**Improvements in glycaemic control after acute moderate-intensity continuous or high-intensity interval exercise are greater in South Asians than white Europeans with nondiabetic hyperglycaemia: a randomised crossover study**

Jack A. Sargeant PhD1,2,\*, Charlotte Jelleyman PhD1,2,3,\*, Nicole A. Coull PhD1,2, Charlotte L. Edwardson PhD1,2, Joseph Henson PhD1,2, James A. King PhD2,4, Kamlesh Khunti FMedSci1,5,6, Matthew McCarthy PhD1,2, Alex V. Rowlands PhD1,2, David J. Stensel PhD2,4, Helen L. Waller PhD1,2, David R. Webb PhD1,2, Melanie J. Davies MD1,2,6, Thomas Yates PhD1,2

\* joint first authors

1 Diabetes Research Centre, University of Leicester, Leicester, UK

2 NIHR Leicester Biomedical Research Centre, Leicester, UK

3 School of Sport and Recreation, Auckland University of Technology, Auckland, NZ

4 School of Sport, Exercise and Health Sciences, Loughborough University, Loughborough, UK

5 NIHR Applied Research Collaboration East Midlands, Leicester, UK

6 Leicester Diabetes Centre, Leicester General Hospital, University Hospitals of Leicester NHS Trust, Leicester, UK

**Corresponding author:** Jack A. Sargeant; Diabetes Research Centre, University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester, UK, LE5 4PW; js928@leicester.ac.uk

**Short running title:** Ethnicity, acute exercise and glycaemic control

**Clinical trials registration:** ISRCTN12337078

**Abstract word count:** 250 words

**Manuscript word count:** 4208 words

**Number of references:** 40

**Number of Tables and Figures:** 2 tables, 2 figures

**Key words**: ethnicity, glycaemic control, impaired glycaemic control, exercise physiology, HIIE, aerobic exercise

**Structured Abstract**

*Objective:* To examine whether circulating metabolic responses to low-volume high-intensity interval (LV-HIIE) or continuous moderate-intensity aerobic (CME) exercise differ between white Europeans and South Asians with nondiabetic hyperglycaemia (NDH).

*Research Design and Methods:* 13 white Europeans and 10 South Asians (combined median (IQR) age 67 (60–68) years, HbA1c 5.9 (5.8–6.1)% [41.0 (39.9–43.2) mmol·mol-1]) completed three 6-hour conditions (sedentary control [CON], LV-HIIE, CME) in a randomised order. Exercise conditions contained a single bout of LV-HIIE and CME respectively (each ending at 2h), with meals provided at 0 and 3h. Circulating glucose (primary outcome), insulin, insulin resistance index (IRI), triglyceride and non-esterified fatty acids were measured at 0, 0.5, 1, 2, 3, 3.5, 4, 5 and 6h. Data were analysed as post-exercise time-averaged area under the curve (AUC), adjusted for age, sex and pre-exercise AUC.

*Results:* Glucose was similar in each condition and ethnicity, with no condition-by-ethnicity interaction (*P*≥0.28). However, insulin was lower in LV-HIIE (mean [95% CI]: -44.4 [-23.7, -65.1] mU·L-1) and CME (-33.8 [-13.7, -53.9] mU·L-1) compared to CON. Insulin responses were greater in South Asians (interaction *P*=0.03) such that values were similar in each ethnicity during exercise conditions, despite being 33% higher in South Asians during CON. IRI followed a similar pattern to insulin. Lipids were unaffected by exercise.

*Conclusions:* Reductions in insulin and insulin resistance after acute LV-HIIE and CME are greater in South Asians than white Europeans with NDH. Further trials are required to examine longer-term impact of LV-HIIE and CME on cardiometabolic health.

Type 2 diabetes (T2D) is a global health problem affecting >400 million people worldwide (1). Characterised by chronic hyperglycaemia and insulin resistance, T2D is associated with increased risk of micro- and macrovascular complications, other metabolic co-morbidities, and earlier death (2,3). More than 300 million further individuals are estimated to have elevated circulating glucose concentrations in the fasted state (impaired fasting glucose), in response to a glucose challenge (impaired glucose tolerance) or both, but do not yet reach diagnostic criteria for T2D (1). These individuals with “non-diabetic hyperglycaemia” (NDH) are at high risk of developing T2D and subsequent complications (1,4), whilst dysregulated post-prandial metabolism, even at sub-clinical levels, independently predicts future cardiovascular events (5).

Physical inactivity and low cardiorespiratory fitness (CRF) are independent risk factors for T2D, and strategies to promote physical activity or improve CRF (e.g. structured exercise training) reduce T2D incidence in the general population and people with NDH (6,7). Regular physical activity and/or exercise provide diverse cardiometabolic benefits, some of which (including improved glucose and lipid metabolism) occur acutely after just a single bout (8–11). Consequently, promotion of physical activity and structured exercise constitute key components of both T2D prevention programmes and management consensus reports (1,2,11,12).

The impact of high-intensity interval exercise (HIIE) on cardiometabolic health has received increasing attention over the past 10-15 years (13–15), and HIIE now features within consensus reports for T2D management alongside continuous moderate-intensity aerobic (CME) and resistance exercise training (2,11). Several HIIE protocols exist, varying in intensity and duration of both exercise and recovery intervals. However, an approach comprising 10x1-minute intervals at near-maximal aerobic capacity, interspersed with 1-minute intervals of active recovery (referred to as “low-volume(LV)-HIIE” hereafter), has been utilised as a pragmatic model to support high-intensity exercise in clinical populations, eliciting diverse metabolic benefits in individuals with or at risk of T2D (16–20).

South Asian individuals have approximately two- to four times greater age-standardised risk of T2D than white Europeans, and higher T2D prevalence for a given BMI (21). They may also transition from NDH to T2D quicker than white Europeans and are typically diagnosed with T2D up to 12 years earlier in life (21,22). Whilst the mechanisms underpinning this increased risk are diverse, complex and not fully understood, greater insulin resistance across the life course appears to constitute a prominent contributing factor (21).

