Effects of acute and chronic stair climbing exercise on metabolic health: A systematic review

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Abstract

Background: Stair climbing exercise (SE) provides a feasible approach to elevate physical activity, but the effects on metabolic health are unclear. We systematically reviewed the currently available evidence on the effects of SE on fasting and postprandial glycaemia and lipidaemia. **Methods:** Studies were included if they investigated the effects of acute or chronic (at least 2 weeks) SE on fasting and/or postprandial glycaemic (insulin and glucose) and lipidaemic (triacylglycerols and non-esterified fatty acids) responses in healthy, prediabetic or type 2 diabetic adult populations. PubMed, Web of Science and Scopus were searched for eligible studies until July 2022. **Results:** 25 studies (14 acute and 11 chronic) were eligible for review. Acute bout(s) of SE can reduce postprandial glycaemia in individuals with prediabetes and type 2 diabetes (8 of 9 studies), but not in normoglycemic individuals. The effects of acute SE on postprandial lipidaemic responses and SE training on both fasting and postprandial glycaemia/lipidaemia were unclear. **Conclusion:** Acute SE may reduce postprandial glucose concentrations in people with impaired glycaemic control, but high-quality studies are needed. More studies are needed to determine the effect of chronic SE training on postprandial glucose and lipid responses, and the acute effects of SE on lipid responses.

Keywords: Impaired glucose control, type 2 diabetes, postprandial glycaemia, postprandial lipidaemia, stair climbing exercise

Introduction

Low levels of habitual physical activity together with prolonged sedentary behaviour are known to impair metabolic health, including an elevation of fasting and postprandial glucose and lipid concentrations (1-5). Importantly, an increase in postabsorptive and postprandial glycaemia (e.g., glucose and insulin concentrations) and lipidaemia (e.g., triacylglycerols [TAGs] and non-esterified fatty acids [NEFAs]) will increase the likelihood of developing to type 2 diabetes, cardiovascular diseases, as well as premature morbidity and mortality (6, 7). The prevalence and burden of both type 2 diabetes and cardiovascular disease remains extremely high worldwide (8, 9). As such, there remains an urgent need to develop feasible and effective strategies to increase population physical activity levels and improve metabolic health.

There is good evidence that various types of acute and chronic exercise, including moderate intensity continuous exercise, resistance exercise and high-intensity interval exercise, can improve fasting and postprandial glycaemia and lipaemia in both healthy individuals and individuals with impaired glucose and lipid metabolism (e.g., prediabetes and type 2 diabetes) (10-18). However, there are various obstacles that may impede the adoption of, and adherence to, these types of exercise, such as the distance to the appropriate facilities, costs associated with gym memberships, the difficulties of using specialised (gym) equipment, dislike of unfamiliar (gym) environments, limited time to travel to exercise locations, and bad weather (19). Overall levels of exercise adherence is low in the general population (20, 21), and potentially lower in people with type 2 diabetes (22, 23), and this represents a key public health challenge (24). Providing alternative and straightforward approaches to increasing exercise/physical activity that overcome some of the key barriers may be part of an effective solution.

Walking is promoted as an effective and easily available form of physical activity, but there is some evidence from randomised controlled trials (RCTs) that the intensity may not be sufficient to improve key aspects of metabolic health (e.g., glucose and TAGs) (25, 26). The addition of stair climbing could be an easy way to increase the intensity of walking physical activity, potentially resulting in more pronounced effects on metabolic health. The combined concentric and eccentric component of ascending and descending stairs has also been hypothesised to elicit greater skeletal muscle adaptations and metabolic health benefits (27, 28). Additional benefits of stair climbing exercise (SE) are that it requires no extra skills/techniques, no equipment (beyond access to a set of stairs), and it can easily be performed at home or in an office setting.

Recent studies have suggested that acute (e.g., single bout and multiple bouts) and long-term SE (i.e., several weeks of training) interventions can reduce postprandial glucose concentrations and improve lipid profile (25, 29, 30), but there are also several studies reporting no beneficial effects (31-33). The inconsistent results might be caused by various SE protocols (i.e., duration and intensity), different populations, and different methods of assessing postprandial glucose and lipid control. Accordingly, whilst SE may be practical approach to increase moderate-vigorous intensity physical activity, the efficacy of SE for improving the metabolic health is not certain. Therefore, the purpose of the current study is to conduct a systematic review of experimental studies on the acute and chronic effects of SE on glucose and lipid responses in adults with and without type 2 diabetes.

