Sports Medicine and Health Science 7 (2025) 393–403

Contents lists available at ScienceDirect

Sports Medicine and Health Science

journal homepage: www.keaipublishing.com/smhs

Review

Effects of amount, intensity, and mode of exercise training on the metabolic syndrome: A narrative review

Garrett A. Moseley [a], Katherine A. Collins-Bennett [b,c], William E. Kraus [b,d], Leanna M. Ross [b,d,*]

[a] Duke University School of Medicine, Durham, NC, United States
[b] Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, United States
[c] Department of Population Health Sciences, Duke University School of Medicine, Durham, NC, United States
[d] Division of Cardiology, Department of Medicine, Duke University School of Medicine, Durham, NC, United States

ARTICLE INFO

Keywords:
Overweight
Obesity
Cardiometabolic health
Aerobic training
Resistance training
Lifestyle medicine

ABSTRACT

Purpose: The purpose of this narrative review is to: 1) summarize findings from the three Studies of a Targeted Risk Reduction Intervention through Defined Exercise (STRRIDE) randomized trials regarding the differential effects of exercise amount, intensity, and mode on metabolic syndrome (MetS); and 2) compare the STRRIDE findings with other published randomized exercise trials related to changes in MetS.

Methods: A literature review was performed to investigate the effects of exercise on composite measures of MetS. PubMed was searched between October 2023 and December 2023. To be included in this review, studies must have employed a randomized study design, whereby exercise amount, intensity, or mode was varied.

Results: Findings from the STRRIDE trials and other randomized exercise trials suggest: 1) there is a relationship between exercise energy expenditure (ExEE) and improvements in composite measures of MetS; 2) there may be an asymptotic effect for ExEE beyond which further improvements in MetS are negligible or counterproductive; 3) improvements in composite measures of MetS are closely linked to insulin sensitivity; and 4) without controlling for total ExEE, combined aerobic and resistance training interventions offer the most robust improvements for composite MetS outcomes compared to either mode alone.

Conclusion: Additional, large-scale, randomized exercise trials should be designed to investigate the potential asymptotic effect and associated threshold for ExEE, the interaction between exercise intensity and baseline insulin sensitivity, and the independent effects of exercise mode on MetS.

1. Introduction

Metabolic syndrome (MetS) is characterized by a cluster of underlying, interrelated cardiometabolic disease risk factors, including abdominal adiposity, elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), elevated blood pressure, and elevated fasting glucose.[1] MetS raises an individual's morbidity and mortality risk, including the risk of developing atherosclerotic cardiovascular disease, diabetes mellitus, neurovascular disease, and certain cancers.[2–4] In the United States, over one-third of adults meet the criteria for MetS.[5] A Scientific Statement from the American Heart Association and National Heart, Lung, and Blood Institute highlights the prime emphasis in MetS management is to mitigate the modifiable, underlying risk factors (*i.e.,* obesity, physical inactivity, atherogenic diet, and smoking) through lifestyle changes to improve the components of MetS.[4] Then, if absolute risk is high enough, consideration can be given to incorporating pharmacotherapy to reduce low-density lipoprotein cholesterol, blood pressure, and glucose.[4] Moreover, recent evidence suggests the combination of newer pharmacotherapies, such as Glucagon-like peptide 1 (GLP-1) receptor agonist therapy, with lifestyle modification may yield greater improvements in MetS severity compared to pharmacotherapy alone.[6] Therefore, lifestyle modification, such as exercise training, remains critical to both MetS prevention and treatment.

Numerous previous reviews have investigated the effects of exercise training – including aerobic training (AT), resistance training (RT), and combined aerobic/resistance training (AT/RT) – on the *individual* components of MetS, as defined by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III)[4] and/or the International Diabetes Federation (IDF) guidelines.[7] In general, these

* Corresponding author. 3475 Erwin Road, Aesthetics Bldg., Rm 254, Durham, 27705, NC, United States.
E-mail address: leanna.ross@duke.edu (L.M. Ross).
Peer review under the responsibility of Editorial Board of Sports Medicine and Health Science

https://doi.org/10.1016/j.smhs.2025.03.006
Received 15 October 2024; Received in revised form 4 March 2025; Accepted 18 March 2025
Available online 19 March 2025

Abbreviations

AT	Aerobic training
ATP III	Adult Treatment Panel III
AT/RT	Combined aerobic and resistance training
95% *CI*	95% Confidence interval
ExEE	Exercise energy expenditure
GLP-1	Glucagon-like peptide 1
HAMI	High-Amount/Moderate-Intensity group
HAVI	High-Amount/Vigorous-Intensity group
HDL-C	High-density lipoprotein cholesterol
HIIT	High-intensity interval training
HOMA-IR	Homeostatic model assessment of insulin resistance
HR	Heart rate
IDF	International Diabetes Federation
KKW	Kilocalories of exercise energy expenditure/kilogram of body weight/week
LAMI	Low-Amount/Moderate-Intensity group
LAVI	Low-Amount/Vigorous-Intensity group
MetS	Metabolic syndrome
MICT	Moderate-intensity continuous training
NCEP	National Cholesterol Education Program
OR	Odds ratio
RT	Resistance training
STRRIDE	Studies of a Targeted Risk Reduction Intervention through Defined Exercise
$\dot{V}O_2$	Oxygen consumption rate

reviews found variations in exercise amount, intensity, and mode lead to differential effects on the individual components of MetS.[8–18] However, to our knowledge, no prior review has explored these moderating effects of exercise amount, intensity, and mode on *composite* measures of MetS. Given the additive nature of risk factors in MetS, such an investigation is necessary.[19] Composite measures of MetS include overall MetS prevalence, the number of individual MetS criteria met (often referred to as a "MetS sum score"), and a continuous MetS *z*-score.[20]

The three Studies of a Targeted Risk Reduction Intervention through Defined Exercise (STRRIDE) randomized trials investigated the effects of various exercise amounts, modes, and intensities on markers of cardiometabolic risk – including the aforementioned composite measures of MetS – in participants with overweight or obesity and dyslipidemia (STRRIDE I and STRRIDE AT/RT) or prediabetes (STRRIDE-PD).[21–23] The purpose of this narrative review is to: 1) summarize findings from the STRRIDE randomized trials regarding the differential effects of exercise amount, intensity, and mode on MetS composite measures; and 2) compare the STRRIDE findings with other published randomized exercise trials which investigated dose- and mode-specific changes in MetS composite measures.

2. Materials and methods

2.1. The STRRIDE randomized exercise trials

A detailed description of the three STRRIDE randomized trials has been provided elsewhere.[24–26] Of the 948 participants originally recruited and enrolled across the three STRRIDE trials, a total of 387 participants who completed the three trials and had pre- and post-intervention data available for all five MetS criteria were included in this narrative review. Participants were randomized to either a control group or one of ten intervention groups.

