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# Sex differences in postprandial glucose response to short bouts of exercise: A randomized controlled trial

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ABSTRACT

*Objectives:* The objective of this study was to assess sex differences in PPG responses to short stair stepping bouts, and to describe their intensity and metabolic cost.
*Design:* Crossover trial.
*Methods:* 34 participants (age: 25.9 ± 5.5 y; women = 14) underwent 4 oral glucose tolerance tests (OGTT) during rest or with stair-stepping bouts at self-selected, moderate pace for 1, 3, and 10 min. Blood was collected every 15 min during the OGTTs and assessed for glucose. Participants also underwent maximal aerobic capacity assessment. Expired gases were collected during capacity testing, and each stair-stepping bout.
*Results:* Normalized to body weight there was no significant interaction for sex with stair-stepping trials ($p = 0.445$, $\eta_p^2 = 0.03$), or time ($p = 0.069$, $\eta_p^2 = 0.09$), or trial by time ($p = 0.264$, $\eta_p^2 = 0.04$). Women had higher mean glucose values than men (15(CI = 3, 27)%, $p = 0.015$). iAUC also showed no interaction of sex*trial ($p = 0.059$, $\eta_p^2 = 0.09$). Women had higher iAUC values ($mean\Delta = -29(-48, -11)$%, $p = 0.003$). There was a main effect for trial with 10min showing the largest reduction from control for women (e.g. AUC −10(−6, −13)%, $p < .001$) and men (−8(2, 13)%, $p = .010$). Metabolic cost of the stair stepping bouts showed no interaction of sex*trial ($p = 0.715$, $\eta_p^2 = 0.01$) and no difference between sexes ($mean\Delta = -1.3(-5.9, 3.4)$%, $p = 0.571$). Intensity was higher for women for the 3 min (60 ± 11 vs. 48 ± 9%$VO_2$max, $p = 0.003$) and 10 min (67 ± 8 vs. 54 ± 12%$VO_2$max, $p = 0.002$) bouts. Moreover, both sexes underestimated the true intensity of stepping.
*Conclusions:* Both sexes had similar responses to short bouts of exercise, which they perceived as less intense than indicated by objective assessment. Stair stepping reduces postprandial glucose response with similar effectiveness for both sexes.
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## 1. Introduction

Women have been understudied in biomedical science.[1,2] Often times it is assumed that their responses are the same as men, but that is not always the case.[2,3] Sex differences in physiological responses are often underappreciated because there is insufficient data on when they occur, what their effect sizes are, and what caused them.[1] One area where sex differences exist is macronutrient processing including glucose uptake and metabolism.[4,5] Postprandial glucose is a particularly suitable marker for disease risk assessment as it is independently associated with developing metabolic complications including cardiovascular disease, diabetes, and obesity.[6] For people who do not have overt diabetes, the association of postprandial glucose and disease risk is even larger than for HbA1c.[7] Since the relationship of postprandial glucose and disease risk is continuous, lowering postprandial glucose is beneficial regardless of threshold values.[8] Decreasing post-meal hyperglycemia is therefore a beneficial strategy for lowering disease risk for prediabetic, diabetic, and apparently healthy individuals.[7,9,10] This has important implications for disease risk and an urgent need for the study of sex differences related to the prevention of metabolic disease has been identified.[5,11]

Sex differences in postprandial glucose responses have been reported but may be influenced by fitness levels and/or body size.[5,12,13] Further, there are also sex differences in response to

*Abbreviations:* AUC, area under the curve; BMI, body mass index; CHO, carbohydrate; GE, gross efficiency; HbA1c, glycated hemoglobin; iAUC, incremental area under the curve; OGTT, oral glucose tolerance test; PPG, postprandial blood glucose; RPE, rating of perceived exertion; $VO_2$max, maximal oxygen consumption.