Methods

This review was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (34) and is registered at the International Prospective Register of Systematic Reviews (PROSPERO) with registered number (CRD42020221691).

Search strategy

The systematic literature search was performed using three electronic databases: PubMed, Web of Science and Scopus. The databases were searched up until the end of July 2022. The search was restricted to the English language and original research published in peer-reviewed journals (preprints and grey literature were not included). The following keywords were used to identify relevant articles: ("stair*" OR "stepping") AND ("glucose" OR "glycemia" OR "glycaemia" OR "free fatty acids [FFAs]" OR "lipemia" OR "non-esterified fatty acids [NEFAs]" OR "triglycerides OR triacylglycerols" OR ''insulin'' OR ''insulinemia'').

Eligibility criteria

The Population, Intervention, Comparison, Outcome and Study (PICOS) framework was used to determine the inclusion criteria for studies (35). Studies were included based on the following inclusion criteria:

1) (P) Participants: males and females aged 18 years or above. Healthy (i.e., normoglycaemia; fasting glucose < 100 mg/dL) and individuals with prediabetes (fasting glucose: 100−125 mg/dL) and type 2 diabetes (fasting glucose: ≥125 mg/dL) were included.
2) (I) Intervention: included studies had to involve either an acute (single bout and/or multiple bouts throughout the day) or chronic (multiple bouts over at least 2 weeks) SE intervention, and include a detailed description of the SE protocol (e.g., the type of SE protocol [i.e., ascending and/or descending], intensity (e.g., heart rate [HR], $\%HR_{max}$, %HRR, rating of perceived exertion [RPE] or step pace), number of sessions, duration of SE, as well as the intervention period for chronic training. We excluded studies involving bench stepping as it is biomechanically different from stair climbing (where all movement is forward) and may result in different physiological effects.

3) (C) Comparator: for acute studies, a suitable no-exercise control trial needed to be included to serve as the comparator. For chronic training studies, both randomised controlled trials and single-arm intervention studies were considered eligible, with study design considered when interpreting the findings. In the case of RCTs, the eligible comparator was a time-matched no intervention control group, whereas for single arm intervention studies comparisons were made between pre- and post-training time points.
4) (O) Outcome: The outcome variables of interest were blood glucose, insulin, TAGs and NEFAs. Studies included at least one of those outcomes in the postprandial state for acute studies, and within the fasting and/or postprandial state for training studies. No restrictions were placed on the method of blood sampling; studies using intravenous cannulation, venepuncture, fingerstick sampling or continuous glucose monitoring (CGM) were included.
5) (S) Study design: RCTs or non-randomised controlled trials (non-RCTs) were both included.

Studies were excluded if they met any of the following criteria:

1) A non-SE control (non-exercise) trial was not included in an acute study and/or the protocol of SE, such as type, intensity, frequency, and duration, was not explicitly stated. Studies involving bench stepping exercise on only one stair were also excluded.
2) Studies investigating the effects of SE combined with other types of exercise or dietary interventions (e.g., intermittent fasting or low calories diets) were excluded because it is not possible to determine the isolated effects of SE.
3) Any study reusing data from a previous study, without containing any new measurements for at least one glycaemic or lipidaemic parameter.
4) No formal statistical analysis was provided in the published paper.
5) Studies published in non-English language, commentaries, letters, reviews, conference

abstracts, poster abstracts.

A Microsoft Excel spreadsheet was developed to track eligibility status. First, the titles and abstracts were independently assessed by these two authors (J-YH and Y-JL) and initially coded as 'yes', 'no' or 'maybe' for inclusion. The same two authors then reviewed the full texts of the 'yes' and 'maybe' studies, and disagreements regarding the inclusion of any study were resolved by discussion with a third reviewer (Y-CC). In addition to the database search, the reference lists of all included studies were checked to identify additional eligible articles. **Fig. 1** provides an overview of the study selection process.