2.1.1. STRRIDE I (8-month intervention duration; Tables 1 and 2)

(1) Low-Amount/Moderate-Intensity (LAMI): Exercise energy expenditure (ExEE) of 14 kilocalories (kcal)/kg of body weight/week (KKW) at an intensity of 40%–55% peak oxygen consumption ($\dot{V}O_2$)
(2) Low-Amount/Vigorous-Intensity (LAVI): ExEE of 14 KKW at an intensity of 65%–80% peak $\dot{V}O_2$
(3) High-Amount/Vigorous-Intensity (HAVI): ExEE of 23 KKW at an intensity of 65%–80% peak $\dot{V}O_2$

2.1.2. STRRIDE AT/RT (8-month intervention duration; Tables 1 and 3)

(4) Aerobic training only (AT): ExEE of 14 KKW at an intensity of 65%–80% peak $\dot{V}O_2$
(5) Resistance training only (RT): 3 sets/day, 8–12 repetitions/set, for 8 exercises total per session for 3 days/week. RT included four upper-body and four lower-body exercises designed to target all major muscle groups
(6) Combined aerobic and resistance training (AT/RT): AT ExEE of 14 KKW at an intensity of 65%–80% peak $\dot{V}O_2$ plus 3 sets/day, 8–12 repetitions/set, for 8 exercises total per session for 3 days/week. RT included four upper-body and four lower-body exercises designed to target all major muscle groups

2.1.3. STRRIDE-PD (6-month intervention duration; Tables 1 and 4)

(7) LAMI: ExEE of 10 KKW at an intensity of 40%–55% $\dot{V}O_2$ reserve
(8) High-Amount/Moderate-Intensity group (HAMI): ExEE of 16 KKW at an intensity of 40%–55% $\dot{V}O_2$ reserve
(9) HAVI: ExEE of 16 KKW at an intensity of 65%–80% $\dot{V}O_2$ reserve
(10) Clinical lifestyle: ExEE of 10 KKW at an intensity of 40%–55% $\dot{V}O_2$ reserve combined with a dietary intervention designed to achieve 7% body weight reduction

2.1.4. Metabolic syndrome measures

In STRRIDE I and STRRIDE-PD, waist circumference was measured horizontally at the minimal waist, the narrowest portion of the torso between the xiphoid process and the umbilicus. In STRRIDE-AT/RT, waist circumference was measured around the abdomen at the level of the iliac crest. For all three STRRIDE studies, two blood pressure readings were taken at rest and averaged. For STRRIDE I and STRRIDE-AT/RT, HDL-C and triglyceride concentrations were determined from fasting plasma samples using 400 MHz nuclear magnetic resonance spectroscopy profilers at LipoScience, now Labcorp (Morrisville, NC, USA), as previously described.[27,28] Glucose levels for STRRIDE I and AT/RT were determined from fasting plasma samples at the beginning of an intravenous glucose tolerance test using an oxidation reaction (YSI 2300, Yellow Springs, OH, USA). In STRRIDE-PD, plasma glucose, HDL-C, and triglyceride concentrations were measured using a Beckman Coulter DxC600 clinical analyzer (Brea, CA, USA).

For all three STRRIDE trials, a modified MetS *z*-score and MetS sum score using the ATPIII criteria were calculated pre- and post-intervention. The equations used to calculate the modified MetS *z*-scores using baseline standard deviations (*SD*) for each criterion among all participants in the STRRIDE trials were as follows: Women's modified MetS *z*-score = [(50 − HDL)/*SD*] + [(TG − 150)/*SD*] + [(fasting blood glucose − 100)/*SD*] + [(waist circumference − 88)/*SD*] + [(mean arterial pressure − 100/*SD*]; and Men's modified MetS *z*-score = [(40 − HDL)/*SD*] + [(TG − 150)/*SD*] + [(fasting blood glucose − 100)/*SD*] + [(waist circumference − 102)/*SD*] + [(mean arterial pressure − 100)/*SD*]. As opposed to a true *z*-score, the modified MetS *z*-score does not follow a normal distribution with mean zero and *SD* of one. Thus, to compare modified *z*-scores to traditional *z*-scores, the modified score would need to be divided by the number of components (which is the same as dividing by 5 in this case). A negative score indicates a lesser risk. The MetS sum score was calculated for each participant as the sum of individual MetS criteria met. Overall MetS prevalence was determined by the number of individuals meeting three or more of the five MetS criteria. To note, given the purpose of this review is to summarize the effects of exercise alone on composite measures of MetS, the clinical lifestyle intervention group in STRRIDE-PD was not included in the discussion.

2.2. Literature search procedures

A review of the literature was performed to investigate the effects of exercise on composite measures of MetS. PubMed was searched between October 2023 and December 2023. A variety of MeSH and text terms were employed using the PICO framework, including terms such as metabolic syndrome, exercise, aerobic, endurance, strength, resistance, high-intensity interval training, energy expenditure, volume, and dose-response. To be included in this review, studies had to employ a randomized study design, whereby exercise amount, intensity, or mode was varied. Additionally, to accurately control for exercise amount, only randomized exercise trials that provided explicit energy expenditure prescriptions, estimations, or calculations – typically noted in units of kcal, kilo- or megajoules (kJ/MJ), or metabolic equivalent-hours or metabolic equivalent-minutes (MET-hrs/MET-min) per week – were included. Finally, studies had to include an aerobic component in at least one arm. Studies with coexisting dietary components were included if the diet was equivalent among all groups (including control) or if more than two exercise arms did not have a dietary component. Studies with concurrent pharmacologic interventions were excluded. Of note, one dose-response randomized exercise trial that quantified ExEE was excluded due to mathematical inconsistencies in the MetS *z*-score calculation and subsequent analysis and interpretation.

3. Results

3.1. Aerobic exercise amount and intensity effects

3.1.1. STRRIDE findings

In STRRIDE I, the LAMI ([−0.8 ± 1.6], $p < 0.01$) and HAVI ([−1.4 ± 1.7], $p < 0.001$) groups significantly improved their modified MetS *z*-scores from baseline to post-intervention (Table 2). There was a significant difference between the HAVI (−1.4 ± 1.7) and LAVI (−0.3 ± 1.4) groups at post-intervention for modified MetS *z*-scores ($p = 0.001$). Similarly, the LAMI (−0.5 ± 1.1) and HAVI (−0.5 ± 1.1) groups significantly improved their MetS sum score from baseline ($p < 0.01$ for each) and compared to controls ($p < 0.006$ for each). All exercise groups decreased their prevalence of MetS (LAMI: 18 to 10; LAVI: 17 to 15; and HAVI: 18 to 10 individuals).

In STRRIDE-PD, the LAMI ([−0.9 ± 1.8], $p < 0.01$) and HAVI ([−1.0 ± 1.9], $p < 0.01$) groups significantly improved their modified MetS *z*-scores from baseline to post-intervention (Table 4). However, only the LAMI group significantly changed their MetS sum score from baseline to post-intervention ([−0.3 ± 0.8], $p < 0.05$). Both the LAMI (27–24) and HAMI (21–19) groups decreased their prevalence of MetS, while HAVI increased their prevalence of MetS (16–17).

Table 1
Overview of exercise prescriptions in the STRRIDE randomized trials.

Intervention group	*n*	[a]ExEE	Intensity
[b]**STRRIDE I**			
Control	41	–	–
[c]LAMI	41	14 [d]KKW	40%–55% peak $\dot{V}O_2$
[e]LAVI	45	14 KKW	65%–80% peak $\dot{V}O_2$
[f]HAVI	44	23 KKW	65%–80% peak $\dot{V}O_2$
STRRIDE AT/RT			
[g]AT (LAVI)	30	14 KKW	65%–80% peak $\dot{V}O_2$
[h]RT	31	3 days/week, 3 sets/day, 8-12 reps, 8 exercises	Progressive
AT/RT	25	14 KKW + 3 days/week, 3 sets/day, 8-12 reps, 8 exercises	65%–80% peak $\dot{V}O_2$
STRRIDE-PD			
LAMI	35	10 KKW	40%–55% $\dot{V}O_2$ reserve
[i]HAMI	31	16 KKW	40%–55% $\dot{V}O_2$ reserve
HAVI	32	16 KKW	65%–80% $\dot{V}O_2$ reserve
Clinical lifestyle intervention	32	10 KKW + Diet	40%–55% $\dot{V}O_2$ reserve

Abbreviations.
[a] ExEE = exercise energy expenditure.
[b] STRRIDE = Studies of a Targeted Risk Reduction Intervention through Defined Exercise.
[c] LAMI = Low-Amount/Moderate-Intensity.
[d] KKW = kcal exercise energy expenditure/kilogram of body weight/week.
[e] LAVI = Low-Amount/Moderate-Intensity.
[f] HAVI = High-Amount/Vigorous Intensity.
[g] AT = Aerobic training.
[h] RT = Resistance training.
[i] HAMI = High-Amount/Moderate-Intensity.