South Asians also have lower CRF and perform less physical activity (particularly moderate-to-vigorous-intensity physical activity; MVPA) than white Europeans (21,23,24), with one study demonstrating that CRF accounted for >66% of the difference in insulin resistance between these ethnicities (23). Cross-sectional analyses suggest that South Asians may require greater habitual physical activity than white Europeans to confer similar cardiometabolic risk, but the benefits observed for a given increase in physical activity may be greater (25). Accordingly, recent experimental evidence demonstrated that the acute postprandial benefits of light-intensity walking in older adults were greater in South Asians than in white Europeans, with a separate trial in young adults showing similar ethnic differences in post-prandial lipid metabolism on the day after a strenuous bout of exercise (26,27). Whether similar ethnic differences exist in responses to acute moderate- or high-intensity exercise in individuals with NDH has not been explored.

This study examined whether the effects of acute LV-HIIE or CME on circulating glucose and lipid metabolism differ between white European and South Asian men and women with NDH. We hypothesised that glucose and lipid metabolism would be improved after each exercise bout, with greater effects observed in South Asians compared to white Europeans.

**Research Design and Methods**

*Ethical approval and study registration*

Ethical approval was provided by an NHS Research Ethics Committee (15-EM-0259) and participants gave informed, written consent to participate. Clinical trials registration was completed prior to participant recruitment (ISRCTN12337078).

*Overview of study design*

This study used a single-site, randomised, crossover design, in which South Asian and white European men and women completed three experimental conditions ((a) sedentary control [CON], (b) LV-HIIE and (c) CME) in a randomised order, stratified by sex and ethnicity. Each condition lasted 6 hours and was separated by approximately 1-week washout. Participants remained seated and rested throughout each condition, except when completing a single bout of LV-HIIE (total 25 minutes) or CME (35 minutes) within the second hour of respective conditions. The primary outcome was post-exercise time-averaged total area under the curve (AUC) for plasma glucose.

*Participant eligibility and recruitment*

White European and South Asian men and post-menopausal women were recruited. South Asian ethnicity was defined as anyone identifying themselves as “Asian” or “Asian British (Indian, Pakistani, Bangladeshi)”, and white Europeans were those identifying as “white/Caucasian” and descending from any European country. Participants were aged 50 - 74 years, with weight-stable BMI ≥27.5 or ≥25.0 kg·m-2 if white European or South Asian, respectively (all <5 kg self-reported weight change within preceding 6 months). Participants had NDH, defined as HbA1c between 5.7 - 6.4 % (39 - 47 mmol·mol-1) or a 2-hour plasma glucose concentration between 7.8 - 11.0 mmol·L-1 in response to a standard 75g oral glucose tolerance test (OGTT) performed at our centre within the preceding 12 months (1). Participants with controlled hypertension/dyslipidaemia were eligible, provided they met all other inclusion criteria, but participants were otherwise free from diagnosed chronic metabolic disease. Individuals that self-reported ≥3 sessions of vigorous-intensity exercise per week (≥20 minutes per session) were excluded, as were those with self-reported contraindications to exercise or other study procedures.

Participants were recruited via primary care services, community events, poster advertisement and existing research databases. Interested individuals underwent telephone pre-screening, and those deemed eligible were invited to attend the laboratory for full screening and enrolment procedures.

*Experimental Procedures*

Preliminary visit

Self-reported physical activity was determined using a frequency recall questionnaire for various transport-related, sport and leisure-time physical activities. Body mass, height and waist circumference were measured to the nearest 0.1 kg, 0.1 cm and 0.5 cm, respectively. A venous blood sample was collected for the measurement of HbA1c, total cholesterol and HDL. Seated, rested blood pressure was measured manually by a qualified healthcare professional and reviewed by a specialist cardiac nurse alongside medical history and resting electrocardiography (ECG) (Cardiofax GEM, Nihon Kohden Corp., Japan). Individuals with resting cardiac arrhythmias or other potential contraindications to exercise were reviewed by a study clinician and either cleared to proceed or withdrawn from the study as appropriate.

Participants then completed a progressive maximal exercise test on a motorised treadmill (Woodway PPS 70 Plus, Woodway USA Inc., USA), with ECG and blood pressure monitoring throughout. After a 3-minute warm-up, participants walked at a self-selected “brisk walking” speed, at a gradient increasing, from 0%, by 1% per minute. Heart rate (HR) was recorded throughout, as were expired gases for the measurement of *V̇*O2 and respiratory exchange ratio (RER) (Metalyser 3B, Cortex Biophysik GmbH, Germany). Participants were instructed to continue for as long as they could, investing maximum effort, and the test continued until volitional exhaustion or participants reached 100% of their age-predicted maximum HR (85% if taking *β*-blockers) and RER ≥1.15. Tests aborted by the cardiac nurse due to adverse symptoms were classified as incomplete, and these participants were withdrawn. After sufficient recovery (≥15 minutes), participants were familiarised with LV-HIIE, performing a condensed protocol of three intervals.

To assess habitual physical activity, participants were asked to wear a tri-axial accelerometer (GENEActiv, ActivInsights Ltd., UK) on their non-dominant wrist for 6 days after the preliminary visit. They were instructed to continue their usual daily activities and encouraged, if possible, to wear the device at all times. A wear log was provided to record if/when the device was removed, along with the time the participants got into and out of bed and an estimate of sleep and wake times. Data were recorded at 100Hz, downloaded using manufacturer software (GENEActiv PC software v2.9), and processed using an R-package GGIR, v1.10.1 (<http://cran.r-project.org>; (28)). The average magnitude of dynamic acceleration corrected for gravity (Euclidean Norm Minus One) was calculated, averaged over 5-second epochs, and expressed in milligravitational units (m*g*). Data were considered valid when the device was worn for ≥16 hours on ≥4 days (including ≥1 weekend day). Time spent sleeping (automated sleep detection), sedentary (<40m*g*), and in light-intensity physical activity (LIPA; 40-100m*g*) or MVPA (>100m*g*) were averaged across valid days. MVPA in bouts of ≥10 minutes was assessed, to reflect periods of structured MVPA and avoid incidental activity.