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**Table 1**
Baseline descriptive values for each sex.

| | Male | Female | *p*-Value |
|---|---|---|---|
| Age (y) | 26.8 ± 6.0 | 24.8 ± 4.5 | 0.309 |
| BMI (kg/m$^2$) | 24.7 ± 2.8 | 24.3 ± 3.1 | 0.669 |
| Weight (kg) | 78.4 ± 1.8 | 64.9 ± 10.04 | 0.002* |
| $VO_{2peak}$ (mL/kg/min) | 44.1 ± 6.1 | 37.9 ± 5.4 | 0.006* |
| Fasting glucose (mg/dL) | 113 ± 12 | 106 ± 9 | 0.058 |

Values are *mean* ± *SD*.
* Significant difference between sexes.

exercise, with women oxidizing more fats, fewer carbohydrates, and producing less hepatic glucose.[4,14,15] For each sex, many factors influence these responses including exercise duration and intensity. An increasing area of interest regarding exercise's effects on postprandial glucose and subsequent disease risk are short, low to moderate intensity exercise interventions aimed to interrupt long periods of sedentary behaviors such as sitting.[16–18] Little is known about sex differences in postprandial glucose response to these types of exercise interventions. Two recent studies explored sex differences and found that women had larger reductions in postprandial glucose with repeated light-moderate intensity, short walking bouts.[18,19] However the authors diligently warn readers that results should be viewed with caution due to low sample sizes and that further investigation is needed.[16,18] We therefore investigated sex differences in postprandial glucose response during stair stepping bouts at self-selected pace and progressively shorter duration, as well as describe the intensity, metabolic cost, and substrate utilization patterns of these bouts. We hypothesized that women would show larger reductions in their postprandial glucose response with stair stepping compared to men.

## 2. Methods

Thirty-four healthy adult participants (males n = 20; females n = 14) with normal fasting glucose values were recruited for the study by the principal investigator and research assistants between October 2016 and August 2017. Descriptive statistics are in Table 1. Two participants did not complete the study due to scheduling difficulty. All participants were categorized as low risk for exercise participation according to American College of Sports Medicine guidelines.[20] Prior to the study, participants completed Physical Activity Recall Questionnaires in order to screen for cardiovascular risk. Fasting blood glucose was measured using a finger-stick glucometer and targeted at values between 80–130 mg/dL as established by the American Diabetes Association. Participants outside of this range were excluded. All participants gave written informed consent. This study was approved by the Institutional Review Board at San Diego State University.

In this randomized controlled, crossover-design trial, subjects visited the lab 5 times. Prior to participating in all trials, participants donned a chest strap heart rate monitor (Polar T31, Polar USA) and sat quietly for 5 min. During the first visit, maximal aerobic capacity ($VO_{2max}$) was determined using a treadmill ramp exercise test until volitional exhaustion. During stage 1 participants walked for 3 min at 3.5mph with a 1% grade. During stage 2, speed and grade were increased to 4mph and 2%, respectively for 1 min. Hereafter, speed and grade were increased by 1mph and 1% for every subsequent 1-min stage. Once speed reached a maximum of 7mph, grade was increased by 1% during each stage until volitional exhaustion.

Prior to all follow up trials, participants were required to fast overnight for at least ten hours, with no restriction on water intake. Caffeine was also restricted during the fasting period. Within one week following max testing, participants returned to the lab for a 60-min resting oral glucose tolerance test (OGTT), serving as the control condition. At the beginning of each OGTT, baseline blood glucose values were obtained from capillarized blood via finger-stick and measured with an over-the-counter glucometer (Nova Max Plus, Nova Biomedical Corp.). Participants then consumed 75 g of dextrose powder mixed into 16oz of water, within ≤5 min. Subsequent blood measurements were taken every 15 min for one hour. At each blood measurement, several samples were obtained until two values were no more than 15 mg/dL apart in accordance with requirements set by the International Organization for Standardization pertaining to blood-glucose monitoring systems (ISO: 15197:2013).

All remaining trials were randomized using a free, open, online random number generator and consisted of an OGTT combined with 1, 3, or 10 min of moderate intensity stair climbing/descending at a self-selected cadence. Following their control trial, participants had been asked to self-select a moderate stepping pace of 90–110 steps per minute, which they thought they could maintain comfortably for ten minutes. This pace was held constant across all trials. A digital metronome was used to set the pace during each trial. Stair climbing bouts started at 18, 25, or 27 min once the dextrose solution had been finished for the 10, 3, and 1-min trials, respectively. This was to allow for blood collection and measurement at the 30-min time point. The stair climbing/descending was done continuously in a stairwell of 21 steps. Rating of perceived exertion (RPE) was provided by participants based on the 1–10 Borg scale. All laboratory visits were conducted at the same time of day 24 h to one week apart and participants were asked to maintain similar exercise and diet habits 48 h prior to each trial.