3.1.2. Previous published findings

Few randomized exercise trials have investigated the relationship between aerobic exercise amount (quantified by ExEE) and/or intensity on composite measures of MetS. Here we discuss the major findings related to composite MetS measures from ten randomized exercise trials and relate these findings to the STRRIDE trials (Tables 5–7).

In general, a greater ExEE is associated with greater improvements in composite MetS measures.[21,29–32] Fogelholm et al. studied the effects of exercise on weight maintenance by examining two *absolute* aerobic exercise amounts (*i.e.*, not relative to body weight) matched for intensity after an initial diet-induced weight loss phase.[29] Following the 12-week body weight reduction phase, premenopausal women with obesity ($n = 65$ with complete data across timepoints) were randomized to one of three weight maintenance groups for 40 weeks: 1) Control (diet-counseling only); 2) Walk-1 – 4.2 MJ per week at 50%–60% heart rate reserve (HRR) for 2–3 h per week; or 3) Walk-2 – 8.4 MJ per week at 50%–60% heart rate reserve (HRR) for 4–6 h per week. All groups followed a low-fat diet during the weight maintenance phase. Before weight reduction, 27 of the 65 participants had MetS. After weight reduction (*i.e.,* start of the weight maintenance phase), only 11 participants had MetS. During the weight maintenance phase, all groups either decreased or remained stagnant in MetS prevalence (Control: 4 to 3; Walk-1: 3 to 3; Walk-2: 4-1).

The DREW study examined two *relative* aerobic exercise amounts (*i.e.*, relative to body weight) matched for intensity, focusing on MetS prevalence and severity among postmenopausal women with overweight or obesity.[30] Participants ($n = 408$) were randomized to either a control group or one of three aerobic exercise groups for six months: 1) 4 KKW at 50% peak $\dot{V}O_2$; 2) 8 KKW at 50% peak $\dot{V}O_2$; or 3) 12 KKW at 50% peak $\dot{V}O_2$. A significant dose-response relationship was found between ExEE and improvements in the MetS *z*-score ($p = 0.02$ for trend; Control: [3.30 ± 1.0] to [3.24 ± 0.9]; 4 KKW: [3.19 ± 0.9] to [3.10 ± 0.9]; 8 KKW:

Table 2
Baseline and change scores for MetS composite characteristics from STRRIDE I by group.

	Control ($n = 41$)			[a]LAMI ($n = 41$)			[b]LAVI ($n = 45$)			[c]HAVI ($n = 44$)		
	Baseline	Change	p	Baseline	Change	p	Baseline	Change	p	Baseline	Change	p
[d]Modified MetS z-score	−0.7 (2.1)	0.0 (1.5)	[e]NS	−0.5 (2.4)	−0.8 (1.6)	**	−1.0 (2.5)	−0.3 (1.4)	NS	−0.9 (3.0)	−1.4 (1.7)	***
[f]ATPIII Score	2.1 (1.1)	0.1 (0.9)	NS	2.4 (1.0)	−0.5 (1.1)	**	2.2 (1.3)	−0.2 (1.1)	NS	2.2 (1.4)	−0.5 (1.1)	**
Prevalence	16	3	–	18	−8	–	17	−2	–	18	−8	–

Abbreviations.
[e]NS = not significant; [f]ATPIII Score = sum of Adult Treatment Panel III metabolic syndrome criteria; Data presented as means (standard deviation) or, for prevalence, the number of participants meeting three or more of the five MetS criteria; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
[a] LAMI = Low-Amount/Moderate-Intensity.
[b] LAVI = Low-Amount/Moderate-Intensity.
[c] HAVI = High-Amount/Vigorous Intensity.
[d] MetS = metabolic syndrome.

Table 3
Baseline and change scores for MetS composite characteristics from STRRIDE AT/RT by group.

	[a]AT ($n = 30$)			[b]RT ($n = 31$)			AT/RT ($n = 25$)		
	Baseline	Change	p	Baseline	Change	p	Baseline	Change	p
[c]Modified MetS z-score	0.45 (3.59)	−0.76 (2.20)	[d]NS	−0.22 (3.47)	0.13 (1.76)	NS	−1.07 (3.06)	−1.10 (1.70)	**
[e]ATPIII Score	2.63 (1.10)	−0.03 (1.19)	NS	2.19 (1.28)	0.36 (0.99)	*	2.28 (0.98)	−0.64 (1.04)	**
Prevalence	14	0	–	12	7	–	11	−7	–

Abbreviations.
[d]NS = not significant; [e]ATPIII Score = sum of Adult Treatment Panel III metabolic syndrome criteria; Data presented as means (standard deviation) or, for prevalence, the number of participants meeting three or more of the five MetS criteria; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
[a] AT = aerobic training.
[b] RT = resistance training.
[c] MetS = metabolic syndrome.

Table 4
Baseline and change scores for MetS composite outcomes from STRRIDE-PD by group.

	[a]LAMI ($n = 35$)			[b]HAMI ($n = 31$)			[c]HAVI ($n = 32$)			Clinical Lifestyle ($n = 32$)		
	Baseline	Change	p	Baseline	Change	p	Baseline	Change	p	Baseline	Change	p
[d]Modified MetS z-score	1.4 (2.6)	−0.9 (1.8)	***	1.0 (2.1)	−0.6 (1.7)	*	0.5 (3.6)	−1.0 (1.9)	***	0.5 (2.5)	−2.4 (2.0)	***
[e]ATPIII Score	3.3 (0.9)	−0.3 (0.8)	**	3.0 (0.9)	−0.2 (1.0)	[f]NS	2.7 (1.3)	−0.2 (1.1)	NS	2.8 (1.1)	−0.6 (0.9)	***
Prevalence	27	−3	–	21	−2	–	16	1	–	19	−7	–

Abbreviations.
[e]ATPIII Score = sum of Adult Treatment Panel III metabolic syndrome criteria; fNS = not significant; Data presented as means (standard deviation) or, for prevalence, the number of participants meeting three or more of the five MetS criteria; *$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.
[a] LAMI = Low-Amount/Moderate-Intensity.
[b] HAMI = High-Amount/Moderate-Intensity.
[c] HAVI = High-Amount/Vigorous Intensity.
[d] MetS = metabolic syndrome.

[3.15 ± 0.9] to [2.94 ± 0.9]; 12 KKW: [3.16 ± 0.9] to [2.87 ± 1.0]). A post hoc analysis showed a significant difference between the 12 KKW group and the Control group in MetS z-score changes ($p < 0.05$). Both the 8 and 12 KKW groups experienced significantly decreased MetS prevalence (−9% and −19%, respectively; $p < 0.02$ for trend), with both groups being significantly different compared to the control group ($p < 0.05$).

