SYSTEMATIC REVIEW

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The Acute Metabolic and Vascular Impact of Interrupting Prolonged Sitting: A Systematic Review and Meta-Analysis

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Abstract

Objective The aim was to conduct a systematic review and meta-analysis analyzing the impact of up to 24 h of prolonged sitting on postprandial glucose, insulin and triglyceride responses, blood pressure and vascular function, in comparison to sitting interrupted with light- to moderate-intensity physical activity.

Methods To be included, studies had to examine the impact of prolonged sitting lasting < 24 h in apparently healthy males or females of any age. Studies were identified from searches of the MEDLINE, CINAHL and SportDISCUS databases on July 6, 2016. Study quality was assessed using the Downs and Black Checklist; publication bias was assessed via funnel plot.

Results Forty-four studies met the inclusion criteria for the systematic review; of these, 20 were included in the meta-analysis, which compared prolonged sitting to the effects of interrupting sitting with regular activity breaks on postprandial glucose, insulin and triglycerides. When compared to prolonged sitting, regular activity breaks lowered postprandial glucose ($d = -0.36$, 95% confidence interval [CI] -0.50 to -0.21) and insulin ($d = -0.37$, 95% CI -0.53 to -0.20), but not triglyceride responses ($d = 0.06$, 95% CI -0.15 to 0.26). Subgroup analyses indicated reductions in postprandial triglyceride responses only occurred 12–16 h after the intervention. The magnitude of the reductions in glucose, insulin or triglyceride response was not modified by the intensity of the activity breaks, the macronutrient composition of the test meal, or the age or body mass index of participants.

Conclusion Prolonged sitting results in moderate elevations in postprandial glucose and insulin responses when compared to sitting interrupted with activity breaks.

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Key Points

Compared to prolonged sitting, breaking up sitting time with light- or moderate-intensity physical activity results in lower post-meal insulin and glucose levels.

Breaks in sitting time may help reduce post-meal triglyceride levels, but this is not seen until the following day.

1 Introduction

Evidence is emerging that sedentary behavior—that is any activity done while sitting, lying, or reclining, while expending no more than 1.5 metabolic equivalents [1]—is a distinct risk factor for chronic disease morbidity and mortality [2]. One biological explanation for this relationship is that sedentary behavior exerts an acute effect on markers of cardiometabolic risk [3–5]. In 2012, Saunders et al. [5] systematically reviewed the research examining changes in cardiometabolic indicators following exposure to ≤7 days of prolonged sedentary behavior, reporting evidence that prolonged periods of sedentary behavior consistently resulted in significant reductions in insulin sensitivity, glucose tolerance, and increased plasma triglyceride levels [5]. However, of the 25 studies identified at the time, only four examined the impact of sitting per se, as opposed to more unconventional and extreme forms of sedentary behavior, such as bed rest or immobility for medical reasons, which are uncommon in day-to-day life. Further, only five studies published at that time examined exposure to sedentary behavior lasting less than 24 h [5]. Thus, although these findings strongly suggested a physiological impact of several days of extreme and prolonged sedentary behavior, the effects of sedentary behaviors more typical of daily life, both in terms of duration and mode, were not addressed.

In recent years there has been a rapid increase in the volume of experimental research examining the acute impact of prolonged sitting on markers of cardiometabolic risk [3, 4]. A recent systematic review and meta-analysis of observational and experimental studies by Chastin et al. [4] examined the benefit of breaking up prolonged sitting with light- or moderate-intensity physical activity. They concluded that interruptions in sitting could help control postprandial glucose and insulin levels, although they found no effect on postprandial triglyceride levels [4]. However, their search identified just six eligible experimental studies, and did not include research in pediatric populations. To date, no review has examined the impact of the macronutrient composition of the test meal or its time of consumption in relation to postprandial metabolic response. This is an important omission as the timing of a meal challenge may greatly influence the postprandial triglyceride response [6] and could explain why Chastin et al. [4] observed no effect of sitting on postprandial triglyceride levels, despite significant reductions in postprandial glucose and insulin. Further, no existing review has investigated whether the impact of prolonged sitting is consistent across the age span. This is important, as initial studies in children and youth suggested that prolonged sitting may have had less cardiometabolic impact in pediatric populations, when compared with adults [7, 8].

Finally, at present no reviews have examined the impact of prolonged sitting on vascular function, which refers to the ability of the vasculature to appropriately adapt to the conditions and demands of the tissue it supplies. In particular, it is now well understood that the vasculature will adapt during conditions of increased metabolic demand from local vasodilatory signaling, and also as a result of changes in shear stress [9]. Persistent alterations in both the form and function of the vasculature are both associated with poorer cardiovascular health outcomes and directly linked to blood pressure. While the exercise physiology literature has clearly elucidated both the acute and chronic effects of increases in these stimuli for affecting blood pressure and vascular function, the effects of sedentary time are less clear, but early initial reports suggest inactivity may lead to decrements in function, which are similarly associated with poorer health outcomes [10, 11]. It is worth highlighting as well that an association has been noted between high blood glucose and poor vascular function, thus making this a logical area for investigation alongside the more traditional metabolic markers [12].

The purpose of the present study was therefore to systematically review and analyze the impact of up to 24 h of prolonged sitting on postprandial insulin, glucose and triglycerides, as well as blood pressure and vascular function, in comparison to sitting interrupted with light- or moderate-intensity physical activity. A secondary purpose was to determine whether the timing or macronutrient composition of the test meal(s), the intensity of activity breaks, or the age or body mass index (BMI) of study participants differentially influenced any effects of sitting on postprandial insulin, glucose, or triglyceride responses.

2 Methods

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for the transparent reporting of systematic reviews

[13] (PROSPERO ID: CRD42015020907). Inclusion criteria for the studies included in the systematic review are detailed in Sects. 2.1, 2.2, and 2.3.

