time and each exposure variable (MVPA or DGAI-2015) in the Cox regression models.

We also tested a significant multiplicative interaction between MVPA and DGAI-2015 on the association of each with the risk of MetS (both cross-sectionally and longitudinally) by incorporating cross-product

terms in the multivariable-adjusted models. Additionally, we created four cross-classification groups using adherence to 2018 PAG and 2015 DGA (independent variable, MVPA \geq 150 minutes/week vs. $<$ 150 minutes/week [2 groups] \times DGAI-2015 \geq median vs. DGAI-2015 $<$ median [2 groups]) to evaluate the cross-sectional and longitudinal associations of conjoint adherence to the 2018 PAG and the 2015 DGA with odds and risk of developing MetS. Participants who did not meet the 2018 PAG ($<$ 150 minutes/week of MVPA) and had poor adherence to the 2015 DGA (DGA-2015 $<$ median) were classified as the referent group. All models were adjusted for age, sex, accelerometer wear time, number of cigarettes smoked per day, total daily caloric intake, and prevalence of CVD. As a sensitivity analysis, we categorized DGAI-2015 into three groups based on tertile and examine the association of 2015 DGA (tertile of DGAI-2015) with odds and incidence of MetS to evaluate dose-response relation in which participants who met the 2018 PAG (MVPA \geq 150 minutes/week) had progressively lower odds or risk of MetS with increasing adherence to the 2015 DGA.

A two-sided value of $P < 0.05$ was considered statistically significant for all models while the value of $P < 0.10$ was used to determine statistically significant multiplicative interaction. All analyses were performed using SAS software version 9.4 (SAS Institute Inc, Cary, NC).

Results

Participant characteristics

The baseline characteristics by sex are presented in Table 1. The average time spent in MVPA was 27.4 ± 20.7 minutes/day and 52.7% of participants met the criteria of the 2018 PAG (MVPA \geq 150 minutes/week). The average scores of the DGAI-2015 were 61.1 (52.1 [DGA-2015 $<$ median, poor adherence], and 70.0 [DGA-2015 \geq median, higher adherence]). Only 28% of participants were characterized as both meeting the 2018 PAG and having higher adherence to the 2015 DGA. However, 47% of participants either met the 2018 PAG (MVPA \geq 150 minutes/week) or had higher adherence to the 2015 DGA. The characteristics of participants excluded from the analysis are presented in **Supplementary Table 1**. Adherence to the 2018 PAG was associated with higher adherence to the 2015 DGA (DGA-2015 \geq median; odds ratio 0.61, 95% CI, 0.51–0.72; $p < .001$). For the cross-sectional analysis, 66% of participants provided 7 days of valid accelerometry data (23% [6 days of valid accelerometry data], 8% [5 days of valid accelerometry data], and 3% [4 days of valid accelerometry data]). Similarly, 66%, 22%, 8%, and 2% of participants provided 7, 6, 5, and 4 days of valid accelerometry data, respectively, at baseline for the longitudinal analysis.

Table 1. Sample Characteristics.

	Men (n=1,086)	Women (n=1,293)
Age (years)	47±8	47±9
Body mass index (kg/m ²)	28.9±4.7	26.8±6.0
Waist circumference (inches)	40.2±4.8	36.1±5.9
SBP (mm Hg)	121±13	113±14
DBP (mm Hg)	78±8	72±9
Antihypertensive medication, n (%)	222 (20.5)	173 (13.4)
Hypertension, n (%)	303 (28.0)	222 (17.2)
Fasting blood glucose (mg/dL)	100.3±19.7	92.4±13.7
Diabetes, n (%)	63 (5.8)	43 (3.3)
Total cholesterol (mg/dL)	187±35	187±35
Triglycerides (mg/dL)	129±83	95±59
HDL-C (mg/dL)	51±14	67±18
LDL-C (mg/dL)	110±30	101±30
Lipid-lowering medication, n (%)	247 (22.7)	130 (10.1)
Smoking, n (%)	99 (9.1)	102 (7.9)
Total caloric intake (kcal/day)	2,106±660	1,913±594
DGAI-2015 (0-100)	58.0±10.7	65.3±9.7
Accelerometer wear time (minutes/day)	934.0±102.7	911.8±88.4
Sedentary time (minutes /day)	657.8±70.1	668.9±67.1
Light intensity PA (minutes /day)	129.7±49.6	123.2±42.2
MVPA (minutes /day)	29.9±21.5	25.3±19.9
Total PA (minutes /day)	159.6±59.9	148.5±51.0
MVPA ≥150 minutes/week, n (%)	641 (59.0)	613 (47.4)
MetS, n (%)	361 (33.2)	223 (17.3)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; DGAI, dietary guidelines for Americans adherence index; MVPA, moderate to vigorous physical activity; PA, physical activity; MetS, metabolic syndrome