Ades et al. investigated the effects of two cardiac rehabilitation programs with varying exercise amounts and intensities on cardiometabolic risk.[31] Adults with coronary heart disease, body mass index > 27 $kg \cdot m^{-2}$, and abdominal obesity ($n = 74$) were randomized to one of two five-month rehabilitation programs: 1) Standard Cardiac Rehabilitation – 700–800 kcal per week at 65%–70% peak $\dot{V}O_2$ for 25–40 min per session for three sessions per week combined with a hypocaloric diet; or 2) High-Calorie Cardiac Rehabilitation – 3 000–3 500 kcal per week at 50%–60% peak $\dot{V}O_2$ for 45–60 min per session for 5–7 sessions per week combined with a hypocaloric diet. Among all participants, the prevalence of MetS was reduced from 59% to 31%, with the average MetS sum score decreasing from (2.76 ± 1.02) to (1.96 ± 1.05) ($p < 0.001$). The High-Calorie group showed a significantly greater reduction in the MetS sum score ([3.1 ± 1.2] to [1.9 ± 1.1]) compared to the Standard Group ([2.4 ± 0.7] to [2.0 ± 1.0]) ($p = 0.01$).

Morales-Palomo et al. assessed the effects of three different exercise training programs – different by session duration, peak intensity, and type (interval versus continuous) – on MetS in 121 sedentary, middle-aged adults with MetS.[32] Participants were randomized to one of four groups for 16 weeks: 1) High-Amount/High-Intensity Interval Training (HIIT) – ~440 kcal per session with 4 by 4 min at 90% maximum heart rate (HR_{max}) with 3 min recovery at 70% HR_{max} for 43 min per session; 2) Low-Amount/HIIT – ~290 kcal per session with 10 by 1 min at 100% HR_{max} with 1.5 min recovery at 65% HR_{max} for 35 min per session; 3) High-Amount/Moderate-Intensity Continuous Training (MICT) – ~440 kcal per session at 70% HR_{max} for 50 min per session; or 4) Inactive Control. Participants in the High-Amount/HIIT (−41%, $p < 0.01$) and High-Amount/MICT (−52%, $p < 0.01$) groups significantly decreased their MetS z-scores, whereas changes were not significant in the Low-Amount/HIIT (−24%, $p = 0.21$) or Control groups (20%, $p = 0.22$). As the two high-amount groups were matched for ExEE, these findings

Table 5
Summary of randomized exercise trials evaluating the impact of aerobic exercise amount, controlling for intensity, on MetS composite outcomes.

Study	*n*	Population	Training type/intervention length	Groups ([a]ExEE; Intensity)	Measure(s)	Results
Fogelholm et al.[29]	82	Premenopausal women [b]BMI: 30–45 kg·m^{-2} Physically inactive Healthy 30–45 years	12-week weight reduction phase followed by 40-week weight maintenance phase via aerobic exercise (walking)	*Walk-1 + Diet:* 4.2 [c]MJ/week at 50%–60% [d]HRR; ~2–3 h/week *Walk-2 + Diet:* 8.4 MJ/wk at 50%–60% HRR; ~4–6 h/week *Control (diet only)*	[e]MetS Prevalence	*MetS Prevalence* All groups decreased or remained the same Changes in Walk-2 significantly differed from Control
Earnest et al.[30]	408	Postmenopausal women BMI: 23.2–40.9 kg·m^{-2} Systolic blood pressure: 120–160 mmHg Sedentary 45–75 years	6-month aerobic intervention (ergometers and treadmills); 3–4 sessions/week	*Low Amount:* 4 [f]KKW at 50% peak $\dot{V}O_2$ *Moderate Amount:* 8 KKW at 50% peak $\dot{V}O_2$ *High Amount:* 12 KKW at 50% peak $\dot{V}O_2$ *Non-Exercise Control*	MetS *z*-score MetS Prevalence	*MetS z-score* Significant dose-response relationship Significant difference in change between 12 KKW and Control *MetS Prevalence* Significant decrease in 8 and 12 KKW groups Changes in both groups significantly differed from Control
Reichklender et al.[39]	61	Caucasian men BMI: 25–30 kg·m^{-2} with fat % ≥ 25% Sedentary Healthy 20–40 years	11-week aerobic intervention (running, bicycling, elliptical training, or rowing); 6–7 days/week	*Moderate Amount/Moderate-Vigorous Intensity:* 300 kcal/session at > 70% $\dot{V}O_{2max}$ for 3 days/week and 50%–70% $\dot{V}O_{2max}$ all other days; ~180 min/week *High Amount/Moderate-Vigorous Intensity:* 600 kcal/session at > 70% $\dot{V}O_{2max}$ for 3 days/week and 50%–70% $\dot{V}O_{2max}$ all other days; unknown session duration (> 180 min/week) *Sedentary Control*	MetS sum score MetS Prevalence	*MetS Sum Score* Significant decrease in both exercise groups *MetS Prevalence* Significant decrease in both exercise groups Significant difference in change between both exercise groups and Control

Abbreviations.
[a] ExEE = exercise energy expenditure.
[b] BMI = body mass index.
[c] MJ = megajoules.
[d] HRR = heart rate reserve.
[e] MetS = metabolic syndrome.
[f] KKW = kcal exercise energy expenditure/kilogram of body weight/week.

suggest greater aerobic ExEE is the main factor driving beneficial MetS changes, as compared to type (interval versus continuous) and peak intensity (70% HR_{max} versus 100% HR_{max}) of the training program.

Similar improvements in composite MetS measures have been observed in other trials with equivalent ExEEs.[32–36] In the RUSH trial, untrained participants ($n = 81$) were randomized to either: 1) HIIT – ~1 800 kcal per week at 95%–110% individual aerobic threshold-HR with 1-3-min recovery periods at 70%–75% individual aerobic threshold-HR plus additional continuous sessions at the individual aerobic threshold [~85% HR_{max}] for ~53 min per session; or 2) Sedentary Control that transitioned to Moderate Intensity Continuous Exercise (MICE) – ~1 900 kcal per week at 70%–82.5% individual aerobic threshold-heart rate for ~57 min per session.[33] Each exercise program lasted 16 weeks with 3–4 sessions per week. Both exercise groups improved their modified MetS *z*-scores (HIIT: [−2.06 ± 1.31], $p \leq 0.001$ and MICE: [−1.60 ± 1.77], $p < 0.001$) with no significant differences between groups ($p = 0.291$). Both groups decreased their MetS sum scores (HIIT: [−0.55 ± 0.62], $p < 0.001$ and MICE: [−0.70 ± 0.59], $p < 0.001$), with no significant difference between exercise groups ($p = 0.336$). Last, exercise-induced changes in both parameters significantly differed from the Control group ($p = 0.001$ for both).