[INSERT FIGURE 1 ABOUT HERE]

Data extraction and synthesis

The results in this review were analysed through a process of narrative synthesis after standardised data was extracted from each of the included studies. Data extraction was conducted by one reviewer (J-YH) and then verified by two reviewers (Y-JL and Y-CC). The authors extracted the following data from each included article: (1) first author's name and publication year; (2) participants' characteristics (e.g., age, health status and weight status); (3) study design; (4) characteristics of the SE protocols (e.g., intensity and duration, etc.) and (5) outcome measures (i.e., outcomes extracted for the narrative review were measures of blood glucose [including results from CGM], insulin, TAGs and NEFAs). A p value of < 0.05, presented in the original studies, was used across the studies to determine the significant effects of SE intervention on the outcomes of interest.

Study risk of bias assessment

The quality of the studies included in the review was assessed using the Cochrane Collaboration's risk of bias (RoB) 2.0 tool for crossover (acute studies) and parallel-arm study designs (training studies) (36). Assessments were performed independently by two authors (Y-CC and RM) with disagreements discussed between the two reviewers discussed until a consensus was reached.

Results

Study selection

A total of 1403 article titles and abstracts were initially retrieved from the search. Of these, 844 were duplicates and were immediately removed. A total of 559 articles were then screened by the title and abstract. After this first stage of screening, 25 articles were eligible for full-text screening, and 7 articles were removed for the following reasons: 1) commentaries article (n = 1), 2) intervention criterion (n = 3), 3) unclear SE protocol (n = 1), 4) reused data from previous study (n = 1), and 5) no formal statistical analysis presented (n = 1). This left 18 eligible articles from the formal search with one additional article identified from the search of reference lists from these articles (37). In addition, 6 of the included articles involved more than one trial, either comparing different SE protocols (29-31), different populations (27, 38), and/or they included both acute and chronic sub-studies (39). In total, 25 unique studies are included in this review. There were 14 studies investigating the acute effects of SE (14, 27, 28, 33, 37-44) and 11 studies examining the training effects of SE (25, 29-32, 39, 45, 46). The flow chart of the systematic search is presented in **Fig.1**.

The study characteristics of acute stair climbing exercise

The characteristics of the acute studies are summarized in **Table 1**. Overall, 14 studies (13 randomised controlled crossover studies and 1 non-randomised controlled crossover study) were identified including 220 participants, aged between 23 and 72 years. These studies were

performed in populations who were metabolically healthy (n = 5 studies, 99 participants) (33, 38, 42, 44), in people with prediabetes (n = 5 studies, 128 participants) (14, 27, 28, 40, 43), and in people with type 2 diabetes (n = 4 studies, n = 37 participants) (27, 37, 39, 41). Nine studies used a single bout of SE (27, 28, 37, 39, 40, 42-44) and 5 studies involved multiple shorter bouts of SE spread across the day (14, 33, 38, 41). The majority of studies involved both ascending and descending SE (27, 28, 33, 37, 39-44), but 3 studies examined the effects of ascending SE only (14, 38). The relative intensity of the SE exercise (based on HR according to ACSM criteria (47)) was light-intensity (50−63% HR_{max}) in 3 studies (38, 43), moderate-intensity (64−76% HR_{max}) in 9 studies (14, 27, 28, 33, 37, 39, 40, 42, 44), and vigorous intensity (77−93% HR_{max}) in 1 study (41). In 1 study the SE was performed at self-selected pace between 90−110 steps/min but they did not report an objective measurement of relative intensity (44).

Acute effects of stair climbing exercise on glucose, insulin, TAGs and NEFA responses

In total, 14 studies investigated the acute effects of SE on postprandial glucose and insulin responses. In people with prediabetes, all 5 studies reported a reduction in postprandial glycaemic concentrations following either a single bout (27, 28, 40, 43) or after multiple shorter bouts performed throughout the day (14). Findings were similarly consistent in people with type 2 diabetes, 3 out of 4 studies reported positive effects of SE on postprandial glycaemic responses (27, 37, 41) with 1 study reported no effect on a 24-h glucose AUC measured using CGM (39). On the other hand, findings were inconsistent in people who were metabolically healthy, with positive effects on postprandial glycaemia observed in one study (44) and no effect observed in another two studies (33, 38). These inconsistent findings may be explained using different SE protocols and participant characteristics (33, 38, 44). In terms of insulin responses, one study found that postprandial insulin was reduced in healthy individuals after a single bout of 3 and 10 min SE but not in 1 min SE (42) and postprandial insulin AUC were decreased in healthy middle-aged individuals with obesity, but not in younger individuals without obesity,

using the same multiple bout SE protocol (38). No difference in postprandial insulin concentrations were found in 3 studies which applied single bouts of SE in either individuals with prediabetes (27, 28) or individuals with type 2 diabetes (27).