Experimental visits

A schematic of experimental conditions is provided in Supplemental Figure S1. Participants arrived at the laboratory at approximately 08:00 hours, after an overnight fast of ≥10 hours. After ensuring compliance with standardisation instructions and confirming willingness to continue, an intravenous cannula (Braun, Pennine Healthcare, UK) was inserted into an antecubital vein. Following a period of habituation (30 – 60 minutes), conditions were initiated with the collection of a venous blood sample (0 hours), with further samples collected at 0.5, 1, 2, 3, 3.5, 4, 5 and 6 hours, for measurement of circulating glucose, insulin, triglyceride (TG) and non-esterified fatty acids (NEFA). Identical mixed meals were provided at 0 and 3 hours, and consumed within 15 minutes. Meal composition was standardised approximately between participants, prescribed according to baseline body weight (mean ± SD: 7.9±0.8 kcal·kg-1;62±2% CHO, 21±2% fat, 17±1% protein), and each participant consumed the same meals during each of their respective conditions. Meals typically consisted of white bagel and full-fat margarine with either (a) full-fat cheddar cheese, fruit jelly and orange juice, or (b) a meal-replacement shake made with whole milk, with small variations between participants according to food preferences or dietary requirements.

LV-HIIE contained 10x1-minute intervals on a motorised treadmill at the same brisk walking speed self-selected during the preliminary visit, and a gradient predicted to elicit 90% of peak *V̇*O2 (“*V̇*O2 peak”). Intervals were interspersed with 1-minute active recovery, walking at 3.5 km·h-1 and 0% gradient. CME contained 30 minutes continuous walking at the same brisk walking speed and a gradient predicted to elicit 65% of *V̇*O2 peak. Both exercise bouts were preceded by a 3-minute warm-up and followed by a 2-minute cool-down (each 3.5 km·h-1, 0% gradient), such that the total duration of LV-HIIE and CME were 25 and 35 minutes, respectively. LV-HIIE and CME each concluded at 2 hours within respective conditions. Therefore, to account for differences in duration, CME commenced 10 minutes earlier than LV-HIIE. HR and rating of perceived exertion (RPE) (29) were recorded at regular intervals throughout each bouts. These protocols have been suggested to be closely matched for external work (30).

Standardisation procedures

Before all visits, participants refrained from alcohol and strenuous physical activity for 48 and 72 hours respectively, and attended the laboratory using motorised transport. Participants also recorded all food and energy-containing beverages for 48 hours before their first condition and replicated this before subsequent conditions. Physical activity and standing beyond that prescribed in the exercise bouts were restricted throughout conditions, with an activPAL thigh-worn accelerometer (PAL Technologies, UK) worn throughout to confirm compliance with these instructions. Data were processed using proprietary software (﻿activPAL Professional Research Edition, PAL Technologies, UK), and time spent sitting and stepping during conditions was calculated.

Biochemical analyses

HbA1c, plasma glucose and serum total cholesterol, HDL and TG were analysed using standardised quality-controlled enzymatic assays by the clinical pathology laboratories of University Hospitals of Leicester NHS Trust. Plasma NEFA was analysed in a similar manner by Nottingham University Hospitals NHS Trust. Plasma insulin was measured using electrochemiluminescence assay (Meso Scale Diagnostics, USA), with analysis of a given sample repeated if the co-efficient of variation (CV) between two duplicates was >20%; the mean intra-plate CV of all analyses was <7.8%.

*Sample size*

Assuming a standardised difference of 1 (30,31), a within-person correlation of 0.7 (unpublished data from previous studies in our laboratory (32)) and *p*<0.05, we required 22 participants to complete all experimental procedures, to detect (a) a condition-by-ethnicity interaction with 80% power (assuming a change in glucose AUC that is twice as large in one group than the other), and (b) a main effect of condition within each ethnicity with >90% power (≥8 required per group). To allow 10% non-compliance and full counterbalancing, our target sample size was 12 per group.

*Data inclusion*

Participants were included in analyses of a given outcome if >50% of data for that outcome were available for each condition. Missing data within included participants were imputed using a regression method previously reported for acute experimental studies (26), with age, sex, ethnicity, BMI, HbA1c and condition as predictors. Imputations were performed for 4.3% of primary outcome data (glucose) and 5.2% of secondary outcomes data (insulin, TG and NEFA).

*Statistical analysis*

Time-averaged total AUC for glucose, insulin, TG and NEFA during pre- and post-exercise periods were calculated using the trapezium rule. AUC for glucose and insulin during each period were multiplied to form an insulin resistance index (IRI), as previously described (26). Descriptive data are presented as median (IQR) and frequency, for continuous and categorical variables, respectively. Outcome data are presented as mean [95% CI], unless otherwise specified.

Data were analysed using generalised estimating equations with an exchangeable correlation matrix, using commercially-available software (SPSS v26, IBM, USA). Glucose, insulin, IRI and TG analyses used a gamma distribution due to positively skewed data. All models contained an interaction term between ethnicity and condition, and were adjusted for age, sex and pre-exercise AUC. Results for condition, ethnicity and condition-by-ethnicity are reported. To aid interpretation, values across each condition are reported stratified by ethnicity and for the combined study population (provided in supplemental materials). Comparisons between exercise conditions and CON within each ethnicity were performed as exploratory analyses. Probability (*p-*)values <0.05 were considered statistically significant.

**Results**

*Participant flow and characteristics*

As detailed in Supplemental Figure S2, 1118 individuals were invited to participate in the study. Sixty-eight underwent telephone pre-screening and 36 were enrolled (white European [M/F] vs. South Asian [M/F]: 17 [8/9] vs. 19 [11/8]). Nine participants were excluded after full screening, with the remaining 27 randomised to an experimental condition sequence. Four individuals withdrew after randomisation, two of whom had completed one experimental condition. The remaining 23 (13 [6/7] vs. 10 [7/3]) completed the study and comprised the full analysis set (Table 1).

The white European group were older and had greater proportion of female participants than the South Asian group. The South Asian group had higher BMI and obesity prevalence, but lower median body weight. HbA1c was similar between groups, but the South Asian individuals were more insulin resistant as indicated by higher HOMA-IR, which was driven by higher fasting insulin.