Weatherwax et al. investigated the effects of prescribing aerobic exercise intensity – based on HRR percentage or ventilatory threshold – on composite MetS outcomes while progressively increasing exercise intensity and amount relative to body weight among previously sedentary adults.[34] Participants ($n = 38$) were randomized to: 1) Standardized Intensity – based on percent HRR with increasing intensity and amount across the intervention ranging from 40% to 65% HRR at 5.6–15.4 KKW for ~168 min per week; 2) Individualized Intensity – based on ventilatory threshold with increasing intensity and amount across the intervention ranging from HR < ventilatory threshold-one to HR ≥ ventilatory threshold-two at 5.6–15.4 KKW for ~131 min per week; or 3) Control for 12 weeks. Both exercise groups significantly improved their modified MetS *z*-scores (Standardized Intensity: [−2.0 ± 3.1] to [−2.8 ± 2.8], $p = 0.01$ and Individualized Intensity: [−3.3 ± 2.3] to [−3.9 ± 2.2], $p = 0.04$), with no significant differences between exercise groups or compared to Control.[34,37]

Most recently, Heiston et al. assessed the impact of two weeks of interval versus continuous aerobic training on MetS severity among physically inactive adults with prediabetes and overweight or obesity.[36] Participants ($n = 28$) were randomized into two groups: 1) Continuous Exercise – (321 ± 76.2) kcal per session at 70% peak HR (HR_{peak}) for 60 min per session; or 2) Interval Exercise – (357 ± 69.7) kcal per session with alternating 3 min intervals at 90% HR_{peak} followed by 50% HR_{peak} for 60 min per session. Prior to training, 13 of the 28 participants were classified as having MetS. The Continuous and Interval groups reduced MetS prevalence by 21% and 14%, respectively. Both groups significantly improved their modified MetS *z*-scores (Continuous: [−0.76 ± 1.85] to [−1.08 ± 2.40] and Interval: [0.33 ± 3.03] to [−0.40 ± 3.2]; time effect: $p = 0.04$), with no significant differences between groups ($p = 0.40$). There were no significant changes over time in MetS sum scores for either group (time effect: $p = 0.14$).

3.1.3. Evidence for an asymptotic effect for ExEE

Although weekly ExEE appears to be a primary driver for improving composite MetS outcomes in many studies, this pattern is not universal.[21,23,38,39] Project FINE examined the effects of two different exercise amounts, while keeping intensity constant, on measures of insulin sensitivity, metabolic risk, and quality of life.[39] Sedentary, Caucasian men with overweight aged 20–40 years ($n = 61$) were randomized to an Inactive Control group or one of two exercise groups for 11 weeks: 1) Moderate-Amount/Moderate-Vigorous Intensity – 300 kcal per session

Table 6
Summary of randomized exercise trials evaluating the impact of aerobic exercise intensity, controlling for amount, on MetS composite outcomes.

Study	*n*	Population	Training type/intervention length	Groups ([a]ExEE; Intensity)	Measure(s)	Results
Earnest et al.[35]	42	Men [b]BMI: 25–36 $kg\cdot m^{-2}$ Sedentary Waist circumference ≥ 38” Waist-to-hip ratio > 0.95 30–60 years	3-month aerobic intervention (treadmill); 3–4 sessions/week	[c]*HIIT*:12 [d]KKW with intervals at 90%–95% $\dot{V}O_{2max}$ with 2 min recovery periods at 50% $\dot{V}O_{2max}$ [e]*MICT*: 12 KKW at 50%–70% $\dot{V}O_{2max}$	[f]MetS *z*-score MetS sum score)	*MetS z-score* Significant decrease in both groups *MetS sum score* Significant decrease in both groups
Kemmler et al.[33]	81	Men BMI: < 35 $kg\cdot m^{-2}$ Untrained 30–50 years	16-week aerobic intervention (running); 3–4 sessions/week	*HIIT:* ~1 800 kcal/week with intervals at 95%–110% individual aerobic threshold-[g]HR with 1–3 min recovery periods at 70%–75% individual aerobic threshold-HR and additional continuous sessions at the individual aerobic threshold (~85% HR_{max}); ~53 min/session *Sedentary Control → Moderate-Intensity Continuous Exercise:* initial sedentary control group with crossover into moderate-intensity continuous exercise group. ~1 900 kcal/week at 70%–82.5% individual aerobic threshold-HR; ~57 min/session	Modified MetS *z*-score MetS sum score	*Modified MetS z-score* Significant decrease in both exercise groups Changes in both groups significantly differed from Control *MetS sum score* Significant decrease in both exercise groups Changes in both groups significantly differed from Control
Weatherwax et al.[34,37]	38	Men and women Sedentary 30–75 years	12-week intervention (primarily aerobic, with resistance portion in last 4 weeks); 3 days/week	*Standardized Intensity:* determined based on %[h]HRR ranging from 40% to 65% HRR at 5.6–15.4 KKW for ~168 min/week *Individualized Intensity:* determined based on ventilatory ranging from HR < [i]VT1 to HR ≥ VT2 at 5.6–15.4 KKW for ~131 min/week *Control*	Modified MetS *z*-score MetS Prevalence	*Modified MetS z-score* Significant decrease in both exercise groups *MetS Prevalence* Decrease in both exercise groups
Heiston et al.[36]	28	Men and women BMI: 25–45 $kg\cdot m^{-2}$ Sedentary Prediabetes	2-week aerobic intervention (cycle ergometry); 6 sessions/week	*Continuous Exercise*: (321 ± 76.2) kcal/session at 70% HR_{peak}; 60 min/session *Interval Exercise:* (357 ± 69.7) kcal/session at alternating 3 min intervals at 90% HR_{peak} followed by 50% HR_{peak}; 60 min/session	Modified MetS *z*-score MetS sum score MetS prevalence	*Modified MetS z-score* Significant decrease in both groups *MetS sum score* No significant changes *MetS prevalence* Significant decrease in both groups

Abbreviations.
[a] ExEE = exercise energy expenditure.
[b] BMI = body mass index.
[c] HIIT = high-intensity interval training.
[d] KKW = kcal exercise energy expenditure/kilogram of body weight/week.
[e] MICT = moderate-intensity continuous training.
[f] MetS = metabolic syndrome.
[g] HR = heart rate.
[h] HRR = heart rate reserve.
[i] VT = ventilatory threshold.

at > 70% $\dot{V}O_{2max}$ for three days per week and 50%–70% $\dot{V}O_{2max}$ all other days; or 2) High-Amount/Moderate-Vigorous Intensity – 600 kcal per session at > 70% $\dot{V}O_{2max}$ for three days per week and 50%–70% $\dot{V}O_{2max}$ all other days. Both exercise groups experienced significant decreases in the MetS sum score (High-Amount: [2.2 ± 0.3] to [1.5 ± 0.3], $p < 0.05$ and Moderate-Amount: [1.8 ± 0.3] to [1.1 ± 0.2], $p < 0.05$), with changes not being significantly different from the Control group ($p = 0.08$). Both exercise groups significantly decreased overall MetS prevalence (High-Amount: 9 to 2, $p < 0.01$ and Moderate-Amount: 5 to 1, $p < 0.05$), and these changes were significantly different compared to the Control group ($p < 0.05$ for both). Thus, compared to exercise for ~2 000 kcal per week (Moderate-Amount group), exercising for ~3 800 kcal per week (High-Amount group) did not yield significantly greater changes in composite MetS outcomes. These findings suggest an asymptotic effect for ExEE, beyond which further improvements in MetS may be minimal or negligible.[39]

While a high amount of vigorous-intensity exercise (HAVI: ~2 000 kcal per week) led to the greatest improvements in composite MetS outcomes in STRRIDE I, a low amount of moderate-intensity exercise (LAMI: ~1 200 kcal per week) provided benefits similar to HAVI, whereas the low amount of vigorous-intensity (LAVI: ~1 200 kcal per week) did not achieve the same magnitude of improvement in MetS composite outcomes. In STRRIDE-PD, a low amount of moderate-intensity exercise (LAMI: ~1 000 kcal per week) resulted in similar or greater improvements in composite MetS outcomes compared to high amounts of moderate (HAMI:~1 600 kcal per week) and vigorous-intensity exercise (HAVI:~1 600 kcal per week). This apparent asymptotic effect for ExEE suggests additional programmatic factors, such as exercise intensity, may influence improvements in composite MetS outcomes.