There were only a small number of studies that examined the effect of acute SE on postprandial lipid responses (NEFAs and TAGs) (33, 37, 38, 41, 42). One study reported a reduction in NEFA responses in healthy individuals with obesity, but not in healthy lean individuals (38). A further two studies reported no effect of acute SE on NEFA responses in people type 2 diabetes (37, 41). There were no beneficial effects on postprandial TAGs responses in all acute SE interventions in healthy participants (33, 38, 42) and none of the included studies examined postprandial TAG responses in prediabetes and type 2 diabetes pateints.

[INSERT TABLE 1 ABOUT HERE]

The study characteristics of chronic stair climbing exercise

The characteristics of the chronic SE studies are summarized in **Table 2**. Overall, 11 studies (7 RCTs and 4 non-RCTs) were identified with a total of 187 participants, aged from 19 to 68 years. These studies were performed in participants who were categorized as metabolically healthy (n = 7 studies, 143 participants) (25, 30-32, 46), in people with prediabetes (n = 2 studies, 30 participants) (29), and in people with type 2 diabetes (n = 2 studies, 14 participants) (39, 45). The length of the training intervention ranged between 2 to 12 weeks. There were 7 studies where the training was fully supervised (29-31, 39) and 4 studies where the training sessions were performed in a free-living environment with either partial or without supervision (25, 32, 45, 46).

In terms of the mode of SE, 5 studies compared the independent effects of ascending or descending SE in separate arms (29-31), with the rest including both ascending and descending SE (25, 31, 32, 39, 45, 46). The majority of SE interventions (based on HR according to ACSM criteria (47)) were performed at moderate-intensity (64−76% HR_{max} or RPE between 12−15 from the 6−20 scale) (25, 30, 39, 45), but 2 studies involved vigorous intensity (77−93% HR_{max})(31). In the other 2 studies, SE was performed at a self-selected pace (50−90 steps/min), and they did not report a measure of relative exercise intensity (32, 46). Moreover, 6 studies progressively increased training volumes (1−2 bouts of SE every 1−2 week) but the same SE intensity for 5 days per week for 8 weeks (32, 46) or 2 to 3 days per week for 12 weeks (29, 30). 5 studies conducted the same SE training protocol (e.g., frequency and intensity) 3 times per week for 6 weeks (31, 39) or 12 weeks (25). One study performed daily SE after every meal (breakfast, lunch and dinner) for 2 weeks (45).

In addition, 10 studies reported post-training sampling, with overnight fasting (45), 48 h (30), 60 h (32, 46), 72 h (31, 39) and 96 h (29) after last training session. One study did not report the timing of post-training sampling (25). In terms of outcome measurements, 6 of 11 training studies only collected fasting blood samples (25, 30-32, 45, 46), and 4 of 11 assessed both fasting and postprandial using either a 2-h OGTT (29, 31) or a 24-h mixed meal CGM assessment (39).

Training effects of stair climbing exercise on glucose, insulin and TAGs responses

In total, 11 studies investigated the training effects of SE on either glycaemic and/or insulinaemic responses and the majority of these studies (7 studies) collected only fasting samples. Two studies reported the independent positive effects on both ascending and descending SE after 8 weeks training on reducing glucose and insulin concentrations in older prediabetic individuals with overweight and obesity (29), with more pronounced effects after

descending SE (29). Mixed results were found in the glycaemic/insulinaemic responses after SE training in people who were normoglycaemic or in people with type 2 diabetes (25, 30, 31, 39, 45, 46). For example, Kang & Ahn, 2019 (25) have reported reduced fasting glucose concentrations in an older adult population, but the intervention was longer (12 weeks), and the SE session duration was also more prolonged (40 min). Similarly, Chow et al (30) reported reduced fasting insulin concentrations after an 8-week SE intervention in young females, but the finding was not consistent across descending SE (reduced fasting insulin) and ascending SE (no effect observed). However, Allison et al (31) reported no significant changes in fasting or OGTT-derived insulin and glucose responses following a 6-week low volume SE (3 × 20-s maximal stair ascends) intervention in young inactive females, whilst Godkin et al (39) reported no change in fasting insulin, mean 24-glucose, time in hyperglycaemia or glycaemic variability following a similar SE intervention (3 × 60-s high intensity stair climbs) in people with type 2 diabetes.