Note: Values are mean±SD unless otherwise indicated; Hypertension was defined by SBP/DBP ≥ 140/90 mmHg or the use of antihypertensive medications; Diabetes was defined as a fasting blood glucose ≥126 mg/dL or use of insulin or oral hypoglycemic agents.

Cross-sectional associations of adherence to the 2018 PAG and 2015 DGA with the prevalence of MetS

The individual and conjoint cross-sectional associations of adherence to the 2018 PAG and 2015 DGA with the prevalence of MetS are shown in Tables 2 and Fig. 1 (**Additional file 1**), respectively. The prevalence of MetS was 24.6% (n = 584/2,379). After adjusting for covariates, participants who met the 2018 PAG had lower odds of MetS, compared to those who did not. Likewise, participants with higher adherence to the DGA (DGAI-2015 ≥ median) had lower odds of MetS, compared to those with poor adherence (DGAI-2015 < median). Results were similar in analyses examining the MVPA and DGAI-2015 as continuous variables (Table 2). Every 10 minutes per day increase in MVPA or 10-point increase in DGAI-2015 was associated with 18% or 19% lower odds of prevalent MetS, respectively (Table 2).

Table 2. Cross-sectional associations of adherence to the 2018 PAG and 2015 DGA with the presence of MetS.

2018 PAG Adherence	#MetS/#total	OR	95% CI	P value
MVPA <150 min/week	358/1,125	Referent		
MVPA ≥150 minutes/week	226/1,254	0.49	0.40-0.60	<.001
MVPA (per 10 minutes increment)	584/2,379	0.82	0.76-0.88	<.001
2015 DGA Adherence	#MetS/#total	OR	95% CI	P value
DGAI_2015 <median	342/1186	Referent	--	
DGAI_2015 ≥median	242/1193	0.67	0.54-0.83	<.001
DGAI-2015 (per 10 point increment)	584/2,379	0.81	0.74-0.89	<.001
Conjoint association	#MetS/#Total	OR	95% CI	P value
MVPA <150 min/week & DGAI-2015 <median	210/600	Referent		
MVPA ≥150 min/week & DGAI-2015 <median	132/586	0.57	0.43-0.75	<.001
MVPA <150 min/week & DGAI-2015 ≥median	148/525	0.80	0.60-1.06	.12
MVPA ≥150 min/week & DGAI-2015 ≥median	94/668	0.35	0.26-0.47	<.001

Abbreviations: PAG, Physical Activity Guidelines; DGA, Dietary Guidelines for Americans; MetS, metabolic syndrome; OR, odds ratio; CI, confidence interval; MVPA, moderate to vigorous physical activity; DGAI, dietary guidelines for Americans adherence index.

Note: Models adjusted for age, sex, accelerometer wear time, number of cigarettes smoked per day, total calorie intake per day, and prevalence of CVD at exam 2; Accelerometer wear time was excluded in the model evaluating the association between adherence to the 2015 DGA and presence of MetS; Family relatedness was further adjusted as a random variance-covariance factor in the generalized linear models; median DGAI-2015 was 62.1/100; Both PA and diet quality were measured at the second examination cycle (2008-2011); Bold P-values indicate statistical significance.

We observed a significant multiplicative interaction between MVPA and DGAI-2015 on the association of each with odds of MetS ($P_{\text{interaction}} = 0.02$). In the conjoint analysis, we observed that participants who met the 2018 PAG (MVPA ≥ 150 minutes/week) had lower odds of MetS with higher adherence to the 2015 DGA. Participants who met the 2018 PAG and had higher adherence to the 2015 DGA were less likely to have MetS compared to the referent group (i.e., participants who did not meet the 2018 PAG and had poor adherence to the 2015 DGA; Table 2 and Fig. 1 **[Additional file 1]**).