Eighteen individuals (9 [4/5] vs. 9 [7/2]) were compliant with free-living physical activity assessment, each providing 2 valid weekend days and 4 valid weekdays of data. Participants were highly sedentary, with the white European group spending approximately 80 minutes more time sedentary per day than the South Asian group. MVPA in bouts of ≥10 minutes was low in both groups, and lower in South Asians than in white Europeans. The South Asian group had shorter sleep duration (Table 1).

*Compliance with experimental procedures and exercise responses*

As per study design, participants remained seated for almost the entirety of the CON condition (median (IQR) percentage of condition spent sitting: 98.0 (97.4 – 99.2)%), whilst stepping time was negligible (total time: 0.5 (0.2 – 1.2) minutes; percentage of condition: 0.1 (0.0 – 0.3)%). Similarly, as intended, stepping time was 25.3 (25.0 – 26.0) and 37.3 (36.9 – 37.7) minutes during LV-HIIE and CME conditions, respectively.

HR responses were similar across LV-HIIE and CME bouts (mean [95% CI]; 119 [114, 124] vs. 118 [112, 124] beats per min), whilst RPE (recorded at the end of each interval) was marginally higher during LV-HIIE (13 [12, 13] vs. 12 [11, 13] arbitrary units).

*Circulating glucose and insulin responses*

Circulating glucose and insulin concentrations throughout each condition in white European and South Asian groups, are presented in Figure 1. Glucose and insulin concentrations fluctuated over each condition in both groups, increasing transiently after each meal.

Post-exercise glucose AUC did not differ between conditions or ethnicities, and there was no condition-by-ethnicity interaction (*p*≥0.28; Table 2 (stratified values); Supplemental Table S1 (combined population)). However, in the combined study population, insulin AUC was reduced in both exercise conditions compared to CON, by 44.4 [23.7, 65.1] mU·L-1 (mean 32%) and 33.8 [13.7, 53.9] mU·L-1 (24%) in the LV-HIIE and CME conditions, respectively (main effect of condition *p*<0.001; Table 2; Supplemental Table S1). Furthermore, this effect was modulated by ethnicity (interaction *p*=0.03). The reduction after exercise was substantially greater in the South Asian group, to the extent that despite post-exercise insulin AUC being 33% higher during the CON condition in the South Asian group, values were similar in both ethnicities during respective exercise conditions (Table 2). In white Europeans, compared to the CON condition, insulin responses were reduced by 23.2 [9.1, 37.2] mU·L-1 (19%) during LV-HIIE, and by 15.6 [0.4, 30.8] mU·L-1 (13%) during CME. In South Asians, the equivalent reductions with exercise were 65.6 [27.9, 103.4] mU·L-1 (41%) and 52.1 [11.0, 93.2] mU·L-1 (33%) during LV-HIIE and CME, respectively.

Similar patterns were observed for IRI, with values being lower during LV-HIIE and CME conditions compared to CON, by 344 [159, 530] arbitrary units (AU) (35%) and 272 [89, 455] AU (27%), respectively, and with a greater response observed in the South Asian individuals compared to the white Europeans (Figure 2; Table 2; Supplemental Table S1). Compared to the CON condition, IRI was reduced in white Europeans by 158 [71, 244] AU (18%) during LV-HIIE, and by 119 [14, 224] AU (14%) during CME. In South Asians, equivalent reductions in IRI were 531 [169, 892] AU (48%) and 425 [46, 805] AU (38%), respectively.

*Circulating lipids responses*

In both groups and in each condition, circulating TG and NEFA concentrations increased and decreased respectively during the course of each condition (Supplemental Figure S3). Post-exercise TG AUC was similar in each condition and each ethnicity, and there was no condition-by-ethnicity interaction (*p*≥0.09; Table 2; Supplemental Table S1). NEFA AUC was 0.06 [0.02, 0.11] mmol·L-1 higher in the South Asian group compared to the white Europeans (main effect of ethnicity *p*=0.01), but no different between conditions and there was no condition-by-ethnicity interaction (*p*≥0.16; Table 2; Supplemental Table S1).

**Conclusions**

This study demonstrated that a single bout of LV-HIIE or CME had no effect on circulating glucose concentrations in white European or South Asian men or women with NDH. However, LV-HIIE and CME each reduced circulating insulin and IRI compared to prolonged sitting, with greater effects observed in South Asians. Responses were greater in South Asians to the extent that insulin and IRI were similar in both ethnicities during respective exercise conditions, despite each being approximately 30% higher during prolonged sitting in the South Asian group.

There are several possible reasons that our glucose findings contrast our hypotheses, and a separate crossover trial reporting reduced post-exercise glucose during an OGTT in individuals with NDH (33). Definitions and principal diagnostic criteria for NDH and T2D are derived from measures of hyperglycaemia (1). However, the pathophysiology of these inter-related conditions is highly complex, and the regulation of circulating glucose in humans is tightly controlled (4). Several complex adaptive mechanisms typically occur years prior to manifest hyperglycaemia, to maintain normal or minimally-elevated glucose concentrations for as long as possible (4). Therefore, in individuals with early glycaemic dysregulation, non-glucose measures including circulating insulin and indices of insulin resistance may be more sensitive to changes with interventions, particularly acute interventions, than circulating glucose itself; as is the case in the current study. Several studies demonstrate that, in contrast to people with T2D (34,35), circulating glucose concentrations are unaffected by acute exercise in individuals with normoglycaemia (27,36–38), with reductions in circulating insulin apparent in those with overweight or obesity and/or glucose concentrations approaching NDH (37,38). In the current study, whilst all participants met our criteria for NDH (1), it is noteworthy that 16 (70%) had normal fasting glucose (<5.6 mmol·L-1). Furthermore, as exercise intensity increases, proportional utilisation of carbohydrate metabolism also increases, with accordant stimulation of hepatic glucose production (39). In individuals with normoglycaemia or NDH, circulating glucose concentrations at the end of acute moderate-to-vigorous-intensity exercise are often greater than those immediately before, with effects extending into the post-prandial period of meals coming shortly after exercise (33,36,37). It is therefore plausible that in our recruited population, any favourable effects of acute exercise promoting a reduction in circulating glucose may have been masked by simultaneous increases in hepatic glucose output during and after exercise. Importantly, however, we sampled mixed venous blood from an antecubital vein, and therefore changes in glucose uptake or output in different tissues cannot be inferred. Thus, this remains a speculative explanation that warrants further investigation.