Overall, 6 studies investigated changes in blood TAG concentrations after SE interventions ranging from 2 to 12 weeks in length. No studies measured changes in fasting NEFA concentrations. The concentrations of fasting TAGs were decreased following 8 weeks of SE training in healthy, middle aged, overweight/obese individuals (25, 46) and after 12 weeks of training in middle aged, overweight/obese people with prediabetes (29). No effect of SE was observed in one study in young healthy lean individuals after 8 weeks of training (32), and following 2 weeks of SE training in males and females with type 2 diabetes (45).

[INSERT TABLE 2 ABOUT HERE]

Quality Assessment

Overall, 5 of 14 acute studies were rated as having "some concerns" for risk of bias (36%; (33, 38, 41, 44)), whilst 9 out of 14 studies were rated as having a high risk of bias. The main reasons for the high risk of bias ratings were due to concerns in the randomisation process, the potential for carryover effects and concerns in the statistical analysis (64%; (14, 27, 28, 37, 39, 40, 42, 43)). In addition, 3 of 11 SE training studies were rated as having "some concerns" for risk of bias (27%; (30, 32)) and 8 out of 11 studies were rated as having high risk of bias. This was mainly due to lack of a non-exercise control group (73%; (25, 29, 31, 39, 45, 46)). The results of bias assessment are shown in the **Fig 2 and Fig 3.**

[INSERT FIGURE 2 ABOUT HERE]

[INSERT FIGURE 3 ABOUT HERE]

Discussion

The aim of this study was to systematically review the effects of acute and chronic SE on the glycaemic and lipidaemic responses in individuals with healthy, prediabetic and type 2 diabetic status. We found consistent evidence that acute bout(s) of SE, prior to feeding or after meal consumption, can attenuate postprandial glucose concentrations in individuals with impaired glucose control (i.e., prediabetes and type 2 diabetes). There were mixed results for the acute effects of SE on postprandial glycaemia and insulinaemia in normoglycaemic individuals. Furthermore, there is mixed evidence which on the balance suggests that there might be a beneficial effect of SE training on fasting glucose and TAG concentrations in middle-aged individuals who were overweight and had prediabetes. However, the quality of the available SE training studies was low (high potential risk of bias) and thus further high-quality research is needed. Finally, although the currently available evidence suggests there is no effect of acute

SE on postprandial lipid responses, only limited studies have investigated this, and thus no clear conclusions can be drawn at this time.

Effects of acute stair climbing exercise on postprandial glycaemic responses

Postprandial hyperglycaemia is strongly associated with adverse health outcomes including an increased risk of cardiovascular disease and type 2 diabetes (48). Moreover, studies have shown that exaggerated postprandial glucose excursions are a particularly important consideration for individuals with impaired glycaemic control; indeed, even in individuals with well controlled type 2 diabetes according to HbA1c, a significant proportion of the day can be spent in (postprandial) hyperglycaemia (49).

The present review provides some evidence that in people with pre- and type 2 diabetes, acute SE exercise with a self-selected comfortable and/or predetermined pace (mostly moderate intensity) and performed approximately 20−120 min after a meal, can reduce postprandial glucose excursions. Indeed, this finding was consistent across all 5 of the available studies in prediabetic populations (14, 27, 28, 40, 43) and 3 out of 4 studies in people with type 2 diabetes (27, 37, 41). This effect appears to be independent of participant age (young (40, 43), middle-aged (14, 27, 28) or elder individuals (27, 37, 41)) and the method of assessment of glycaemic control (e.g., OGTT (14, 37, 40) *versus* mixed meal tests (14, 27, 28, 41, 43)). Furthermore, reductions in glucose concentrations at one or more time points after a meal have been observed with a range of different SE protocols (e.g., the duration of the SE bouts ranged from 1 to 10 min), but there is some evidence of a potential dose response, with studies reporting more pronounced improvement in glycaemic control (e.g. reduction in glucose AUC) with longer (3 and 10 min) compared to shorter bouts (1 min) of SE (40, 43). It is also interesting to note that the improvements in postprandial glycaemia following acute SE in people with either pre-diabetes or type 2 diabetes have been observed in the absence of any change in postprandial