2.1 Population

Studies of apparently healthy males and females of all ages were eligible for review. In line with previous research, individuals were deemed to be apparently healthy if they had not received a positive disease diagnosis [14–16]. Those with risk factors for disease, but without a positive diagnosis (e.g., elevated fasting glucose or blood pressure below the threshold for the diagnosis of diabetes or hypertension) were therefore included in this review. In line with previous research, individuals with overweight/obesity, but without a positive diagnosis for other chronic disease, were considered apparently healthy [15, 16]. Studies in which participants were selected on the basis of existing disease (e.g., diabetes or cardiovascular disease) were excluded from this review to ensure that study participants would be sufficiently homogeneous for inclusion in meta-analyses. There were no restrictions on the age or sex of the participants.

2.2 Intervention and Comparator

To be included in this review, studies must have exposed participants to a period of uninterrupted sitting lasting no more than 24 h. Studies with longer periods of sitting were included if they measured the outcomes of interest within the first 24 h of sitting (all data beyond 24 h were excluded from this review). The comparator had to include some form of light- or moderate-intensity physical activity. In comparison to prolonged sitting, the benefits of vigorous-intensity exercise are well-established. Therefore, to limit the scope of the current manuscript, it was felt that focusing on light- and moderate-intensity activity breaks would provide the greatest contribution to the published literature. There were no specific criteria about the duration of the activity, which could be prolonged (e.g., several hours of standing or walking) or intermittent (e.g., a 2-min walk-break every 20 min). Activity was defined as light- ($<50\%$ maximum oxygen uptake [VO_{2max}]) or moderate-intensity exercise ($>50\%$ VO_{2max} to $<65\%$ VO_{2max}) following the Howley [17] guidelines for aerobic, leisure, and occupational physical activity.

2.3 Outcomes

To be included in the present review, all studies were required to report on the impact of prolonged sitting on one or more of the following health indicators: postprandial glucose, insulin, and triglyceride concentrations measured in plasma, serum, interstitial fluid or whole blood, blood pressure, arterial stiffness (collected via pulse wave velocity via tonometry, or beta-stiffness with ultrasound), or flow-mediated dilatation (a non-invasive measure of vascular reactivity to a shear stress).

2.4 Search Strategy and Study Selection

A systematic search was conducted using the databases MEDLINE, CINAHL, and SportDISCUS (all via EBSCO-host) on July 6, 2016. The search strategy was created with the help of a research librarian (Fig. 1). Only articles published in English were included in the review, and no limits were placed on the date of publication.

Using Covidence software (Covidence.org, Melbourne, Australia), two separate reviewers screened titles and abstracts of potentially relevant articles. Articles deemed potentially relevant by either reviewer were obtained for full-text review. The full-text review was also performed by two separate reviewers; at this stage any discrepancies between reviewers were decided via consensus. The reference list of each study identified in the initial database search and the library of each co-author were also reviewed to identify any potentially relevant studies.

2.5 Quality of Evidence

The risk of bias and strength of evidence was assessed by one reviewer (HA) using the Downs and Black Checklist

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 1.  MW "Sedentary Lifestyle"
 2.  "sedentary behav*"
 3.  sitting
 4.  "breaks from sitting"
 5.  "breaks in sitting"
 6.  "sitting breaks"
 7.  "standing breaks"
 8.  or/ 1-7
 9.  MW Insulin
10.  MW Blood Pressure
11.  MW Blood glucose
12.  MW Triglycerides
13.  "reactive hyperemia"
14.  "vascular function"
15.  "flow mediated dilation"
16.  "augmentation index"
17.  MW Pulse Wave Analysis
18.  "central blood pressure"
19.  or/ 9-18
20.  8 and 19
21.  remove duplicates from 20
22.  Restricted to "Human" and "English Language"
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Fig. 1 Medline search strategy

[18]. This 27-point checklist assesses the strength of reporting, external validity, internal validity, and power. As some questions are worth more than 1 point, the maximum score that a study can receive is 32.

2.6 Data Extraction

Data extraction was conducted by one author and verified by another, with any disagreements resolved by consensus. Descriptive characteristics were extracted from each included study, including the BMI of participants and the intensity of the activity as well as mean and standard deviation (SD) for outcomes of interest. For studies that measured the postprandial insulin, glucose or triglyceride responses, incremental area under the curve (iAUC) or total area under the curve (AUC) were extracted in the form (e.g., net or positive iAUC) provided in the individual manuscripts as mean and SD for both the prolonged sitting and activity-based interventions. Where 95% confidence intervals (CIs) or standard errors were reported, SDs were calculated, assuming a t distribution if the sample size was less than $n = 70$. If an AUC (either incremental or total) was not reported, or only presented in a figure, the authors were contacted and asked to provide the relevant information. The amount of carbohydrate, fat and protein provided by the meal challenge(s) and the timing of the meal in relation to the activity were also extracted from relevant studies.

2.7 Meta-Analysis

Studies were included in the meta-analysis if they compared the effect of prolonged sitting to performing repeated short bouts of light to moderate activity, henceforth referred to as regular activity breaks, on postprandial glucose, insulin or triglyceride concentrations. To ensure that interventions were sufficiently homogeneous for comparison, only interventions with activity breaks less than 10 min in duration and a total exposure of < 24 h of uninterrupted sitting were included in meta-analyses. This was done as periods of activity lasting > 10 min are typically considered an activity "bout", rather than simply a break in sedentary time. Thus, although studies with bouts of activity lasting > 10 min were included in the narrative review, they were not included in meta-analyses. Meta-analyses were used to calculate summary estimates for the effect of regular activity breaks compared to prolonged sitting on postprandial glucose, insulin and triglyceride responses. The overall summary estimate for each outcome was calculated as a standardized mean difference (95% CI) using the METAN command in STATA version 14.1 (StataCorp, College Station, USA); fixed effects were assumed and individual study results weighted by the inverse of their variance. Evidence of heterogeneity was assessed using a Cochran's Q with a significance level

of < 0.05, and I^2 values used to judge the degree of heterogeneity, with values above 50% considered to be important. Some studies included more than one regular activity break intervention or measured postprandial responses at multiple time points. To facilitate appropriate weighting of studies in the meta-analysis, only one comparison from each study could be included. Where multiple arms involved different intensities of activity break, only the comparison between the intervention with the lower intensity activity break and prolonged sitting was included. Where the postprandial response was measured at multiple time points (e.g., concurrently with the intervention period and the day following the intervention period), only the response measured concurrently with the intervention was included. Publication bias was assessed through visual inspection of funnel plots. Meta-regression was used to examine the association between the carbohydrate or fat content (in grams) of the test meal and the standardized effect size, as well as the association between age of participants (in years) or BMI (kg/m^2) and the standardized effect size.