3.1.4. Evidence of a state-dependent effect for exercise intensity

Among individuals with overweight or obesity and mild-to-moderate dyslipidemia, evidence from STRRIDE I indicates moderate-intensity exercise yields greater improvements in composite MetS outcomes compared to vigorous-intensity exercise, when ExEE is controlled at approximately 1 200 kcal per week.[21] Among individuals further along the MetS disease spectrum, specifically those with overweight or obesity and prediabetes, STRRIDE-PD found moderate-intensity exercise at approximately 1 000–1 600 kcal per week yielded the greatest

Table 7
Summary of randomized exercise trials evaluating the impact of aerobic exercise amount and intensity on MetS composite outcomes.

Study	n	Population	Training type/intervention length	Groups ([a]ExEE; Intensity)	Measure(s)	Results
Ades et al.[31]	74	Men and women [b]BMI: 27–45 kg·m^{-2} Coronary heart disease Abdominal obesity 44–84 years	5-month cardiac rehabilitation program (primarily walking; cycle, rowing, and arm ergometers also used); 3 or 5–7 days/week	*Standard Cardiac Rehabilitation + Hypocaloric Diet:* 7–800 kcal/week at 65%–70% peak $\dot{V}O_2$; 25–40 min/session for 3 sessions/week *High-Calorie Cardiac Rehabilitation + Hypocaloric Diet*: 3 000–3 500 kcal/week at 50%–60% peak $\dot{V}O_2$; 45–60 min/session for 5–7 sessions/week	[c]MetS sum score MetS prevalence	*MetS prevalence* Decreased in both groups *MetS sum score* Decreased in both groups The High-Calorie group had a significantly greater reduction compared to the Standard group
Ramos et al.[38]	99	Men and women ≥ 3/5 MetS risk factors	16-week aerobic intervention (treadmill or cycle ergometer); 3 or 5 days/week	*High-Amount/[d]HIIT:* ~(1 003 ± 360) kcal/week with 4 × 4 min bouts at 85%–95% [e]HR_{peak} with 3 min recovery at 50%–70% HR_{peak}; 3 days/week for 114 min/week *Low-Amount/HIIT*: ~(412 ± 121) kcal/week with 1 × 4 min bout at 85%–95% HR_{peak}; 3 days/week for 51 min/week *High-Amount/[f]MICT*: ~(959 ± 300) kcal/week at 60%–70% HR_{peak}; 5 days/week for 150 min/week	Modified MetS z-score	*Modified MetS z-score* Significant decrease in all groups
Morales-Paloma et al.[32]	121	Men and women BMI: (32.5 ± 4.8) kg·m^{-2} ≥ 3/5 MetS risk factors Sedentary (57 ± 8) years	16-week aerobic intervention (cycle ergometer); 3 sessions/week	*High-Amount/HIIT:* ~440 kcal/session with 4 × 4 min at 90% HR_{max} with 3 min recovery at 70% HR_{max}; 43 min/session *Low-Amount/HIIT:* ~290 kcal/session with 10 × 1 min at 100% HR_{max} with 1.5 min recovery at 65% HR_{max}; 35 min/session *High-Amount/MICT:* ~440 kcal/session at 70% HR_{max}; 50 min/session *No Exercise Control*	MetS z-score	*MetS z-score* High-Amount/HIIT and High-Amount/MICT significantly decreased

Abbreviations.
[a] ExEE = exercise energy expenditure.
[b] BMI = body mass index.
[c] MetS = metabolic syndrome.
[d] HIIT = high-intensity interval training.
[e] HR = heart rate.
[f] MICT = moderate-intensity continuous training.

improvements among exercise-only groups, regardless of ExEE.[23] This mismatched finding in LAMI between STRRIDE-PD and STRRIDE I may be due to the more advanced insulin-resistant state in STRRIDE-PD participants.

In the EX-MET study, adults with MetS ($n = 99$) were randomized to one of three groups for 16 weeks: 1) High-Amount/HIIT – ~(1 003 ± 360) kcal per week with 4 by 4 min bouts at 85%–95% HR_{peak} with 3 min recovery at 50%–70% HR_{peak} for 114 min per week; 2) Low-Amount/HIIT – ~(412 ± 121) kcal per week with 1 by 4 min bouts at 85%–95% HR_{peak} for 51 min per week; or 3) High-Amount/MICT – ~(959 ± 300) kcal per week at 60%–70% HR_{peak} for 150 min per week.[38] All groups showed significant improvements in their modified MetS z-scores (High-Amount/HIIT: [−0.6 ± 1.2], $p < 0.05$; Low-Amount/HIIT: [−1.6 ± 2.1], $p < 0.05$; High-Amount/MICT: [−0.9 ± 1.7], $p < 0.05$), with no significant differences among groups ($p = 0.08$). Compared to High-Amount/HIIT (−42%) and High-Amount/MICT (−57%), participants without type 2 diabetes had the largest magnitude of modified MetS z-score reduction with Low-Amount/HIIT (−126%). In contrast, participants with type 2 diabetes showed attenuated reductions in modified MetS z-score, particularly with Low-Amount/HIIT (−51%) and High-Amount/HIIT (−1%).

The Insulin Sensitivity of Aerobic Interval Conditioning trial further supports the state-dependent effect of aerobic exercise intensity using interval training.[35] Sedentary men aged 30–60 years with overweight or obesity ($n = 42$) participated in a 12-week exercise training intervention divided into: Part 1) a 6-week ramp up and steady state period of MICT – 12 KKW at 50%–70% $\dot{V}O_{2max}$ followed by Part 2) randomization into either a) HIIT – 12 KKW with intervals at 90%–95% $\dot{V}O_{2max}$ with 2-min recovery periods at 50% $\dot{V}O_{2max}$ for 6 more weeks; or b) continued MICT for six more weeks. Both a MetS sum score and MetS z-score were calculated for each group. Measures of insulin resistance (*e.g.*, homeostatic model assessment of insulin resistance [HOMA-IR]) were obtained at both 24 h and 72 h after the last exercise session. Both groups significantly reduced their MetS sum scores (HIIT: [−1.14 ± 1.15], $p < 0.05$; MICT: [−1.03 ± 1.68], $p < 0.05$). Among men with lesser baseline HOMA-IR (*i.e.,* more insulin sensitive), only HIIT resulted in significant improvements in the MetS z-score ($p < 0.05$). Conversely, compared to HIIT, MICT showed numerically greater, though not statistically significant, improvements in the MetS z-score among men with greater baseline HOMA-IR (*i.e.,* more insulin resistant). In addition, there was a relationship between baseline insulin resistance, exercise intensity, and HOMA-IR improvements. Men with a greater baseline HOMA-IR in MICT significantly improved their HOMA-IR at the 24 h post-training timepoint ($p < 0.05$). In contrast, regardless of baseline HOMA-IR, men in HIIT significantly improved their HOMA-IR at 24 h and 72 h post-training ($p < 0.05$). These findings suggest individuals who are more insulin sensitive at baseline may respond better to high-intensity interval exercise. In comparison, individuals who are more insulin resistant at baseline may benefit more from low-amount moderate-intensity aerobic exercise.[21,23,35,38]

3.2. Exercise mode effects

3.2.1. STRRIDE findings

In STRRIDE AT/RT, only the combined group (AT/RT) significantly improved their modified MetS z-score ([−1.10 ± 1.70]; $p = 0.004$) and MetS sum score ([−0.64 ± 1.04], $p < 0.01$). The AT only group showed a trend toward improvement in modified MetS z-score ([−0.76 ± 2.20]; $p = 0.067$) (Table 3). The change in the modified MetS z-score for the AT/RT group was significantly different from RT only group ($p < 0.05$), and the AT only group showed a trend towards a significant difference compared to RT only ($p < 0.10$). Although no statistical comparisons were performed, the prevalence of MetS remained unchanged in the AT only group (14 individuals at pre- and post-intervention), decreased from 11 to 4 individuals in the AT/RT group, and increased from 12 to 19 individuals in the RT only group.