insulin responses (27, 28), perhaps indicating that acute SE improves glycaemia via insulin-independent mechanisms (discussed below). Collectively, the currently available evidence supports that SE can be used as an effective and ready-to-perform strategy to decrease postprandial glycaemia for individuals with impaired glucose control (e.g., prediabetes and type 2 diabetes). However, the high risk of bias score for the majority of the included studies, means that these findings should be interpreted with some caution.

Mechanistically, the improvement in glycaemic control after acute SE is probably explained by an increase in exogenous glucose oxidation together with increases in glucose and insulin delivery due to enhanced blood flow to skeletal muscle during acute bouts of exercise (1, 50). Indeed, skeletal muscle rapidly activates glucose uptake during moderate intensity exercise by inducing translocation of glucose transporter 4 (GLUT4) molecules to the cell surface within 5 min of exercise initiation (50, 51). This mechanism results in an increase in skeletal muscle glucose uptake which is independent and additive to the effects of insulin (52, 53). This mechanistic suggestion remains speculative, however, as to our knowledge, no studies have investigated the mechanisms for improved glycaemic control following acute SE. Future studies should investigate the molecular mechanisms through which acute SE improves glycaemic control.

Interestingly, some studies have compared SE to walking (28) and cycling (27) in people with prediabetes and type 2 diabetes. A single bout of 6 min SE, compared to walking, showed a greater reduction of postprandial glucose concentrations (28). This effect may be a result of the higher exercise intensity (e.g., greater HR and estimated oxygen consumption and lactate levels) in SE compared to walking (28). In another study with better standardisation of exercise intensity (e.g., same HR and RPE), a single bout of 8 min SE was superior to cycling for reducing postprandial glucose concentrations (27). Although both concentric and eccentric

muscle contraction are involved in SE and cycling, the support of body weight that is involved during the SE could be a potential reason why better improvements in glycaemic control were found SE compared to cycling.

Postprandial glycaemic control is also an important consideration in individuals who would be classified as "normoglycaemic" according to diagnostic criteria for type 2 diabetes. Studies have shown that there is a causal effect of postprandial spikes in blood glucose after a meal and the risk of cardiovascular and metabolic related diseases not only in individuals with prediabetes and type 2 diabetes but also in normoglycaemic individuals (48, 54, 55). The present review revealed mixed findings on the effects of SE on postprandial glycaemic/insulinaemic responses and, overall, it is not possible to conclude that there is a beneficial effect of acute SE in this population (33, 38, 42, 44). This is perhaps not all that surprising given that there is also mixed evidence for the effects of other types of exercise of postprandial insulin sensitivity and glycaemic control in healthy individuals (56-66). The heterogeneous design of the small number of studies (5 studies only) is likely to explain the mixed findings, with differences in population characteristics (lean vs obese), SE protocols, and the composition of the meal and/or outcome assessment methods the most likely driving factors. Indeed, there is evidence from one study that, despite identical study methods and SE protocols, SE improved postprandial insulin responses in overweight/obese but not in lean individuals (38). Similarly, another study showed that the improvement in glycaemic control following multiple shorter bouts of SE was only present in people with elevated baseline blood glucose concentrations (14). It is also worth noting that any potential improvements in glycaemic control in normoglycaemic individuals are likely to be subtle because the capacity for skeletal muscle glucose uptake is already high, particularly in those who are young and lean. As such, studies with small sample sizes and low statistical power may lack the sensitivity to be able to detect any change.