Previous evidence in a European population suggests that 20% reduction in insulin AUC during an OGTT may confer approximately 10% reduction in coronary mortality risk (40). Therefore, whilst acknowledging that the effect in South Asians is not known, and that the current study was an acute crossover trial, these data suggest that the magnitude of post-exercise insulin reduction observed in our study may be clinically meaningful (white European vs. South Asian: LV-HIIE 19% vs. 41%, CME 13% vs. 33%). Our findings that reductions in insulin and IRI were greater in South Asians than in white Europeans also extends evidence from two previous studies exploring the impact of regular light-intensity walking to break prolonged sitting (26,32). In these previous analyses, reductions in insulin and IRI after light-intensity walking were greater in South Asians compared to white Europeans. However, post-walking concentrations in South Asians were still similar to prolonged sitting in white Europeans (26,32). In the current study, the effects of LV-HIIE and CME on circulating insulin and IRI were not only greater in South Asians, but greater to the extent that values were similar in both ethnicities during respective exercise conditions. This experimental finding supports observational evidence that physical inactivity and low CRF may be prominent factors contributing to the excess risk of insulin resistance and cardiovascular disease in South Asians (23,24). This study, therefore, adds to mounting evidence highlighting the public health importance of targeting low levels of physical activity and CRF in South Asian communities, to address inequalities in cardiometabolic health. Furthermore, it suggests that both CME and LV-HIIE are effective at acutely improving insulin resistance in South Asians, supporting an evidence-base that allows for greater personalisation of exercise interventions in South Asian communities.

Whilst fasted NEFA and TG concentrations were higher in South Asians in the current study, as previously reported (26,27), neither were affected by exercise. This is likely due to the duration of observation in the current study, which was limited to 4 hours post-exercise. Evidence suggests that the impact of acute exercise on post-prandial lipid metabolism may only become apparent when examined several hours later (10).

Important strengths of this study include the fully-powered randomised crossover design, with strict standardisation procedures and robust analytical methods in a multi-ethnic population. Whilst acknowledging that the intended sample size to allow full counterbalancing was not reached (*n*=24), we emphasise that the number of participants recruited met the minimum required according to our *a priori* sample size calculation (total *n* ≥22, *n* ≥8 per group). Certain limitations and consequences of our study design are also noteworthy. Experimental procedures were performed in a laboratory setting, thus limiting ecological validity. Our results also predominantly reflect changes in post-prandial metabolism, as participants were fed twice within the 6-hour conditions (approximately 90 minutes prior to the exercise bouts and 1 hour following them). Participants were middle-aged to older adults (range 50 to 73 years) and thus results cannot be generalised to younger or older individuals. Similarly, we recruited a migrant South Asian population living in the UK. Therefore, results may not be generalisable to South Asians living elsewhere, particularly in low- or middle-income countries. Some differences in participant characteristics between groups were apparent (most prominently age, sex distribution, systolic blood pressure and obesity prevalence). Age and sex were included *a priori* as covariates within our statistical analysis plan, but nevertheless the potential for other between-group differences to confound our results cannot be excluded. Most prominently, this study examined the effects of a single bout of LV-HIIE and CME. Whilst each have been shown to elicit cardiometabolic benefits for individuals with NDH or T2D when performed regularly (i.e. exercise training) (6–12,14,15), data in South Asians are lacking and evidence from other ethnic groups or multi-ethnic cohorts may not be generalisable. Cultural sensitivity in terms of appeal, uptake and sustainability of different physical activity/exercise interventions also remains an essential consideration. Therefore, trials examining the long-term impact of different approaches to promoting physical activity and structured exercise in South Asians, including LV-HIIE and CME, are greatly needed.

In conclusion, a single bout of LV-HIIE or CME reduces circulating insulin concentrations and IRI, but not glucose or lipids, for up to 4 hours post-exercise in white European and South Asian men and women with NDH. Greater effects were observed in South Asians to the extent that values for insulin and IRI were similar in each ethnicity during respective exercise conditions, despite 30% higher responses during prolonged sitting in South Asians. Intervention trials specifically in South Asians are required to assess the efficacy and effectiveness of LV-HIIE and CME over a prolonged period to further examine their potential to improve cardiometabolic health in this high-risk group.

**Acknowledgements**

Funding statement

This research was supported by the NIHR Leicester Biomedical Research Centre and the NIHR Applied Research Collaboration East Midlands.

Conflicts of interest statement

JAS and TY have received a grant in support of an investigator-initiated trial from AstraZeneca, unrelated to the current study. KK chaired the Public Health Guidance on Detection and Prevention of Diabetes. MJD has acted as consultant, advisory board member and speaker for Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca and Janssen, an advisory board member for Servier and Gilead Sciences Ltd and as a speaker for NAPP, Mitsubishi Tanabe Pharma Corporation and Takeda Pharmaceuticals International Inc. She has received grants in support of investigator and investigator-initiated trials from Novo Nordisk, Sanofi-Aventis, Lilly, Boehringer Ingelheim, AstraZeneca and Janssen. CJ, NAC, CLE, JH, JAK, MM, AR, DJS, HLW and DRW have no conflicts of interest to disclose.

Author contributions

CJ, KK, MJD, and TY generated the study idea and designed the protocol. JAS, CJ, NAC, CLE, JH, JAK, MM, AVR and HLW contributed to data collection and/or analysis of study outcomes. JAS and TY performed and interpreted the data analysis and drafted the manuscript. CJ, NAC, CLE, JH, JAK, KK, MM, AVR, DJS, HLW, DRW and MJD reviewed the manuscript providing substantial academic and/or clinical input. All authors approved the final manuscript. ﻿JAS is the guarantor of the work and as such had full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior publication

The study formed part of Charlotte Jelleyman’s PhD studentship, with preliminary data presented in her thesis. An abstract of study findings was accepted for publication at American College of Sports Medicine Annual Meeting 2020; whilst these were not presented due to the COVID-19 pandemic, the abstract will be published in a supplementary issue of *Diabetologia*.