3.2.2. Previous published findings

Few randomized exercise trials assess ExEE when an RT arm is included in the study design. Here we discuss the major findings from four randomized exercise trials that investigated the effects of exercise mode on composite MetS outcomes, while also reporting ExEE (Table 8), and how these findings relate to STRRIDE AT/RT.

When considering the impact of exercise mode, composite MetS improvements similarly follow the threshold effect principle for ExEE.[40,41] Kukkonen-Harjula et al. compared AT versus RT on MetS prevalence after a diet-induced weight loss phase.[40] Following a two-month dietary intervention, 90 middle-aged men with abdominal obesity were randomized to one of three weight maintenance groups for six months: 1) Walking (*i.e.,* AT) – 1.7 MJ per session at 60%–70% $\dot{V}O_{2max}$ and dietary counseling; 2) RT – 1.2 MJ per session, performing three sets of eight reps for six exercises and dietary counseling; or 3) Dietary Counseling Control. Both exercise groups trained for 45 min per session, three sessions per week. At baseline, before weight loss, MetS prevalence was 35 out of 61 men with complete MetS data. After the weight loss phase, MetS prevalence decreased to 7 individuals (odds ratio [*OR*]: 0.10; 95% confidence interval [*CI*]: 0.04, 0.22), and remained stable at 6 individuals during the weight maintenance intervention (*OR*: 0.08; 95% *CI*: 0.03, 0.19). There was no statistically significant group-by-time interaction.

Geliebter et al. randomized 81 sedentary adults with overweight or obesity to one of three groups for eight weeks: 1) Hypocaloric Diet Control – liquid-formula diet based on 70% of measured resting metabolic rate at baseline; 2) AT – 150 kcal per session at 55% peak $\dot{V}O_2$ for 30 min per session for three days per week combined with the hypocaloric diet; or 3) RT – 150 kcal per session of progressive weight training at three sets of six or more reps for eight exercises for 60 min per session for three days per week combined with the hypocaloric diet.[41] At baseline, MetS was prevalent in 11 of the 81 participants and decreased to 4 participants post-intervention ($p = 0.01$). Across groups, the *OR* for MetS prevalence post-versus pre-intervention was 0.33 (95% *CI*: 0.1–1.1) and the MetS sum score significantly decreased ([1.6 ± 1.0] pre-intervention to [1.2 ± 0.9] post-intervention, $p = 0.004$), with no significant differences among groups ($p > 0.35$). The authors noted the lack of an additive effect of either AT or RT on MetS may be due to the relatively small caloric deficit produced by the exercise training compared to the magnitude of caloric deficit elicited by the dietary portion of the intervention.[41]

Similar to STRRIDE AT/RT, the HART-D study compared the effects of aerobic and resistance training alone to a combined AT/RT program. In HART-D,[42] sedentary adults with type 2 diabetes ($n = 262$) were randomized to one of four groups for a nine-month exercise training program: 1) AT – 12 KKW at ~65% peak $\dot{V}O_2$ for ~140 min per week; 2) RT – 2 sets of 4 upper body exercises, 3 sets of 3 lower body exercises, and 2 sets of core exercises, all for 10–12 reps and performed 3 days per week for ~141 min per week; 3) AT/RT – 10 KKW at ~65% peak $\dot{V}O_2$ plus a modified resistance program 2 days per week for ~145 min per week; or 4) Non-Exercise Control. In a secondary analysis, both the AT only and AT/RT groups significantly decreased their MetS sum scores (AT mean change: 0.59, 95% *CI*: 1.00, −0.21 and AT/RT mean change: 0.79, 95% *CI*: 1.4, −0.35) compared to the control ($p = 0.028$ and $p = 0.005$; respectively) and RT groups ($p = 0.02$ and $p = 0.003$; respectively). The prevalence of MetS significantly decreased over time in the AT only (56%–43%) and AT/RT (55%–46%) groups. Of note, the authors attempted to equalize the training dose among groups by decreasing the aerobic dose to 10 KKW in the combined AT/RT group and equalizing training duration across groups, in contrast to STRRIDE AT/RT, in which the AT/RT group represented a combination of the full AT and RT doses. However, neither STRRIDE AT/RT nor HART-D provided explicit ExEE doses for the RT arms, thus limiting the interpretability of the modality-independent findings.

Recent evidence incorporating real-time estimation of ExEE in both AT only and combined AT/RT suggests the effects of exercise modality may be secondary to ExEE.[43] Moreno-Cabañas et al. conducted a 16-week intervention among middle-aged, inactive adults with overweight or obesity and MetS.[43] Participants ($n = 66$) were randomized into one of two groups and exercised three days per week: 1) HIIT – 455 kcal per session of aerobic cycling with 5 by 4 min bouts at 90% HR_{max} with 3 min recovery periods at 70% HR_{max} for 50 min per session; or 2) HIIT plus RT – 419 kcal per session of aerobic cycling with 4 by 4 min bouts of a similar structure for 38 min per session followed by three sets of 12 reps of three lower body exercises. ExEE did not significantly differ between groups ($p = 0.149$). Both groups significantly improved their modified MetS *z*-scores by a similar magnitude (HIIT alone: [−0.12 ± 0.31]; HIIT + RT: [−0.12 ± 0.29]) with no significant group by time interaction ($p = 0.976$). Notably, in contrast to the full-body routines of the HART-D and STRRIDE AT/RT studies, the RT component from Moreno-Cabañas et al. only involved lower body movements, which may partially explain why no significant differences between groups were detected.

4. Discussion

Findings suggest there is a relationship between ExEE and MetS, with a potential threshold of ~1 000–1 200 kcal per week needed to achieve significant improvements in composite MetS measures.[21,29–36,40,41] However, dose-dependent improvements beyond 1 200 kcal per week are not universal, and factors such as exercise intensity appear to play a prominent role depending on an individual's insulin sensitivity.[21,23,35,38,39]

The state-dependent, modulatory effects of exercise intensity on MetS may have biological plausibility given the pathophysiologic development and progression of MetS, which is closely linked to insulin resistance and subsequent lipotoxicity.[44] For instance, in individuals who are insulin sensitive before intervention initiation, intramuscular glycogen depletion and resynthesis from vigorous-intensity exercise may help slow or prevent insulin resistance.[45] However, once an individual becomes insulin resistant, addressing lipotoxicity[44] may become critical. Thus, for individuals with insulin resistance before intervention initiation, moderate-intensity exercise may be equally or more important for improving MetS due to fatty acid oxidation dependence and the potential to reduce lipotoxicity by preventing fatty acid intermediates from accumulating in the intramyocell.[46]

Another consideration for understanding the relationship between exercise intensity and MetS relates to systemic inflammation. As highlighted by a recent review by Figueiredo et al. while both HIIT and moderate-intensity aerobic exercise yield beneficial acute and chronic anti-inflammatory effects in individuals with metabolic disorders, acute exercise performed to the point of exhaustion (*i.e.*, maximal exercise) was less associated with an anti-inflammatory phenotype and often resulted in elevated levels of pro-inflammatory cytokines such as TNF-α.[47] As chronic, low-grade inflammation through pro-inflammatory cytokines such as TNF-α is closely linked to the development of MetS,[44] there may be a point beyond which increasing exercise intensity may become counterproductive in patients with MetS.