Effects of acute stairs climbing exercise on postprandial lipemic responses

Previous meta-analyses have demonstrated a ~15–25% decrease in postprandial TAGs following running and cycling between 30–110 min at 40–75% $\dot{V}O_{2max}$ (67) and small reduction in postprandial TAGs when breaking sitting with short bouts of physical activity compared to prolonged sitting (68). However, there was no effect of acute bout(s) SE on postprandial TAGs reported in any of the 4 available studies revealed in this review, either in young healthy lean and overweight individuals (33, 38, 42). There was also limited evidence for any changes in NEFA concentrations, with only one study showing an effect in obese but not in lean individuals (38), and two other studies showing no effect in people with type 2 diabetes (37, 41). Together, these findings suggest that SE has limited effects on postprandial lipid concentrations. However, it is important to note that there is relatively less research on the effects of SE on postprandial lipaemia compared to postprandial glycaemia and, as such, an important finding of this review is the need for more research in this area. Nevertheless, one potential reason for the lack of effect observed in the studies conducted to date is the short duration and low exercise volume of SE (e.g., in 5 of 6 trial arms the duration of SE was lower than 10 min), with previous research suggesting that higher exercise duration and/or volume is an important driver of the effect of aerobic exercise on lowering postprandial lipids (69). Moreover, studies have shown that exercise performed 12–16 h prior to a meal seems to produce the most dramatic and consistent decrease in postprandial lipidaemia (67) and in the current review studies were between 1–9 h timeframe which might be another reason for the lack of observed effects of SE on lipemic responses.

Effects of chronic SE training on insulin and glycaemic responses in healthy, prediabetes and type 2 diabetes populations

Whilst the acute effects of exercise are generally thought to be more important for improving glycaemic control, there is some evidence that chronic adaptations to exercise *training* can enhance insulin sensitivity and glycaemic control after the acute effects of the last training bout have subsided (70). There are 11 studies that have investigated the training effects of SE on blood glucose and insulin concentrations, with 7 in healthy individuals (25, 30-32, 46), 2 in prediabetic individuals (29) and 2 in people with type 2 diabetes (39, 45).

There is evidence both for and against a beneficial effect of chronic SE on markers of insulin sensitivity and glycaemic control. For example, studies have reported improvements in insulin sensitivity in older adults with prediabetes following a 12-week SE intervention (29), whilst other studies in people with type 2 diabetes have reported no changes following 2–6 week SE interventions (39, 45). Similarly, in healthy normoglycaemic populations, studies have reported both favourable effects (25, 30) and no significant changes (31, 46). There are a wide variety of possible explanations for these mixed findings, but there are three key themes that are worthy of further discussion. Firstly, it is notable that most studies investigating chronic SE have relied on fasting indices and this may miss the beneficial effects of training-induced skeletal muscle adaptations upon insulin sensitivity and glycaemic control, which are mostly likely to be observed postprandially (71). Secondly, there is some tentative evidence of a dose-response effect in the literature to date. For example, two studies investigating particularly low volumes of SE (3 × 20 s or 3 × 60 s stair climbs per session) over 6 weeks reported no improvements (31, 39), whereas studies that have reported beneficial changes have tended to use either higher volumes of SE per session and/or longer training interventions (25, 30). Finally, it is important to highlight that many of the studies conducted to date have had very small sample sizes and, given the associated technical/biological/random error associated with repeated assessments of insulin sensitivity and glycaemic control (72), the statistical power of these studies to detect improvements is low. To illustrate this point, in the study by Allison et al (31), which had a

412 sample size of n=11, there was a 10% mean reduction in insulin AUC and a 12% mean
413 improvement in insulin sensitivity following 6-weeks of low volume SE in healthy inactive
414 women, but both findings were statistically non-significant. Taken together, there is a clear
415 need for further larger studies in both healthy and clinical cohorts, investigating a variety of
416 doses of chronic SE, on both fasting and (particularly) postprandial insulin sensitivity and
417 glycaemic control.
418
419 An additional theme from the chronic SE studies that is important to highlight is the potential
420 for descending SE to result in more profound improvements in insulin sensitivity and glycaemic
421 control compared with ascending SE (29, 73). Interestingly, these more pronounced effects
422 appear to occur despite lower relative exercise intensity (i.e., heart rate) and RPE with
423 descending SE (29). The reason descending SE demonstrated greater beneficial effects is
424 unclear, but a possible mechanism could be an attenuated circulating inflammatory response
425 (e.g., component 1q, apelin and adropin) caused by mechanical pressure through repeated bouts
426 of eccentric muscle contraction (73). Nevertheless, the practical application of the more
427 pronounced effects of descending SE is somewhat unclear, as in a real-world setting,
428 performing a bout SE for health would most likely necessitate a combination of both ascending
429 and descending SE.
430
431 Overall, the findings of this review have revealed a clear contrast in findings between the effects
432 of acute and chronic SE on markers of glycaemic control and insulin sensitivity in people with
433 pre- or type 2 diabetes. Specifically, there is a clear and consistent pattern of evidence (albeit
434 from studies of mixed quality) that acute bouts of SE can improve glycaemia, whereas the
435 effects of chronic SE several days after the final session has been performed are unclear. This
436 has important practical implications: for people with pre- or type 2 diabetes who are interested
437 in using SE as a method to manage blood glucose control, the current evidence suggests that a