Expired gases were collected continuously throughout the treadmill max test, and 5 min before, during, and 15 min after stair stepping using a softmask worn by the participants. Respired gases were analyzed via open-circuit indirect calorimetry (K4B$^2$ Mobile Metabolic Analyzer, Cosmed, USA or Oxycon Mobile, CareFusion Corporation, CA, USA).

%$VO_2$peak was determined by dividing the highest oxygen consumption rate of a 15 breath running average[21] over the entire measurement period by $VO_2$peak.

$VO_2$ and $VCO_2$ measurements during the last 3 min of the 10 min bout were used to calculate fat and carbohydrate used during the exercise (assuming negligible contribution of protein oxidation), using stoichiometric formulae based on exercise intensity as previously described.[22]

$$\text{Fat (g/min)} = 1.695 \times VO_2 - 1.701 \times VCO_2$$

$$\text{CHO (g/min)} = 4.210 \times VCO_2 - 2.962 \times VO_2 (50\text{–}75\%\, VO_2 max) \text{ or}$$

$$4.344 \times VCO_2 - 3.061 \times VO_2 (40\text{–}50\%\, VO_2 max)$$

If the respiratory exchange ratio was greater than 1, fat oxidation rate was set to 0.

Gross efficiency (GE) was calculated as Work performed/Oxygen consumed, where Work performed was calculated as steeping rate (steps per min) * step height (18 cm) * 0.5 * stepping time (min) * force (i.e. body weight). Conversion factor for $O_2$ consumed to kcal was 5 kcal/l.

Statistical analyses were performed using SPSS, version 24. Data were normalized to body weight to account for size differences except for those measurements that are dependent on body weight (i.e. relative $VO_2$max and gross mechanical efficiency) or categorical (i.e. RPE). Tests of Normality were conducted with the Shapiro–Wilk test using the Bonferroni correction for multiple comparisons. Data were analyzed using a 4 (trial) × 5 (time) × 2 (sex) three-way analysis of variance (ANOVA) with repeated measures and LSD adjustments for post hoc pairwise comparisons tests. Violations of the assumption of sphericity were adjusted with the

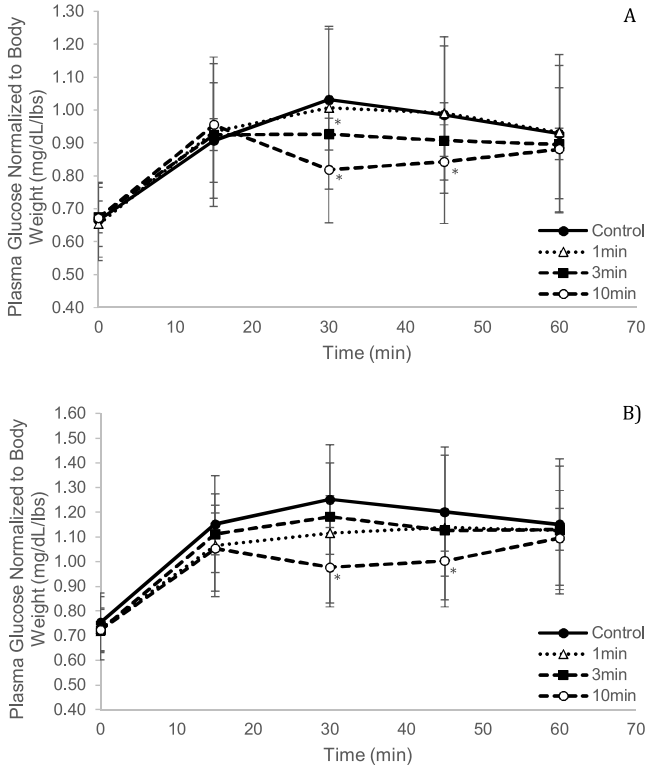


**Fig. 1.** Plasma glucose responses for (A) men and (B) women.
*Indicates significant difference from control ($p < 0.05$).

Greenhouse–Geisser correction if estimated epsilon ($\varepsilon$) was <0.75 or undefined and the Huynh–Feldt correction if >0.75.

Categorical data (RPE) were analyzed for sex difference with the non-parametric Mann–Whitney test for each stair stepping trial.

The $\alpha$-level was set a priori at 0.05 to determine statistical significance for this secondary analysis of an existing data set. Values are presented as *mean* (95%*CI*) for outcomes of inferential statistical analysis, *mean* ± *SD* for descriptives and *median* (*IQR*) for non-parametric analysis.