The effects of exercise modality independent of ExEE on MetS composite outcomes remain poorly understood, primarily due to varying study designs and populations (*e.g.,* RT prescriptions, health status, and medications). In STRRIDE AT/RT, the combined AT/RT group represented a combination of full AT and RT doses, while HART-D attempted to equalize the training dose across all intervention groups. Some evidence suggests the effects of exercise modality may be secondary to ExEE; however, the RT component from Moreno-Cabañas et al.[43] only involved lower body movements, which may have influenced the results. Regardless of the study design, the combined AT/RT programs offered

Table 8
Summary of randomized exercise trials evaluating the impact of exercise modality on MetS composite outcomes.

Study	*n*	Population	Training type/intervention length	Groups ([a]ExEE; Intensity)	Measure(s)	Results
Kukkonen-Harjula et al.[40]	90	Men [b]BMI: 30–40 $kg \cdot m^{-2}$ Waist circumference > 100 cm Relative inactivity 35–50 years	2-month weight reduction phase followed by 6-month weight maintenance phase via aerobic (walking) or resistance exercise; 3 days/week	*Walking ([c]AT) + Dietary Counseling*: 1.7 [d]MJ/session at 60%–70% $\dot{V}O_{2max}$ [e]*RT + Dietary Counseling*: 1.2 MJ/session; 3 × 8 reps for 6 exercises *Dietary Counseling Control*	[f]MetS Prevalence	*MetS Prevalence* Decreased in weight loss phase No change in weight maintenance phase
Geliebter et al.[41]	81	Men and women BMI: 25–52 $kg \cdot m^{-2}$ Sedentary Healthy 19–49 years	8-week aerobic (cycle and arm ergometers) or resistance intervention; 3 days/week	*AT + Hypocaloric Diet*: 150 kcal/session at 55% peak $\dot{V}O_2$; 30 min/session *RT + Hypocaloric Diet:* 150 kcal/session of progressive weight training with 3 sets of 6+ reps for 8 exercises for 60 min/session *Hypocaloric Diet Control*	MetS sum score MetS Prevalence	*MetS sum score* Significantly decreased across time *MetS Prevalence* Decreased across time
Earnest et al.[42]	262	Men and women BMI: (34.9 ± 5.9) $kg \cdot m^{-2}$ A1c: 6.5%–11.0% Sedentary 30–75 years	9-month aerobic (treadmill), resistance, or combined intervention; 3–5 days/week	*AT*: 12 [g]KKW at ~65% peak $\dot{V}O_2$ for ~140 min/week *RT*: 2 sets of 4 upper body exercises, 3 sets of 3 lower body exercises, and 2 sets of core exercises, all for 10–12 reps and performed 3 days/week for ~141 min/week *AT + RT:* 10 KKW at ~65% peak $\dot{V}O_2$ plus modified resistance program 2 days/week for ~145 min/week *Non-Exercise Control*	MetS sum score MetS Prevalence	*MetS sum score* Significant decrease in AT and AT/RT groups Changes in AT and AT/RT significantly different from Control and RT *MetS Prevalence* Significantly decreased in AT and AT/RT groups
Moreno-Cabañas et al.[43]	66	Men and women BMI: (32 ± 5) $kg \cdot m^{-2}$ ≥ 3/5 MetS risk factors Sedentary (56 ± 7) years	16-week aerobic (cycling) or combined (aerobic + resistance) intervention; 3 days/week	[h]*HIIT:* 455 kcal/session with 4 + 1 × 4 min intervals at 90% [i]HR_{max} with 3 min recovery periods at 70% HRmax; 50 min/session *HIIT + RT:* 419 kcal/session of similar structure for 38 min/session followed by 3 sets of 12 reps of 3 lower body exercises	Modified MetS *z*-score	*Modified MetS z-score* Significant decrease in both groups

Abbreviations.
[a] ExEE = exercise energy expenditure.
[b] BMI = body mass index.
[c] AT = aerobic training.
[d] MJ = megajoules.
[e] RT = resistance training.
[f] MetS = metabolic syndrome.
[g] KKW = kcal exercise energy expenditure/kilogram of body weight/week.
[h] HIIT = high-intensity interval training.
[i] HR = heart rate.

the most robust improvements in composite MetS outcomes.[22,42] The mechanisms by which combination training elicits these notable improvements remain unclear.

4.1. Strengths and limitations

Strengths of this review include: 1) the assessment of composite MetS outcomes, allowing for a sensitive interpretation of the effects of exercise on MetS as a distinct condition, and 2) the inclusion of studies with explicit ExEE prescriptions, enabling a more accurate assessment of the independent effects of exercise amount, intensity, and mode on MetS. This review also has limitations to consider. We did not compare the effects of combined lifestyle interventions to exercise alone, so the conclusions in this review should be interpreted in the context of exercise-only interventions. Additionally, the study populations varied substantially in age, gender, race, baseline health status, and other characteristics, limiting the generalizability of the findings. Last, there was substantial heterogeneity in study designs, intervention durations, composite MetS outcomes measured, and procedures for prescribing and estimating ExEE among the included studies. Additional, longer-term randomized exercise trials with sufficient ExEE relative to body mass are needed to: 1) determine whether an asymptotic effect for ExEE on MetS severity exists; 2) assess the interaction between baseline insulin sensitivity and exercise intensity on composite MetS outcomes; and 3) evaluate the independent effects of exercise mode on MetS.

5. Conclusions

The summation of findings in this narrative review include: 1) achieving a sufficient level of energy expenditure (~1 000–1 200 kcal per week) at either moderate or vigorous intensity is critical for exercise to ameliorate MetS severity; 2) while a relationship between aerobic energy expenditure and MetS severity may exist, there is likely a threshold beyond which further improvements are limited based on increasing energy expenditure alone; 3) the moderating effects of exercise intensity on composite MetS outcomes may be related to an individual's baseline insulin sensitivity; and 4) without controlling for total exercise energy expenditure, combined AT/RT interventions offer the most robust improvements for composite MetS outcomes compared to either mode alone. As the prevalence of MetS continues to grow, continued development of exercise programs as accessible, cost-effective means to prevent or reduce MetS severity is of importance. Given the existing data, drawing definitive recommendations for the optimal exercise programming for MetS remains unclear. Thus, further investigation is critical to identify the optimal exercise intervention characteristics that focus on combinations of mode, intensity, and amount for MetS prevention and treatment.

CRediT authorship contribution statement

Garrett A. Moseley: Writing – original draft, Conceptualization. **Katherine A. Collins-Bennett:** Writing – review & editing, Conceptualization. **William E. Kraus:** Writing – review & editing, Supervision, Conceptualization. **Leanna M. Ross:** Writing – review & editing, Supervision, Conceptualization.

Funding

Leanna M. Ross is supported by the American Heart Association Career Development Award 23CDA1051777 and National Institute on Aging grant 5P30AG028716-18. No other funding was used to directly support the preparation of this narrative review.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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