Subgroup analyses were performed to assess the modifying effect of the intensity of the activity breaks (moderate, light or standing) and the timing of the meal challenge (measured concurrently with activity breaks or the following day). For studies in which more than one intensity of activity break was compared with prolonged sitting, all intensities were included in the forest plots. However, the test for differences between subgroups assumes independence between subgroups, so to facilitate a valid comparison, with similar n in each group, subgroup analyses were repeated using only the comparison between lowest intensity of activity break and prolonged sitting. Similarly a single study measured postprandial responses both concurrently with the activity breaks and the day following the activity. Both arms are presented in the forest plot; however, the statistical results of the subgroup analysis are confined to the responses measured on the following day.

3 Results

3.1 Narrative Synthesis

A total of 2668 individual studies were identified via the search process, after which 120 were selected for full-text review (Fig. 2). Of these, 76 were excluded because they did not meet the inclusion criteria: 60 studies employed an ineligible intervention or comparator (e.g., no sitting condition, activity breaks of vigorous intensity, etc.), 54 studies were excluded for having an ineligible study design (e.g., sitting for more than 1 day, ineligible population or lacking the outcomes of interest, etc.), five papers were reviews
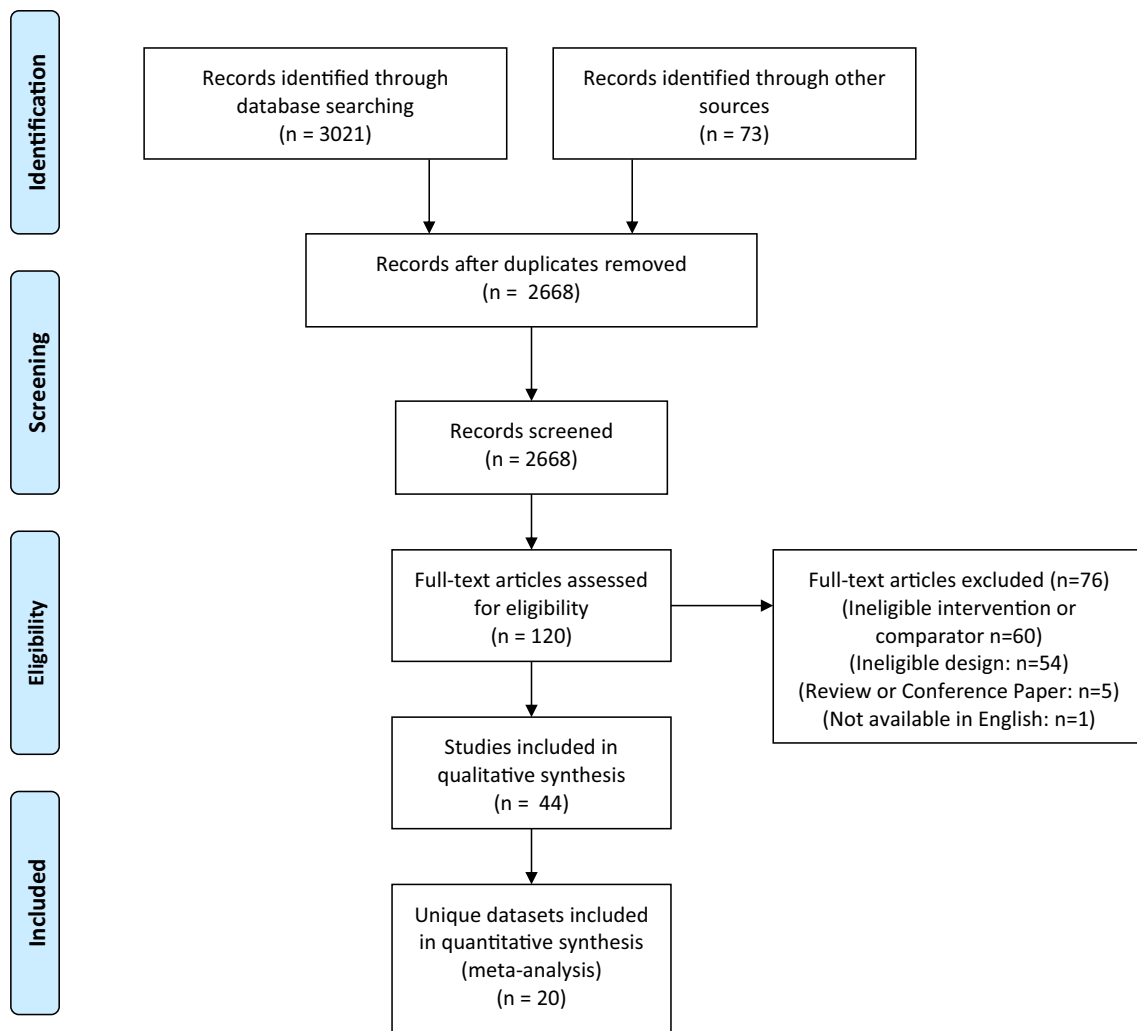
Fig. 2 Flow-chart of publications included in systematic review and meta-analysis (PRISMA diagram). *PRISMA* Preferred Reporting Items for Systematic Reviews and Meta-Analyses

or conference abstracts, and one study was not available in English. Forty-four papers representing 42 separate interventions met all eligibility criteria and were included in this review (see Table 1 and Supplemental Dataset 1 in the electronic supplementary material). The mean (SD) score on the Downs and Black Checklist [18] was 26.5 (2.4) out of a possible 32 points.