## 3. Results

For plasma glucose values, there was no significant interaction of sex with trial ($p = 0.445$, $\eta_p^2 = 0.03$), or time ($p = 0.069$, $\eta_p^2 = 0.09$), or trial by time ($p = 0.264$, $\eta_p^2 = 0.04$), thus indicating a similar postprandial glucose response in both sexes.

There was a significant difference between sexes. Plasma glucose at each time point during the OGTT was on average 15% lower in men than women ($p = 0.015$, *mean*Δ (men–women) = −15(−27,−3)%, Fig. 1).

For AUC values, there was no significant interaction of sex with trial ($p = 0.215$, $\eta_p^2 = 0.05$) but again significant difference between sexes ($p = 0.019$, *mean*Δ = −14(−26, −3)%, Fig. 2A). iAUC showed no significant interaction of sex with trial ($p = 0.059$, $\eta_p^2 = 0.09$). There was a significant difference between sexes ($p = 0.003$, *mean*Δ = −29(−48, −11)%, Fig. 2B.

RPE for the 1 min bout was significantly higher for women (1.0(0.5) vs. men (1.0(1.8), $U = 49.5$, $p = 0.037$, but not for the 3 or 10 min bouts ($U = 86.5$–$96.5$, $p = 0.801$–$0.939$, Fig. 2C).

Objective intensity for men for 1 vs. 3 vs. 10 min bout was 41%(35, 47) vs. 47%(41, 52, $p = 0.031$) vs. 51%(44, 59, $p = 0.005$), respectively. Objective intensity for women for 1 vs. 3 vs. 10 min bout was 47%(39, 56) vs. 61%(53, 69, $p = 0.004$) vs. 67%(62, 73, $p = 0.052$), respectively.

For $\%VO_2$peak there was a significant interaction of sex with trial ($p = 0.021$, $\eta_p^2 = 0.16$). Women performed stair stepping at a higher percentage of their maximal values compared to men for the 3 ($p = 0.003$) and 10 min bouts ($p = 0.002$) but not the 1 min bout ($p = 0.143$, Fig. 2D).

For $O_2$ consumed there was no significant interaction of sex with trial ($p = 0.715$, $\eta_p^2 = 0.01$) and no difference between sexes ($p = 0.571$, *mean*Δ = −1.3(−5.9, 3.4)%). There was also no significant difference in substrate utilization patterns (independent of body weight, fat oxidation *mean*Δ = −7(−17, 3)%, $p = 0.189$, carbohydrate oxidation *mean*Δ = 7(−4, 16)%, $p = 0.193$ or gross efficiency (not normalized to BW, trial by sex interaction: $p = 0.276$, $\eta_p^2 = 0.05$; difference between sexes: $p = 0.979$, *mean*Δ = −0.1(−5.2, 5.1)%).

## 4. Discussion

Contrary to our hypothesis, the results of the current study indicate that after adjusting for weight, men and women showed similar postprandial glucose and metabolic responses following single, short moderate intensity stair stepping bouts. Short, simple exercise bouts are of interest as they can reduce disease risk by countering the detrimental effects of sedentary behaviors such as sitting.[16–18] We purposefully selected stair climbing/descending for several reasons. It is simple, cheap, easy, and familiar to most people. We also found that both men and women underestimated the true intensity of stair stepping. These considerations are noteworthy because the most common barriers to exercise include intensity, perceived discomfort, transport, money, facilities, time, and self-efficacy.[21,23,24] These issues are not applicable for single, short stair stepping at a self-selected intensity, of which participants perceived as very light to light, at least for (the majority) of the general population.

Few other studies have investigated sex differences of short, moderate intensity exercise bouts.[16,18] Bhammar et al.[16] and Dempsey et al.[18] report larger reductions in postprandial glucose for women with repeated bouts of light intensity walking either with a standard meal load or intake adjusted for body weight.[16,18] One of the two studies reported differences, which, while large, did not result in a significant interaction of condition and sex, and the authors warn the reader of a potential type 1 error of their outcome. We also did not observe significant interactions of trials and sex with glucose responses and while there was a strong trend for the iAUC values, exploratory simple effects analysis revealed no significant discrepancies for declines compared to control between sexes ($p = 0.069$–$0.567$). There are notable differences between these previous studies and ours. Firstly, previous studies investigated overweight/obese and/or diabetic participants. These participants showed higher postprandial glucose excursion, which left more room for improvement with exercise. However, we did see significant reductions for both sexes with the 10 min bout thereby ensuring the absence of an absolute flooring effect. There are also differences in the meal provided among the studies. Bhammar et al.[16] provided 2 fixed mixed meals (130 and 68 g of CHO) and snacks (19 g of CHO), while Dempsey et al.[18] provided repeated meals adjusted to estimated energy expenditure (mean CHO load 113–119 g/meal). Our study provided a standard oral glucose tolerance test load (75 g glucose). The overall glucose load was therefore substantially lower in our study and reductions may be proportionally smaller masking sex interactions that may occur with larger loads. However, a 75 g glucose load is standard for an OGTT irrespective of sex and should introduce less variability associated with digestion and absorption of repeated, mixed meals. This in turn should allow for better isolation of the interaction effect of sex and exercise on postprandial glucose. In addition, our study investigated exercise at a self selected pace, while Bhammar et al.[16] and