Longitudinal associations of adherence to the 2018 PAG and 2015 DGA with the incidence of MetS

In our sample of participants who were free of MetS at baseline (**Sample 2**, $n = 1,562$), 287 (18.4%) individuals developed new-onset MetS over an average follow-up of 8 years. After adjusting for covariates, adherence to the 2018 PAG was associated with a lower risk of developing MetS. Similarly, higher adherence to the 2015 DGA (DGAI-2015 ≥ median) was associated with a lower risk of MetS compared to those with poor adherence to the 2015 DGA (DGAI-2015 < median). Additionally, every 10 minutes per day increase in MVPA and each 10-point increase in DGAI-2015 were associated with 8% and 13% lower risk of developing MetS, respectively (Table 3).

Table 3. Longitudinal associations of adherence to the 2018 PAG and 2015 DGA with the incidence of MetS.

2018 PAG Adherence	# Events/# At risk	HR	95% CI	P value
MVPA <150 min/week	141/648	Referent		
MVPA ≥150 min/week	146/914	0.66	0.50-0.88	.004
MVPA (per 10 minutes increment/day)	287/1,562	0.92	0.86-0.99	.03
2015 DGA Adherence	# Events/# At risk	HR	95% CI	P value
DGAI-2015 <median	174/781	Referent		
DGAI-2015 ≥median	113/781	0.68	0.51-0.90	.008
DGAI-2015 (per 10 point increment)	287/1,562	0.87	0.76-0.99	.03
Conjoint association	# Events/# At risk	HR	95% CI	P value
MVPA <150 min/week & DGAI-2015 <median	86/339	Referent		
MVPA ≥150 min/week & DGAI-2015 <median	88/442	0.74	0.51-1.06	.10
MVPA <150 min/week & DGAI-2015 ≥median	55/309	0.78	0.52-1.17	.22
MVPA ≥150 min/week & DGAI-2015 ≥median	58/472	0.48	0.32-0.70	<.001

Abbreviations: PAG, Physical Activity Guidelines; DGA, dietary guidelines for Americans; MetS, metabolic syndrome; HR, hazards ratio; CI, confidence interval; MVPA, moderate to vigorous physical activity; DGAI, diet guidelines for Americans adherence index;

Note: Models adjusted for age, sex, accelerometer wear time, number of cigarettes smoked per day, total calorie intake per day, and prevalence of CVD at baseline; Accelerometer wear time was excluded in the model evaluating the association between adherence to the 2015 DGA and incidence of MetS; median DGAI-2015 was 63.0/100; Both PA and diet quality were measured at the second examination cycle (2008-2011); Bold P-values indicate statistical significance.

We also observed a significant multiplicative interaction between MVPA and DGAI-2015 on the association of each with the risk of MetS ($P_{\text{interaction}} = 0.03$). In our longitudinal analysis, participants who met the 2018 PAG and had higher adherence to the 2015 DGA had a lower risk of MetS when compared to the referent group (MVPA < 150 minutes/week and DGAI-2015 < median; Table 3 and Fig. 1 [Additional file 1]).

Sensitivity Analysis

In cross-sectional analysis, participants with either second or third tertile of DGAI-2015 had lower odds of MetS, after adjusting for covariates (**Supplementary Table 2**). Additionally, among participants who met the 2018 PAG (MVPA ≥ 150 minutes/week), we observed a dose-response relation, with progressively lower odds of MetS as adherence to the 2015 DGA increased (across tertiles of the DGAI-2015). Participants who met the 2018 PAG and had optimal adherence to the 2015 DGA (third tertile of DGAI-2015) were 68% less likely to have MetS compared to participants who did not meet the 2018 PAG and had poor adherence to the 2015 DGA (first tertile of DGAI-2015; **Supplementary Table 3** and **Supplementary Fig. 1**). However, we did not observe an association between either second or third tertiles of DGAI-2015 and risk of MetS compared to the first tertile of the DGAI-2015 prospectively (**Supplementary Table 4**). Only participants who met the 2018 PAG and had optimal adherence to the 2015 DGA (third tertile of DGAI-2015) had lower risk of MetS when compared to the referent group (MVPA < 150 minutes/week and first tertile of DGAI-2015; **Supplementary Table 5** and **Supplementary Fig. 2**).