Forty studies were designed to compare the effect of sitting with that of activity on postprandial glucose, all of which were of crossover design [7, 8, 19–56]. Of these, 23 found that sitting resulted in significantly higher levels of postprandial glucose and/or reduced glucose clearance in comparison to at least one of the activity conditions [20, 23, 26–29, 31–34, 39–45, 50, 52–56]. One study found a significant decrease in postprandial glucose levels in response to sitting [19], and 16 studies observed no significant difference

between sitting and activity [7, 8, 21, 22, 24, 25, 28, 30, 36–38, 47–49, 51].

The impact of sitting compared to activity on postprandial insulin was assessed in 28 crossover studies [7, 8, 19, 22, 23, 25, 27, 30, 32, 34, 37–42, 44, 45, 47, 49–52, 54–57]. Fifteen studies found that sitting resulted in significantly increased postprandial insulin levels when compared to at least one activity condition [22, 23, 25, 27, 32, 37, 39, 41, 44, 45, 50, 54–57], two studies found that sitting significantly reduced insulin levels, while 11 studies found no significant difference between sitting and light or moderate activity [7, 8, 19, 34, 38, 40, 42, 47, 49, 51, 52]. Two studies reported in a single manuscript [30] observed a significant reduction in postprandial insulin following prolonged sitting, when compared to light-intensity walking.

Twenty-two crossover studies examined the impact of sitting compared to activity on postprandial triglyceride levels [7, 8, 19, 21, 22, 25, 28, 30, 35–37, 39–43, 45, 46, 49, 50, 57]. Eight studies found that sitting resulted in significantly higher postprandial triglyceride levels, in comparison to at least one light or moderate activity condition [21, 22, 25, 28, 35, 37, 40, 57]. Fourteen studies observed no difference between sitting and activity [7, 8, 19, 30, 36, 39, 41–43, 45, 46, 49, 50].

Six interventions examined the impact of sitting compared to activity on blood pressure or vascular function [10, 11, 33, 43, 51, 58]. Three studies found that blood pressure was higher during sitting than during light or moderate activity [33, 45, 58], and two studies observed no difference [47, 51]. One study found that flow-mediated dilation was significantly lower during prolonged sitting than during interrupted sitting [10].

3.2 Quantitative Synthesis

Due to the small number of studies and heterogeneity of methods examining blood pressure and vascular function, these outcomes were not examined via meta-analysis. Similarly, studies that compared prolonged sitting with prolonged light- or moderate-intensity activity, operationally defined as bouts of activity greater than 10 min in length, were insufficiently homogeneous for inclusion in meta-analyses. The 20 studies included in the meta-analysis were all of crossover design, and all compared the effects of regular activity breaks and prolonged sitting on postprandial glucose, insulin and/or triglyceride responses.

When compared to prolonged sitting, regular activity breaks lowered postprandial glucose ($d = -0.36$, 95% CI -0.50 to -0.21) (Fig. 3) and insulin ($d = -0.37$, 95% CI -0.53 to -0.20) (Fig. 4) responses, but did not change postprandial triglyceride responses ($d = 0.06$, 95% CI -0.15 to 0.26) (Fig. 5). Neither the I^2 statistic nor the chi-squared test indicated evidence of heterogeneity. Funnel plots (data not shown) did not indicate evidence of publication bias. All but one study included in the meta-analyses [46] employed a randomized design. Removing this study from the meta-analyses did not materially change the above findings (data not shown).

Subgroup analyses indicated that the intensity of the activity break did not modify the effect on postprandial glucose ($p = 0.20$), insulin ($p = 0.38$) or triglycerides ($p = 0.72$). The inclusion of all arms of the studies ($n = 5$) that reported comparisons for breaks of different intensities in this subgroup analysis did not noticeably change the results (glucose: $p = 0.12$; insulin: $p = 0.51$; triglycerides: $p = 0.68$). However, both moderate- and light-intensity activity breaks induced reductions in postprandial glucose (Supplemental Figure S1) and insulin response (Supplemental Figure S2),

while standing breaks did not significantly affect glucose or insulin response. None of the intensities of activity break resulted in changes in postprandial triglyceride response compared to prolonged sitting (Supplemental Figure S3).

Subgroup analyses indicated that timing of the test meal did not modify the effect of regular activity breaks on postprandial glucose ($p = 0.34$) or insulin responses ($p = 0.90$), despite changes in glucose and insulin only being observed concomitantly with the period of activity breaks or prolonged sitting, and not the day following the activity intervention (Supplemental Figures S4 and S5). In contrast, subgroup analysis indicated that meal timing does influence the effect of regular activity breaks on postprandial triglyceride response ($p = 0.01$). A significantly lower postprandial triglyceride response with activity intervention was only observed 12–16 h after the activity (Supplemental Figure S6). These results did not change markedly when the one study that reported postprandial responses both during and the day following activity was included (glucose: $p = 0.34$; insulin: $p = 0.89$; triglycerides: $p = 0.01$)

Meta-regression indicated no evidence of a linear association between the amount of carbohydrate or fat provided in the test meal and the magnitude of the regular activity break-induced reductions in glucose, insulin or triglyceride response (Table 2). Similarly, meta-regression indicated no evidence of a linear association between the magnitude of the regular activity break-induced reductions in glucose, insulin or triglyceride response and either BMI (Table 3) or age of participants (data not shown; all $p > 0.05$).

4 Discussion

The purpose of the present systematic review and meta-analysis was to determine the impact of prolonged sitting lasting up to 1 day on important markers of cardiometabolic risk, in comparison to sitting interrupted with light- or moderate-intensity physical activity. Our results indicate that prolonged sitting results in elevated levels of postprandial glucose and insulin when compared to sitting interrupted with regularly performed light- or moderate-intensity activity breaks. The magnitude of the elevation is consistent with what could be considered a medium effect [59]. Given the effect of raised postprandial insulin and glucose concentrations on increasing the risk of chronic disease morbidity and mortality [60–63], these increases may be clinically relevant if experienced on a regular basis. Based on the Downs and Black Checklist scores, the quality of evidence was high, and we did not observe evidence of publication bias.