higher frequency of SE sessions will be important to maintain the potential benefits. This is not dissimilar to recommendations for other types of physical activity and exercise, where a high frequency of activity is similarly emphasised in clinical guidelines and recommendations (74).

Effects of chronic SE training on lipaemic responses

Only 6 studies in total have investigated the training effects of SE on fasting TAG concentrations, with three studies in healthy individuals (25, 32, 46), two studies in prediabetic individuals (29) and one in type 2 diabetes (45). One study involving 2 weeks of SE training found no effects on TAGs in lean elderly men (45). However, a reduction in fasting TAGs has been reported after 8 weeks of SE in overweight/obese women who were either metabolically healthy or with prediabetes/type 2 diabetes (25, 29, 46). Similar improvements were not observed in the relatively young and lean sedentary women (age of ~20 years) (32). This potentially suggests that body composition might be important moderator of the effect of SE training on fasting TAGs, and this should be investigated.

Key Directions for Future Research

This review has revealed some important directions for future research. Firstly, due to limited available studies, the effect of both acute SE and SE training on lipidaemic responses is unclear and more research is needed in this area. Similarly, most of the SE training studies to date have used fasting blood samples and therefore there is a need to investigate the effect of SE training on postprandial metabolic responses. This is especially the case as it can be argued that postprandial responses are more likely to be influenced by adaptations in skeletal muscle (71). Moreover, the most of SE training studies were classified as having a high risk of bias due to lack of non-exercise control groups, meaning any observed changes cannot be specifically attributed to SE. Therefore, there is a need for randomised controlled trials to determine the true effect of SE training on both fasting and postprandial glycaemia/lipidaemia. There is also a lack

of research investigating different SE protocol permutations on both glycaemic and lipid responses. Indeed, most studies performed SE at moderate-intensity and direct comparisons in the different intensities have not been made. In addition, due to different height and numbers of stairs, unavoidably the total work and energy expenditure is different between studies and so it is challenging to compare SE protocols across studies. Finally, one practical concern of SE for older and/or overweight/obese individuals, or individuals with bone related issues, is the potential for SE to cause knee injuries. Thus, it would be useful for future studies to investigate the safety of SE in these populations, as well as the effect of SE interventions on bone related health. In addition, where studies wish to investigate the potential effects of intensity on the health-related effects of SE, it may be prudent to use load carriage as an alternative to increasing walking/running speed, as a method achieve higher SE intensities (75).

Conclusions

In conclusion, this systematic review revealed some evidence that acute bout(s) of SE with minimum 3 min duration can reduce postprandial glycaemic responses in people with pre- and type 2 diabetes. Conversely, there is inconsistent evidence (fasting) or a lack of available studies (postprandial) showing that SE training can improve glycaemic control in either healthy or pre- and type 2 diabetic populations. Similarly, there is limited research on the acute or chronic effects of SE on lipid responses, and findings are inconsistent. Overall, further high-quality studies are needed to increase the certainty of conclusions that can be made on the effects of both acute and chronic SE on glycaemic/lipidaemic regulation.

Authors' contributions

Y-CC and RM initially designed this project. J-YH and Y-JL searched and reviewed the literature and assessed risk of bias of included studies in consultation with Y-CC and RM. J-

YH extracted data. J-YH and Y-CC wrote the manuscript with inputs and critical feedback from RM. All authors approved the final manuscript.

Statements and Declarations

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Figure Legends

Fig. 1 Modified PRISMA flow diagram for included and excluded studies.

Fig. 2 The bias assessment result of acute SE studies. Visualizing risk of bias as percentage in

each domain.

Fig. 3 The bias assessment result of SE training studies. Visualizing risk of bias as percentage in each domain.