Discussion

Principal findings

The primary finding of our investigation is that adherence to both PA and dietary guidelines in middle-adulthood is inversely associated with odds of MetS cross-sectionally, and with a lower risk of developing MetS later in life prospectively. Particularly, we observed a dose-response association, in which there were lower odds or risk of MetS for those who met both the 2018 PAG and demonstrated higher (\geq median) or optimal (\geq third tertile) adherence to the 2015 DGA, which is suggestive of a potential synergistic effect of PA and diet on cardiometabolic health. Overall, our findings underscore the importance of maintaining both a regular physical activity schedule and following a healthy diet in mid-adulthood in order to lower risk of developing cardiometabolic disease in later life.

Comparison with the literature

Consistent with the current investigation, numerous cross-sectional studies have reported an inverse association between objectively-assessed MVPA and odds of MetS [8, 9, 21, 22]. Additionally, several longitudinal studies have observed an inverse association between adherence to the 2008 PAG, using self-reported MVPA, and incident MetS across different demographic groups, showing approximately 20–60% lower risk of MetS [23–25]. Furthermore, a number of studies have reported inverse associations between healthy dietary patterns and MetS. This includes studies evaluating both cross-sectional and longitudinal relations of dietary patterns such as the 2005 DGAI [10, 11], Dietary Approaches to Stop Hypertension (DASH) score [26], Mediterranean Diet Score (MDS) [27–28], and the Alternative Healthy Eating Index (AHEI) [29] with MetS. In particular, adherence to the 2005 DGA was associated with a lower odds of MetS in the Framingham Offspring Cohort, where an interaction in the relation of the 2005 DGAI with MetS by age was observed, with larger effect sizes reported in adults younger than 55 years [10]. The effect size they observed in adults younger than 55 years is consistent with ours (OR:0.57, 95% CI:0.36–0.92 [highest 2005 DGAI quintile vs. lowest DGAI quintile] in the previous report vs. OR: 0.67, 95% CI:0.54–0.83 [DGAI-2015 \geq median vs. DGAI-2015 < median] or OR:0.58, 95% CI: 0.45–0.75 [highest DGAI-2015 tertile vs. lowest DGAI-2015 tertile] in the current investigation). The present investigation adds to the existing literature by using objectively measured MVPA and the most recent guidelines for both PA and diet. These data strengthen current evidence that adherence to both guidelines in mid-adulthood may confer the lowest risk of MetS, which often precedes overt cardiovascular disease.

Evidence is limited with regards to the conjoint association of adherence to both the PAG and DGA with MetS. Prior clinical intervention studies have highlighted the adoption of both a physically active lifestyle and well-balanced diet to improve cardiometabolic health [30]. In particular, a 1-year intervention study among men with MetS demonstrated a strong reduction in the prevalence of MetS in the combined intervention group (67.4%) compared to a single PA (23.5%) or dietary intervention (35.3%) [31].

In accordance with the present investigation, prior cross-sectional studies in Asian populations have reported that the combination of a sedentary lifestyle with poor diet quality is associated with higher odds of MetS [32, 33]. Differences between our investigation and these previous reports may be due to the use of self-reported PA data, which could lead to overestimation of PA. Similar to the present investigation, other investigators have reported that non-adherence to the 2008 PAG (MVPA < 150 minutes/week) and an unhealthy diet (Healthy Eating Index-2005 < 60th percentile) was associated with a

more than doubling of the odds of MetS compared to adherence to the 2008 PAG (MVPA \geq 150 minutes/week) and a healthy diet (Healthy Eating Index \geq 60th percentile) [34]. However, a direct comparison between this study and ours is challenging due to differences in dietary assessment methods (24-hour recall vs. 150-item FFQ) and the type of accelerometer (uniaxial vs. omnidirectional).

There is a lack of evidence regarding the conjoint association of PA and diet quality with the *incidence* of MetS in a large prospective cohort study. Our results indicate that adherence to both PA and dietary guidelines in middle-adulthood may have synergistic effects on lowering the risk of cardiometabolic disease later in life. Further, we observed that 28% of participants adhered to both the 2018 PAG (MVPA \geq 150 minutes/week) and 2015 DGA (DGAI-2015 \geq median), and 47% adhered to one of the respective guidelines. Only 19% of participants adhere to both guidelines, and 67% adhered to one of the respective guidelines when 2015 DGA was categorized into three groups based on the tertile of DGAI-2015. These data suggest that adherence to both 2018 PAG and 2015 DGA may be a good approach to improve cardiometabolic health for a majority of middle-aged adults.