Table 1 Characteristics of included studies

Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Welle, 1984 [19]	3 male, 3 female	Non-randomized crossover	1. Sitting for 3 h 2. Sitting for 3 h, cycling for 15 min at 50 W during each hour of sitting	Glucose, insulin and triglycerides	Compared to sitting, postprandial glucose levels were elevated at 30, 90 and 150 min post-meal in the cycling condition. There were no differences in insulin or triglycerides across conditions	23
Schlierf, 1987 [57]	12 male, 0 female	Randomized crossover	1. Sitting for 6 h 2. Light-intensity cycling for 90 min and sitting for 4.5 h	Insulin and triglycerides	Compared to sitting, postprandial triglyceride and insulin levels were significantly reduced in the cycling condition	23
Mikines, 1988 [20]	7 male, 0 female	Randomized crossover	1. Sitting for 1 h 2. Cycling at moderate intensity for 1 h	Glucose uptake during hyperinsulinemic clamp	Compared to sitting, glucose uptake was higher following 1 h of cycling	24
Hardman, 1995 [21]	6 male, 6 female	Randomized crossover	1. Sitting for 6 h 2. Walking at a light-intensity for 1.5 h and sitting for 4.5 h	Glucose and triglycerides	Compared to sitting, triglycerides were reduced during the walking condition. There was no difference in glucose levels across conditions	26
Tsetsonis, 1996 [22]	5 male, 4 female	Randomized crossover	1. Sitting for 3 h 2. Walking for 3 h at a light intensity 3. Walking for 1.5 h at a moderate intensity	Insulin, glucose and triglycerides	Compared to sitting, postprandial triglyceride levels were significantly lower following both walking conditions. Postprandial insulin levels were reduced following moderate-, but not light-intensity walking. There were no differences in postprandial glucose across conditions	20
Marion–Latard, 2003 [23]	6 male, 0 female	Randomized crossover	1. 7 h of sitting 2. 6 h of sitting with 1 h of light-intensity walking between the 3rd and 4th h of sitting	Glucose and insulin	Compared to sitting, postprandial insulin and glucose levels were significantly lower during exercise (but not during the rest of the session)	25
Tsofliou, 2003 [24]	0 male, 10 female	Randomized crossover	1. Sitting for 2.5 h 2. Sitting for 2.5 h with a 20-min moderate-intensity walk break	Glucose	There was no difference in glucose levels across conditions	29

Table 1 (continued)

Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Katsanos, 2004 [25]	13 male, 0 female	Randomized crossover	1. Sitting for 5 h 2. Walking for 4 h at a light intensity 3. Walking for 1.5 h at a moderate intensity	Insulin, glucose and triglycerides	Compared to sitting, postprandial insulin and triglyceride levels were reduced following moderate-, but not light-intensity walking. There were no differences in glucose across conditions	24
Høstmark, 2006 [26]	0 male, 39 female	Non-randomized crossover	1. Sitting for 2 h 2. Cycling for 30 min at a light intensity, followed by 1.5 h of cycling	Glucose	Postprandial glucose levels were significantly lower during the cycling condition	23
Aadland, 2008 [27]	6 male, 3 female	Non-randomized crossover	1. Sitting for 2.75 h 2. Sitting for 2.75 h, interrupted with 30 min of light-intensity cycling	Insulin and glucose	Compared to sitting, light-intensity cycling reduced the immediate postprandial glucose and insulin response to a test meal, although the area under-the-curve was not different across conditions	24
Tolfrey, 2008 [28]	8 male, 0 female	Randomized crossover	1. Sitting for 110 min 2. Six alternating 10-min periods of sitting and moderate-intensity jog	Glucose and triglycerides	Compared to sitting, postprandial triglyceride levels, but not glucose levels, were significantly reduced during the moderate exercise condition	21
Nygaard, 2009 [29]	0 male, 14 female	Randomized crossover	1. Sitting for 2 h post-meal 2. Walking at a self-paced slow pace for 15 min immediately after a meal, followed by 1.75 h of sitting 3. Walking at a self-selected slow pace for 40 min immediately after a meal, followed by sitting for 1.33 h.	Glucose	Compared to sitting, postprandial glucose was significantly lower during the 40-min walking condition. Glucose levels in the 15-min walking condition were not different from either of other conditions	28
Hashimoto, 2011 [30]	0 male, 9 female	Randomized crossover	1. 6 h of sitting 2. 6 h of sitting with a 30-min light-intensity walk before an oral fat tolerance test	Glucose, insulin and triglycerides	Compared to sitting, postprandial insulin levels were significantly elevated immediately following exercise. There was no difference in postprandial glucose or triglyceride levels across conditions	27

Table 1 (continued)

Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Hashimoto, 2011 [30]	0 male, 8 female	Randomized crossover	1. 6 h of sitting 2. 6 h of sitting with a 30-min light-intensity walk after an oral fat tolerance test	Glucose, insulin and triglycerides	Compared to sitting, postprandial insulin levels were significantly elevated immediately following exercise. There was no difference in postprandial glucose or triglyceride levels across conditions	27
Stephens, 2011 [31]	7 male, 7 female	Randomized crossover	1. Sitting for 9 h 2. Sitting for 9 h with caloric restriction 3. Minimizing sitting (e.g., standing and walking) for 9 h	Glucose disposal	Compared to prolonged sitting without caloric restriction, minimizing sitting resulted in a 39% increase in the rate of glucose disappearance	29
Dunstan, 2012 [32]	11 male, 8 female	Randomized crossover	1. 7 h of sitting 2. 7 h of sitting with 2 min of light-intensity walking every 20 min 3. 7 h of sitting with 2 min of moderate-intensity walking every 20 min	Glucose and insulin	Compared to sitting, both light- and moderate-intensity walking breaks reduced postprandial glucose and insulin	26
Lunde, 2012 [33]	0 male, 11 female	Non-randomized crossover	1. Sitting for 2 h 2. Self-paced slow walk for 20 min, followed by 100 min of sitting 3. Self-paced slow walk for 40 min, followed by 80 min of sitting	Glucose and blood pressure	Compared to sitting, postprandial glucose was lower during both the walking conditions. Systolic blood pressure was lower in the 40-min, but not 20-min walking condition. There was no difference across conditions in diastolic blood pressure	25
Takaishi, 2012 [34]	8 male, 0 female	Non-randomized crossover	1. Sitting for 2 h 2. Sitting for 2 h with a 7.25-min flat walk at light intensity after 1.5 h of sitting 3. Sitting for 2 h with a 6.5-min bout of moderate stair walking after the first 1.5 h of sitting	Insulin and glucose	Compared to sitting and flat walking, postprandial glucose levels were significantly reduced during and after stair walking. There were no differences in postprandial insulin levels across conditions	25