**References**

1. International Diabetes Federation. IDF Diabetes Atlas, 8th Edition, 2017.

2. Davies MJ, D’Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, et al. Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2018;41(12):2669–2701.

3. Gregg EW, Cheng YJ, Srinivasan M, Lin J, Geiss LS, Albright AL, et al. Trends in cause-specific mortality among adults with and without diagnosed diabetes in the USA: an epidemiological analysis of linked national survey and vital statistics data. Lancet. 2018;391:2430–2440.

4. Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: A high-risk state for diabetes development. Lancet. 2012;379(9833):2279–2290.

5. O’Keefe JH, Bell DSH. Postprandial hyperglycemia/hyperlipidemia (postprandial dysmetabolism) is a cardiovascular risk factor. Am J Cardiol. 2007;100(5):899–904.

6. Balk EM, Earley A, Raman G, Avendano EA, Pittas AG, Remington PL. Combined diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk: A systematic review for the community preventive services task force. Ann Intern Med. 2015;163(6):437–451.

7. Gill JMR, Cooper AR. Physical activity and prevention of type 2 diabetes mellitus. Sport Med. 2008;38(10):807–824.

8. Umpierre D, Ribeiro PA, Kramer CK, Leitao CB, Zucatti AT, Azevedo MJ, et al. Physical activity advice only or structured exercise training and association with HbA 1c levels in type 2 diabetes: A systematic review and meta-analysis. JAMA. 2011;305(17):1790–1799.

9. Kodama S, Tanaka S, Saito K, Shu M, Sone Y, Onitake F, et al. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. Arch Intern Med. 2007;167(10):999–1008.

10. Gill JMR. Exercise and postprandial lipid metabolism - an analysis of the current evidence. Eur J Lipid Sci Technol. 2004;106(2):110–121.

11. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care. 2016;39(11):2065–2079.

12. American Diabetes Association. 3. Prevention or delay of type 2 diabetes: standards of medical care in diabetes-2020. Diabetes Care. 2020;43(Suppl 1):S32–36.

13. Gillen J, Gibala M. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? Appl Physiol Nutr Metab. 2014;39(3):409–412.

14. Weston KS, Wisløff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. Br J Sports Med. 2014;48:1227–1234.

15. Jelleyman C, Yates T, O’Donovan G, Gray LJ, King JA, Khunti K, et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. Obes Rev. 2015;16(11):942–961.

16. Gibala MJ, Little JP, Macdonald MJ, Hawley JA. Physiological adaptations to low-volume, high-intensity interval training in health and disease. J Physiol. 2012;590(5):1077–1084.

17. Little JP, Gillen JB, Percival ME, Safdar A, Tarnopolsky MA, Punthakee Z, et al. Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes. J Appl Physiol. 2011;111(6):1554–1560.

18. Afousi AG, Izadi MR, Rakhshan K, Mafi F, Biglari S, Gandomkar Bagheri H. Improved brachial artery shear patterns and increased flow-mediated dilatation after low-volume high-intensity interval training in type 2 diabetes. Exp Physiol. 2018;103(9):1264–1276.

19. Winding KM, Munch GW, Iepsen UW, Van Hall G, Pedersen BK, Mortensen SP. The effect on glycaemic control of low-volume high-intensity interval training versus endurance training in individuals with type 2 diabetes. Diabetes, Obes Metab. 2018;20(5):1131–1139.

20. RezkAllah SS, Takla MK. Effects of different dosages of interval training on glycemic control in people with prediabetes: a randomized controlled trial. Diabetes Spectr. 2019;32(2):125–131.

21. Sattar N, Gill JMR. Type 2 diabetes in migrant south Asians: mechanisms, mitigation, and management. Lancet Diabetes Endocrinol. 2015;3:1004–1016.

22. Paul SK, Owusu Adjah ES, Samanta M, Patel K, Bellary S, Hanif W, et al. Comparison of body mass index at diagnosis of diabetes in a multi-ethnic population: a case-control study with matched non-diabetic controls. Diabetes, Obes Metab. 2017;19(7):1014–1023.

23. Ghouri N, Purves D, McConnachie A, Wilson J, Gill JMR, Sattar N. Lower cardiorespiratory fitness contributes to increased insulin resistance and fasting glycaemia in middle-aged South Asian compared with European men living in the UK. Diabetologia. 2013;56(10):2238–2249.

24. Williams ED, Stamatakis E, Chandola T, Hamer M. Physical activity behaviour and coronary heart disease mortality among South Asian people in the UK: An observational longitudinal study. Heart. 2011;97(8):655–659.

25. Iliodromiti S, Ghouri N, Celis-Morales CA, Sattar N, Lumsden MA, Gill JMR. Should physical activity recommendations for south Asian adults be ethnicity-specific? Evidence from a cross-sectional study of south Asian and white European men and women. PLoS One. 2016;11(8):e0160024.

26. Yates T, Edwardson CL, Celis-Morales C, Biddle SJH, Bodicoat D, Davies MJ, et al. Metabolic effects of breaking prolonged sitting with standing or light walking in older South Asians and White Europeans: a randomized acute study. J Gerontol A Biol Sci Med Sci. 2020;75(1):139-146.

27. Arjunan SP, Bishop NC, Reischak-Oliveira A, Stensel DJ. Exercise and coronary heart disease risk markers in south Asian and European men. Med Sci Sports Exerc. 2013;45(7):1261–1268.

28. Migueles JH, Cadenas-Sanchez C, Rowlands AV., Henriksson P, Shiroma EJ, Acosta FM, et al. Comparability of accelerometer signal aggregation metrics across placements and dominant wrist cut points for the assessment of physical activity in adults. Sci Rep. 2019;9:18235.

29. Borg G. Percieved exertion as an indicator of somatic stress. Scand J Rehab Med. 1970;2(2):92–98.

30. Little JP, Jung ME, Wright AE, Wright W, Manders RJF. Effects of high-intensity interval exercise versus continuous moderate-intensity exercise on postprandial glycemic control assessed by continuous glucose monitoring in obese adults. Appl Physiol Nutr Metab. 2014;39(7):835–841.