Previous studies have suggested improved endothelial function, insulin resistance, inflammatory profile, and adiposity measures as plausible underlying biological mechanisms mediating associations of PA and diet quality with MetS [35, 36]. However, mechanistic links concerning the conjoint effects of PA and diet quality on MetS are not fully understood. Several intervention studies have demonstrated improved lipid profiles and glycemic control with reductions in blood pressure, body weight, fat mass, visceral fat, and mid-thigh muscle fat content in participants undergoing combined healthy diet and PA interventions compared to a single PA or dietary intervention [37–38]. Moreover, from a behavioral perspective, a meta-analysis conducted by Colcombe et al reported that higher PA is associated with improved cognitive function, which leads to better self-regulatory skills and robust goal-oriented behavior [39]. Thus, higher PA may indirectly promote healthier eating habits. Indeed, adherence to the 2018 PAG was associated with higher odds of adherence to the 2015 DGA (DGAI-2015 \geq median) in our investigation. Further studies are warranted to explore the underlying biological or behavioral mechanisms that may explain the conjoint associations of PA and diet quality with occurrence of the MetS.

There are several strengths of our investigation. The FHS Third Generation cohort is a deeply phenotyped large community-based sample of middle-aged adults, which may reduce selection bias with respect to comorbidities. Furthermore, the comprehensive and detailed assessment of CVD risk factors minimizes residual confounding. We measured PA objectively using an accelerometer to reduce measurement bias. The use of the latest dietary guidelines adherence index (DGAI-2015) as a more comprehensive measure of dietary quality is another strength of our investigation. This approach penalized excessive consumption of energy-dense foods, limiting the possibility that their overconsumption could lead to higher scoring [40]. Lastly, we used a cross-sectional and prospective cohort study design rendering our findings more robust. However, there are limitations that should be recognized. The DGAI-2015 was derived using data from the Harvard semi-quantitative 150-item FFQ, which is a self-administered questionnaire. Therefore, non-differential misclassification may affect our results. Additionally, in the present investigation, we observed significant multiplicative interactions only when MVPA and DGAI-2015

were modeled as continuous variables. However, given that the purpose of the present investigation is to examine the conjoint associations of adherence to the 2018 PAG and the 2015 DGA with MetS and to provide more specific behavioral goals, we evaluated the conjoint associations using categorical variables. All participants in the current investigation were white individuals of European ancestry, limiting the generalizability of our findings to other racial groups. Further studies with a multi-ethnic sample are needed to assess for effect modification by race/ethnicity.

Conclusions

In the present investigation, conjoint adherence to the 2018 PAG and 2015 DGA was associated with the lowest odds of prevalent MetS and lowest risk of developing MetS later in life. These findings emphasize the importance of maintaining adequate PA and consuming a healthy diet in midlife on cardiometabolic health later in life.

Abbreviations

MetS, metabolic syndrome; CVD, cardiovascular disease; PAG, physical activity guidelines; MVPA, moderate to vigorous physical activity; DGA, dietary guidelines; DGAI, dietary guidelines for Americans adherence index; FHS, Framingham Heart Study; FFQ, food frequency questionnaire; HDL-C, high-density lipoprotein cholesterol

Declarations

Acknowledgments

We acknowledge the dedication of the FHS study participants without whom this research would not be possible.

Funding

The Framingham Heart Study (FHS) acknowledges the support of contracts N01-HC-25195, R01-HL131029, HHSN268201500001I, 75N92019D00031 and T32 grant 5T32HL125232 from the National Heart, Lung and Blood Institute, and grants 15GPSGC24800006 from the American Heart Association. The accelerometry study was supported by R01AG047645. Dr. Vasan is supported in part by the Evans Medical Foundation and the Jay and Louis Coffman Endowment from the Department of Medicine, Boston University School of Medicine.

Availability of data and materials

Study data and materials available from the corresponding author on request.

Author Contribution: J.L., M.E.W., and R.S.V conceived the idea for the present investigation. J.L., M.T.B., and M.E.W. drafted the manuscript. J.L., M.E.W., G.T.S., P.T.J., and V.X. contributed to the analysis of data.

N.S., G.T.S., P.T.J., R.S.V., and V.X. provided critical revision of the manuscript. V.X. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable

Ethics approval and consent to participate: Ethics approval was obtained from the Institutional Review Board at the Boston University Medical center and all participants provided informed consent.

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