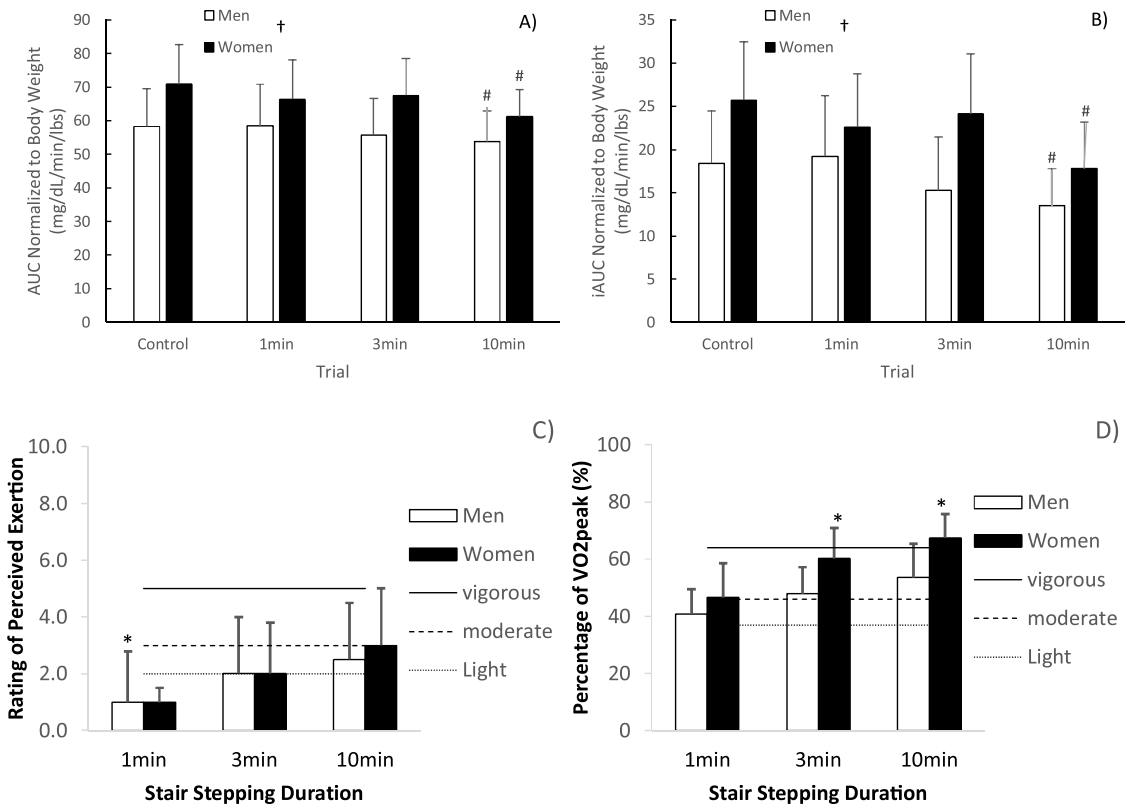


**Fig. 2.** Plasma glucose AUC (Panel A) and iAUC (Panel B) differences between sexes and rating of perceived exertion (Panel C) and VO2peak (Panel D) differences between sexes. Intensity categories upper limits based on ACSM guidelines are indicated with horizontal lines at corresponding levels of the y-axis.
†Indicates significant main effect for sex ($p < 0.05$).
#Indicates significant difference from control at the individual sex level from simple effect post-hoc analysis ($p < 0.05$).
*Indicates significant difference from men at the individual trial level from simple effect post-hoc analysis ($p < 0.05$).