Table 1 (continued)

Author	Sample (*n*)	Design	Arms	Outcomes	Results	Downs and Black score
Tolfrey, 2012 [35]	11 male, 0 female	Randomized crossover	1. Sitting for 110 min 2. Three alternating 10-min periods of sitting and moderate intensity jog 3. Six alternating 10-min periods of sitting and moderate-intensity jog	Glucose and triglycerides	Compared to sitting, postprandial triglyceride levels were significantly reduced following 60, but not 30 min of intermitted exercise. Glucose levels were reduced in both activity conditions	24
Altenburg, 2013 [36]	5 male, 6 female	Randomized crossover	1. 8 h of sitting 2. 8 h of sitting with 8 min of moderate cycling every hour	Glucose and triglycerides	No differences in postprandial glucose or triglycerides across conditions	28
Farah, 2013 [37]	10 male, 0 female	Randomized crossover	1. 8.5 h of sitting 2. 8.5 h of sitting with a 60-min light-intensity walk before breakfast 3. 8.5 h of sitting with a 60-min light-intensity walk after breakfast	Glucose, insulin and triglycerides	Compared to sitting, postprandial triglycerides were reduced when walking was done before, but not after breakfast. Postprandial insulin was lowered by both walking conditions. There were no differences in postprandial glucose across conditions	28
Gonzalez, 2013 [38]	11 male, 0 female	Randomized crossover	1. 2 h of rest 2. 2 h of rest, followed by moderate-intensity running expending a total of 2.9 MJ of energy	Glucose and insulin	There was no significant difference in glucose or insulin across study conditions	28
Hashimoto, 2013 [39]	0 male, 14 female	Randomized crossover	1. 6 h of sitting 2. 6 h of sitting preceded by 30 min of light-intensity walking	Glucose, insulin and triglycerides	Compared to sitting, walking reduced postprandial glucose and insulin levels in the 1st h post-meal. Postprandial triglyceride levels were not different across conditions	26
Miyashita, 2013 [40]	15 male, 0 female	Randomized crossover	1. Sitting for 7.75 h 2. Sitting for 15 min, following by standing for 45 min, for 7.75 h 3. Sitting for 7.75 h with a 30-min brisk self-paced walk in the afternoon	Glucose, insulin and triglycerides	Compared to sitting, postprandial triglyceride and glucose (but not insulin) levels were reduced following the walking condition. There were no differences between the sitting and standing conditions	28

Table 1 (continued)

Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Peddie, 2013 [41]	28 male, 42 female	Randomized crossover	1. Sitting for 9 h 2. Sitting for 9 h with 30 min of light-intensity walking equally spaced throughout the day 3. Sitting for 9 h with 30 min of moderate-intensity walking performed in the morning	Glucose, insulin and triglycerides	Compared to sitting, postprandial glucose and insulin were significantly lower during the light-intensity walking break condition. Postprandial triglyceride levels during prolonged sitting were not different from either activity condition	28
Saunders, 2013 [7]	11 male, 8 female	Randomized crossover	1. Sitting for 8 h 2. Sitting for 8 h with a 2-min light-intensity walk break every 20 min 3. Sitting for 8 h with a 2-min light-intensity walk break every 20 min, and a 20-min moderate-intensity walk in the morning and afternoon	Glucose, insulin and triglycerides	There were no differences in any risk factor across the 3 conditions	28
Sisson, 2013 [8]	9 male, 9 female	Randomized crossover	1. Sitting for 3 h 2. Walking 45 min/h at 1.5 miles/h for 3 h	Glucose, insulin and triglycerides	Compared to 3 h of sitting, walking for 45 min/h resulted in significantly lower insulin levels 3 h post-meal. There were no other significant differences observed in cardio-metabolic health markers	28
Larsen, 2014 [11]	11 male, 8 female	Randomized crossover	1. 7 h of sitting 2. 7 h of sitting with a 2-min light-intensity walk break every 20 min 3. 7 h of sitting with a 2-min moderate-intensity walk break every 20 min	Blood pressure	Compared to sitting, systolic and diastolic blood pressure were significantly reduced during light- and moderate-intensity walk conditions. There were no differences in mean arterial pressure across conditions	29
Thorp, 2014 [42]	17 male, 6 female	Randomized crossover	1. Sitting for 8 h 2. Alternating 30-min periods of sitting and standing for 8 h	Glucose, insulin and triglycerides	Compared to prolonged sitting, alternating sitting and standing resulted in a significant reduction in postprandial glucose. There were no differences in postprandial insulin or triglycerides	28

Table 1 (continued)