31. Francois ME, Baldi JC, Manning PJ, Lucas SJE, Hawley JA, Williams MJA, et al. “Exercise snacks” before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance. Diabetologia. 2014;57(7):1437–1445.

32. Henson J, Edwardson CL, Celis-Morales CA, Davies MJ, Dunstan DW, Esliger DW, et al. Predictors of the Acute Postprandial Response to Breaking Up Prolonged Sitting. Med Sci Sport Exerc. 2020;52(6):1385-1393.

33. Rynders CA, Weltman JY, Jiang B, Breton M, Patrie J, Barrett EJ, et al. Effects of exercise intensity on postprandial improvement in glucose disposal and insulin sensitivity in prediabetic adults. J Clin Endocrinol Metab. 2014;99(1):220–228.

34. Van Dijk JW, Venema M, Van Mechelen W, Stehouwer CDA, Hartgens F, Van Loon LJC. Effect of moderate-intensity exercise versus activities of daily living on 24-hour blood glucose homeostasis in male patients with type 2 diabetes. Diabetes Care. 2013;36(11):3448–3453.

35. Gillen J, Little J, Punthakee Z, Tarnopolsky M, Riddell M, Gibala M. Acute high-intensity interval exercise reduces the postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. Diabetes, Obes Metab. 2012;14:575–577.

36. Hatamoto Y, Goya R, Yamada Y, Yoshimura E, Nishimura S, Higaki Y, et al. Effect of exercise timing on elevated postprandial glucose levels. J Appl Physiol. 2017;123(2):278–284.

37. Douglas JA, King JA, Clayton DJ, Jackson AP, Sargeant JA, Thackray AE, et al. Acute effects of exercise on appetite, ad libitum energy intake and appetite-regulatory hormones in lean and overweight/obese men and women. Int J Obes. 2017;41(12):1737–1744.

38. Arjunan SP, Deighton K, Bishop NC, King J, Reischak-Oliveira A, Rogan A, et al. The effect of prior walking on coronary heart disease risk markers in South Asian and European men. Eur J Appl Physiol. 2015;115(12):2641–2651.

39. Trefts E, Williams AS, Wasserman DH. Exercise and the regulation of hepatic metabolism. Prog Mol Biol Transl Sci. 2015;135:203–225.

40. Pyörälä M, Miettinen H, Laakso M, Pyörälä K. Plasma insulin and all-cause, cardiovascular, and noncardiovascular mortality: the 22-year follow-up results of the Helsinki Policemen Study. Diabetes Care. 2000;23(8):1097–1102.

**Tables**

*Table 1*–Participant characteristics of the whole study population and stratified by ethnicity

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | All | | | White European | | | South Asian | | |
|  | **(n = 23)** | | | **(n = 13)** | | | **(n = 10)** | | |
| Sex (M / F) | 13 / 10 | | | 6 / 7 | | | 7 / 3 | | |
| *Anthropometry* |  |  |  | |  |  | |  |  |
| Age (years) | 67 (60 – 68) | | | 68 (66 – 70) | | | 59 (52 – 67) | | |
| Body weight (kg) | 80.5 (71.9 – 93.8) | | | 84.6 (75.5 – 91.2) | | | 78.7 (68.9 – 96.1) | | |
| BMI (kg·m-2) | 30.0 (28.4 – 32.8) | | | 28.8 (28.4 – 32.8) | | | 30.6 (26.7 – 32.3) | | |
| Obesity prevalence (*n* (%)) \* | 13 (57%) | | | 6 (46%) | | | 7 (70%) | | |
| Waist circumference (cm) † | 100.8 (97.6 – 109.1) | | | 101.6 (98.0 – 106.9) | | | 99.5 (95.0 – 109.5) | | |
| *Glycaemic Control and Insulin Sensitivity* |  |  |  | |  |  | |  |  |
| HbA1c (%) | 5.9 (5.8 – 6.1) | | | 5.9 (5.8 – 6.0) | | | 6.1 (6.0 – 6.1) | | |
| HbA1c (mmol·mol-1) | 41.0 (39.9 – 43.2) | | | 41.0 (39.3 – 42.1) | | | 42.6 (41.8 – 43.2) | | |
| Fasted plasma glucose (mmol·L-1) | 5.3 (5.0 – 5.6) | | | 5.3 (5.1 – 5.7) | | | 5.4 (5.0 – 5.6) | | |
| Fasted plasma insulin (mU·L-1) | 12.6 (8.8 – 16.9) | | | 10.7 (8.6 – 18.7) | | | 15.4 (10.0 – 17.8) | | |
| HOMA-IR | 3.09 (2.11 – 4.31) | | | 2.97 (1.93 – 4.20) | | | 3.38 (2.39 – 4.35) | | |
| Fasted plasma NEFA (mmol·L-1) | 0.47 (0.35 – 0.59) | | | 0.56 (0.40 – 0.65) | | | 0.40 (0.35 – 0.51) | | |
| Adipo-IR | 37.5 (24.2 – 47.5) | | | 37.5 (27.1 – 49.3) | | | 39.3 (20.1 – 50.4) | | |
| *Blood Pressure and Circulating Lipids* |  |  |  | |  |  | |  |  |
| Systolic blood pressure (mmHg) | 136 (118 – 140) | | | 140 (133 – 141) | | | 124 (112 – 140) | | |
| Diastolic blood pressure (mmHg) | 79 (75 – 86) | | | 80 (76 – 89) | | | 76 (71 – 84) | | |
| Total Cholesterol (mmol·L-1) † | 5.1 (4.5 – 5.7) | | | 5.3 (4.4 – 5.6) | | | 5.1 (4.6 – 6.0) | | |
| HDL (mmol·L-1) † | 1.40 (1.15 – 1.60) | | | 1.50 (1.30 – 1.70) | | | 1.30 (1.08 – 1.40) | | |
| Fasted plasma TG (mmol·L-1) | 1.63 (1.25 – 2.36) | | | 1.37 (1.21 – 2.26) | | | 1.74 (1.44 – 2.75) | | |
| *Physical Activity, Fitness, Sedentary Behaviour and Sleep* |  | | |  | | |  | | |
| Absolute *V*̇̇O2 peak (L·min-1) | 2.09 (1.75 – 2.38) | | | 2.21 (1.83 – 2.37) | | | 1.96 (1.68 – 2.41) | | |
| Relative *V*̇̇O2 peak (mL·kg-1·min-1) | 25.0 (21.7 – 27.5) | | | 25.4 (21.9 – 28.8) | | | 25.0 (21.4 – 28.3) | | |
| Sleep duration (min per day) † | 375 (341 – 436) | | | 393 (357 – 472) | | | 343 (293 – 408) | | |
| Sedentary time (min per day) † | 656 (610 – 724) | | | 691 (617 – 709) | | | 611 (596 – 805) | | |
| Light intensity physical activity (min per day) † | 166 (133 – 233) | | | 162 (130 – 201) | | | 170 (154 – 263) | | |
| MVPA (min per day in bouts ≥10 min)† | 5.4 (3.2 – 17.8) | | | 6.0 (5.1 – 24.5) | | | 2.5 (0.0 – 15.4) | | |