Dempsey et al[18] used fixed pace exercise and neither report on sex differences for exercise intensity. Our protocol resulted in significantly higher relative intensities for women compared to men which may account for the higher levels of glucose observed in our study due to greater hepatic glucose release. Similar results would however be expected for fixed pace walking exercise, at least on level ground,[18] as women usually have lower absolute cardiorespiratory fitness values and therefore would be expected to exercise at a higher relative intensity. Lastly, there is also the possibility that differences between sexes particularly for very short bouts only manifest with repeated attempts or repeated feeding. The discrepancy between sexes was largest for the 1 min bout, however it failed to reduce postprandial glucose in either sex. This could be an indication for such a mediating effect of repetitions when differences magnify as they accumulate. Future studies will have to determine whether there is such an effect for repetitions and/or repeated meals.

Of note is that women perceived the shortest bout as less intense than men, albeit both sexes considered it below light intensity. The discrepancy did not carry forward to the longer bouts. In contrast, the exact opposite was the case for our objective measure of exercise intensity (%$VO_2$max) where women had higher values during the 3 and 10 min bouts. We are unsure why these discrepancies occurred. Generally, RPE values are independent of sex[25,26] but this may be different for stair stepping. Median RPE values for both sexes underestimated the objective measure exercise intensity indicating that men and women did not accurately judge their stair stepping intensity. Further studies need to determine whether this underestimation enables people to engage or adhere to higher intensity exercise than they normally would and whether stair stepping of different duration is a preferable mode for either sex. We studied young, healthy participants. The Borg RPE scale has been deemed a valid and reproducible tool to subjectively quantify exercise intensity in many populations including healthy, elderly, and obese, among others.[27] Patients with T2DM do not report higher RPE compared to control during submaximal exercise, however objective measures were significantly higher.[28] Whether the findings regarding the disconnect between subjective and objective measures of intensities from this study expand to other populations remains to be determined. Lastly, though RPE scores for the 1 min bout were statistically significant for women (1.0(0.5) vs. men (1.0(1.8), $U = 49.5$, $p = 0.037$, there is unlikely to be any practical significance or implications to this.

There are several limitations to our study. Women had higher baseline glucose values than men and this carried through all measurement time points resulting in a significant main effect for sex. We are unsure why this discrepancy occurred but since it was consistent, small (<10 mg/dL), and below disease threshold we have no reason to assume that it affected the main outcome of this sex comparison (i.e. interactions).

For the objective intensity measure there was a significant effect for trials within both sexes. Men had significantly different values among all bouts. Women only had significantly lower values for the 1 min compared to 3 and 10 min bouts. Significantly different values indicate that either exercise onset VO2 kinetics had not yet stabilized or that intensity was above critical power. The latter is unlikely since men only reached moderate intensities based on %$VO_2$peak values and women had no significant difference between 3 and 10 min values.

Substrate utilization was only calculated for the last three minutes of the 10 min bout. This ensured sufficient time for exercise onset $VO_2$ kinetics to stabilize but there was no accounting for

changes in intensity for upward and downward stair stepping. However, with an average stepping speed of 102 steps per minute, it took only around 12 s to complete each ascent and descent. After seven minutes of stepping we considered the effects of slight changes in intensity back and forth every 12 s as reasonably stable to derive substrate utilization measurements.

Additionally, we utilized a 75 g OGTT rather than a real meal, thus limiting the ecological validity of our results. It is likely that 75 g glucose load is consumed in combination with other macronutrients by most people. We chose the standard OGTT load to determine proof-of-principle and future research should test whether these effects are seen following mixed meal consumption.

## 5. Conclusion

Normalized for body weight, men and women had similar glycemic and metabolic responses to simple, single, short bouts of stair stepping exercise. Perceived intensity ratings were low-moderate, with both sexes underestimating the intensity of their exercise. Combined with the low cost and ubiquitous availability, stair stepping presents a feasible intervention to reduce postprandial glucose response with similar effectiveness for both sexes.

## Practical implications

- Contrary to recent reports short bouts of stair stepping exercise decrease blood sugar levels similarly in men and women.
- Stair stepping is therefore an equally effective mode of exercise to improve disease risk markers for both sexes.
- Both men and women tend to underestimate the intensity of stair stepping exercise which could help people start or maintain this type of exercise more easily, particularly since stair stepping is also cheap, easy, and ubiquitously available.

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