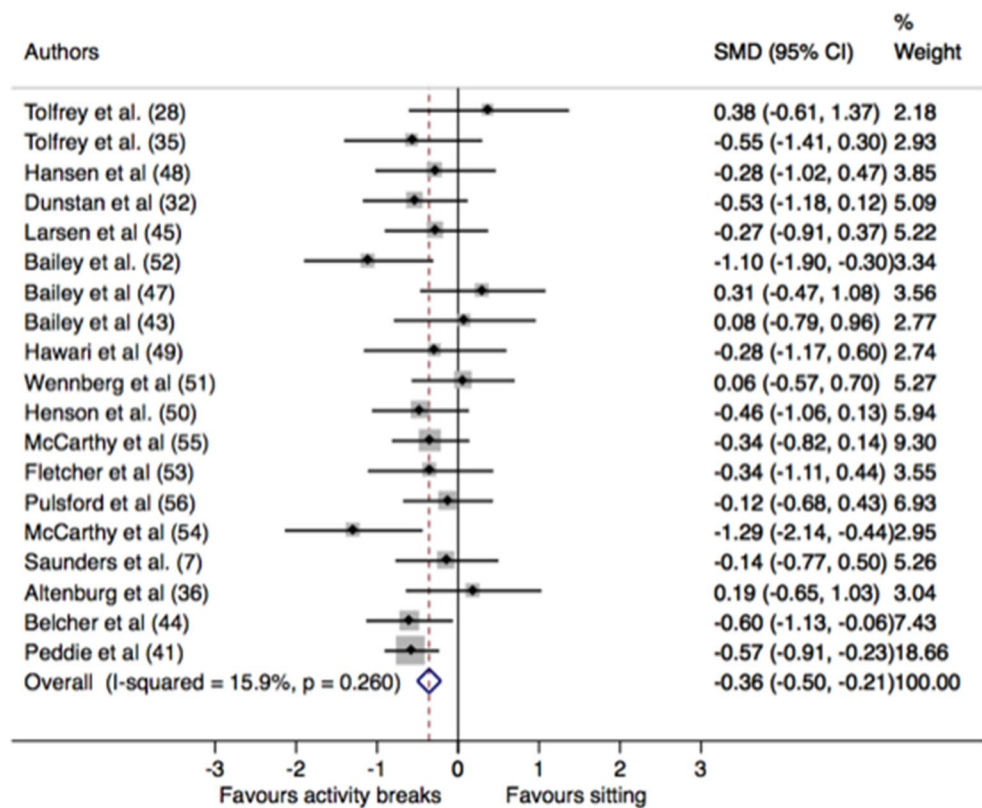| Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Thosar, 2014 [10]	12 male, 0 female	Randomized crossover	1. Sitting for 3 h 2. Sitting for 3 h with a 5-min walk at 2 miles/h during each hour of sitting	Superior femoral artery flow-mediated dilation	Compared to 3 h of sitting, flow-mediated dilation was significantly higher in the activity break condition	29
Bailey, 2015 [43]	7 male, 3 female	Randomized crossover	1. 5 h of sitting 2. 5 h of sitting with 2-min standing breaks every 20 min 3. 5 h of sitting with 2-min light-intensity walking every 20 min	Glucose, triglycerides, and blood pressure	Compared to sitting, walk breaks (but not standing breaks) reduced postprandial glucose. No differences observed for triglycerides or blood pressure across conditions	28
Belcher, 2015 [44]	15 male, 13 female	Randomized crossover	1. Sitting for 3 h 2. Sitting for 3 h, interrupted by 3 min of moderate-intensity walking every 30 min	Glucose and insulin	Compared to sitting, interrupting sitting resulted in a significant reduction in postprandial insulin and glucose levels	26
Larsen, 2015 [45]	11 male, 8 female	Randomized crossover	1. Sitting for 7 h 2. Sitting for 7 h with 2 min of light-intensity walking every 20 min 3. Both repeated for 3 days	Glucose, insulin, triglycerides	Compared to sitting, interrupting sitting resulted in a significant reduction in postprandial glucose and insulin, but not triglyceride levels. Differences were observed on day 1 and maintained on day 3	28
Ross, 2015 [46]	4 male, 8 female	Non-Randomized crossover	1. Sitting for 6 h 2. Sitting for 6 h with 4 min of moderate-intensity activity every 30 min	Triglycerides	No significant difference in triglyceride levels across conditions	28
Bailey, 2016 [47]	6 male, 7 female	Randomized crossover	1. Sitting for 5 h 2. Sitting for 5 h with a 2-min light-intensity walk break every 20 min 3. Sitting for 5 h with a 2-min moderate-intensity walk break every 20 min	Insulin and glucose	Compared to sitting, there were no differences in postprandial glucose or insulin in either of the walking conditions	24
Hansen, 2016 [48]	6 male, 8 female	Randomized crossover	1. Sitting for 2.5 h 2. Sitting for 2.5 h with a 2-min light-intensity walk break every 20 min	Glucose	There was no difference seen across conditions	24

Table 1 (continued)

Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Hawari, 2016 [49]	10 male, 0 female	Randomized crossover	1. Sitting for 8 h 2. Alternating between sitting and standing every 15 min during an 8-h period 3. Performing the following cycle for 8 h: sitting for 5 min, then 10 cycles of standing for 90 s followed by sitting for 30 s, then sitting for an additional 5 min	Insulin, glucose and triglycerides	There were no significant differences observed between conditions	27
Henson, 2016 [50]	0 male, 22 female	Randomized crossover	1. Sitting for 7.5 h 2. Sitting for 7.5 h with a 5-min standing break every 30 min 3. Sitting for 7.5 h with a 5-min self-paced light walk every 30 min	Insulin, glucose and triglycerides	Compared to prolonged sitting, postprandial glucose and insulin were reduced by both standing and walking breaks. There was no difference in triglycerides across conditions	28
Wennberg, 2016 [51]	10 male, 9 female	Randomized crossover	1. Sitting for 7 h 2. Sitting for 7 h with a 3-min light-intensity walk break every 30 min during the last 5 h of sitting	Insulin, glucose, and blood pressure	There were no differences between conditions for any outcome	29
Zeigler, 2016 [58]	2 male, 7 female	Randomized crossover	1. Sitting for 8 h 2. Accumulating 2.5 h of standing and 5.5 h of sitting during an 8-h period 3. Accumulating 2.5 h of walking at 1 mile/h and 5.5 h of sitting during an 8-h period 4. Accumulating 2.5 h of cycling at 20 W and 5.5 h of sitting during an 8-h period	Blood pressure	Compared to sitting, systolic blood pressure was reduced in all three active conditions, while cycling was also lower than standing or walking. Compared to sitting, diastolic blood pressure was reduced in cycling only	28
Bailey, 2017 [52]	14 males, 0 females	Randomized crossover	1. Sitting for 4 h 2. Sitting for 4 h with a 2-min moderate-intensity walk break every 20 min	Insulin and glucose	Compared to prolonged sitting, postprandial glucose was lower during the walk break condition. There was no difference in insulin levels across conditions	26