Data for continuous and categorical outcomes presented as median (IQR) and frequencies, respectively. \* ethnicity-specific BMI thresholds were used to categorise obesity prevalence (BMI ≥30.0 kg·m-2 and ≥27.5 kg·m-2 in white European and South Asian groups, respectively). **†**indicate data not available for all participants; waist circumference: *n* = 22 (1 South Asian female missing), total cholesterol and HDL: *n* = 21 (1 white European male and 1 white European female missing); all sleep, sedentary behaviour and activity variables: *n* = 18 (2 white European males, 2 white European females and 1 South Asian female missing).

Abbreviations: Adipo-IR: adipose tissue insulin resistance index; BMI: body mass index; F: female; HbA1c: glycated haemoglobin; HDL: high-density lipoprotein; HOMA-IR: homeostatic model assessment of insulin resistance; M: male; MVPA: moderate-to-vigorous physical activity; NEFA: non-esterified fatty acids; TG: triglyceride; *V*̇̇O2 peak: peak oxygen uptake.

*Table 2* **–** Post-exercise responses for glucose, insulin, insulin resistance index, triglycerides and non-esterified fatty acids during each condition in each ethnicity group

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **White European** | | |  | **South Asian** | | |  | ***p*-values** | | |
|  |  | *CON* | *LV-HIIE* | *CME* |  | *CON* | *LV-HIIE* | *CME* |  | *trt* | *eth* | *int* |
| *Primary outcome* |  |  |  |  |  |  |  |  |  |  |  |  |
| Glucose (mmol·L-1) |  | 7.29 (6.35, 8.22) | 7.27 (6.40, 8.13) | 7.15 (6.20, 8.11) |  | 6.68 (5.88, 7.49) | 6.37 (5.88, 6.85) | 6.42 (5.91, 6.93) |  | 0.51 | 0.28 | 0.58 |
| *Secondary outcomes* |  |  |  |  |  |  |  |  |  |  |  |  |
| Insulin (mU·L-1) |  | 119.7 (92.8, 146.7) | 96.5 (76.3, 116.7)\*\*\* | 104.1 (87.0, 121.2)\* |  | 159.7 (112.4, 207.0) | 94.1 (74.9, 113.3) **†††** | 107.7 (81.3, 134.0) **†** |  | **<0.001** | 0.45 | **0.03** |
| Insulin resistance index (AU) |  | 874 (658, 1091) | 717 (533, 900)\*\*\* | 755 (586, 925)\* |  | 1115 (708, 1521) | 584 (431, 736) **††** | 689 (484, 894) **†** |  | **<0.001** | 0.93 | **0.03** |
| Triglycerides (mmol·L-1) |  | 1.97 (1.83, 2.11) | 2.03 (1.83, 2.24) | 1.95 (1.71, 2.19) |  | 2.20 (1.91, 2.50) | 2.18 (2.00, 2.36) | 2.25 (2.00, 2.50) |  | 0.95 | 0.17 | 0.09 |
| Non-esterified fatty acids (mmol·L-1) |  | 0.08 (0.04, 0.12) | 0.12 (0.08, 0.16) | 0.16 (0.11, 0.21)\* |  | 0.19 (0.15, 0.22) | 0.19 (0.15, 0.22) | 0.18 (0.14, 0.23) |  | 0.26 | **0.01‡** | 0.16 |

Data presented as mean (95% confidence interval) time-averaged area under the curve; models were adjusted age, sex and pre-exercise AUC; *p*-values are for analyses performed with all data combined (i.e. the entire study population) (trt: effect of treatment condition; eth: effect of ethnicity; int: treatment-by-ethnicity interaction); \*/**†** indicate significant difference from CON condition *within* ethnicity group (\*/**†***p* < 0.05, \*\*/**††***p* < 0.01, \*\*\*/**†***p* ≤ 0.001).; ‡ pairwise comparison: white European: 0.12 (0.09, 0.15) vs. South Asian: 0.18 (0.15, 0.22). Data for each condition in the combined population can be found in Supplemental Table S1.

Abbreviations: AU: arbitrary units; CME: continuous moderate-intensity aerobic exercise conditions; CON: seated, rested control condition; LV-HIIE: low-volume high-intensity interval exercise condition.

**Figure Legends**

*Figure 1 –* Circulating glucose (A-B) and insulin (C-D) responses across experimental conditions for white European (left; filled symbols) and South Asian (right; open symbols) groups

Data are presented as mean (standard error of the mean).

Abbreviations: CME: continuous moderate-intensity aerobic exercise condition; CON: control condition; LV-HIIE: low-volume high-intensity interval exercise.

*Figure 2* – Post-exercise response of the insulin resistance index during each condition in each ethnicity group

Data presented as mean (95% confidence interval); For ease of interpretation, data are normalised to the estimated marginal mean of the adjusted post-exercise AUC during the CON condition in the white European group. \*/# indicate significant differences from the CON condition within each ethnicity group (\*/#*p* < 0.05, \*\*/##*p* < 0.01, \*\*\*/###*p* ≤ 0.001).

Abbreviations: CME: continuous moderate-intensity aerobic exercise condition; CON: control condition; LV-HIIE: low-volume high-intensity interval exercise.