Table 1 (continued)

Author	Sample (n)	Design	Arms	Outcomes	Results	Downs and Black score
Fletcher, 2017 [53]	5 male, 8 females	Randomized crossover	1. Sitting for 6 h with high-energy diet 2. Sitting for 6 h with 2 min of body weight resistance exercises every 20 min with a high-energy diet 3. Sitting for 6 h with usual-energy diet 4. Sitting for 6 h with 2 min of body weight resistance exercises every 20 min with usual-energy diet	Glucose	Compared to prolonged sitting, postprandial glucose was lower with activity breaks in both dietary conditions	26
McCarthy, 2017 [54]	16 male, 18 female	Randomized crossover	1. Sitting for 7.5 h 2. Sitting for 7.5 h with a 5-min light-intensity walk break every 30 min	Insulin and glucose	Compared to prolonged sitting, postprandial insulin and glucose levels were reduced in the walk break condition	30
McCarthy, 2017 [55]	6 male, 7 female	Randomized crossover	1. Sitting for 7.5 h 2. Sitting for 7.5 h with a 5-min of seated arm ergometry every 30 min	Insulin and glucose	Compared to prolonged sitting, postprandial insulin and glucose levels were reduced in the ergometry condition	29
Pulsford, 2017 [56]	25 male, 0 female	Randomized crossover	1. Sitting for 9 h 2. Sitting for 9 h with a 2-min standing break every 20 min during the last 7 h of sitting 3. Sitting for 9 h with a 2-min light-intensity walk break every 20 min during the last 7 h of sitting	Insulin and glucose	Compared to sitting, postprandial insulin and glucose were significantly reduced during the walking, but not standing condition	29

Fig. 3 Effect (Cohen's *d*) of regular activity breaks (< 10 min in duration) compared to prolonged sitting on postprandial glucose responses. Studies are sorted by carbohydrate content of the test meal. The *diamond* indicates the standardized mean difference (SMD) with associated 95% confidence interval for each subgroup. *Shaded* area represents weighting of individual studies

Authors	SMD (95% CI)	% Weight
Tolfrey et al. (28)	0.38 (−0.61, 1.37)	2.18
Tolfrey et al. (35)	−0.55 (−1.41, 0.30)	2.93
Hansen et al (48)	−0.28 (−1.02, 0.47)	3.85
Dunstan et al (32)	−0.53 (−1.18, 0.12)	5.09
Larsen et al (45)	−0.27 (−0.91, 0.37)	5.22
Bailey et al. (52)	−1.10 (−1.90, −0.30)	3.34
Bailey et al (47)	0.31 (−0.47, 1.08)	3.56
Bailey et al (43)	0.08 (−0.79, 0.96)	2.77
Hawari et al (49)	−0.28 (−1.17, 0.60)	2.74
Wennberg et al (51)	0.06 (−0.57, 0.70)	5.27
Henson et al. (50)	−0.46 (−1.06, 0.13)	5.94
McCarthy et al (55)	−0.34 (−0.82, 0.14)	9.30
Fletcher et al (53)	−0.34 (−1.11, 0.44)	3.55
Pulsford et al (56)	−0.12 (−0.68, 0.43)	6.93
McCarthy et al (54)	−1.29 (−2.14, −0.44)	2.95
Saunders et al. (7)	−0.14 (−0.77, 0.50)	5.26
Altenburg et al (36)	0.19 (−0.65, 1.03)	3.04
Belcher et al (44)	−0.60 (−1.13, −0.06)	7.43
Peddie et al (41)	−0.57 (−0.91, −0.23)	18.66
Overall (I-squared = 15.9%, p = 0.260)	−0.36 (−0.50, −0.21)	100.00

Favours activity breaks   Favours sitting

The impact of sitting on postprandial glucose and insulin levels does not appear to be influenced by participant age or the carbohydrate load of test meals. However, the total amount of carbohydrate provided in the test meal(s) in the interventions included in our meta-analyses ranged from 54.9 to 228.5 g. It is possible that larger carbohydrate loads may modify the effect of regular activity breaks on postprandial insulin and glucose. Although the mean BMI of study participants ranged from a low of 16.2 [44] to a high of 32.9 [50], we observed no impact on our findings. These results suggest that the relationship between activity breaks and postprandial insulin, glucose, and triglyceride levels may be consistent across a relatively large range of body weights.

Subgroup analyses indicated that the intensity of activity breaks did not modify their effect on postprandial insulin, glucose, or triglyceride responses. However, it is possible that the small number of studies eligible for this subgroup analysis limited the statistical power to detect small differences. Acknowledging this limitation, it is possible that standing breaks of less than 10 min in duration may be insufficient to reduce postprandial insulin or glucose levels in apparently healthy individuals. Given the small number of studies on this topic, future research

should continue to investigate the impact of standing breaks to determine whether they offer similar benefit as other forms of light and moderate activity in both healthy individuals and in those with type 2 diabetes or impaired glucose tolerance.

We now have a convincing body of high-quality evidence from randomized controlled trials showing that light- to moderate-intensity activity breaks reduce postprandial glucose and insulin concentrations among apparently healthy individuals. Nevertheless, there are still many important questions to answer and knowledge gaps to be filled in this field of research. In particular, more work needs to be done to identify the timing, duration and mode of activity break that are likely to impart the most benefit to specific populations. Thinking more broadly about the implications of this knowledge for public health, we must begin to devise strategies that will enable individuals who habitually sit for long periods to perform activity breaks as part of their everyday routine.

Of the ten studies included in our meta-analysis that examined postprandial triglyceride levels, seven examined triglyceride levels during the intervention, while three examined triglycerides the day following the intervention. Differences in postprandial triglyceride responses were only
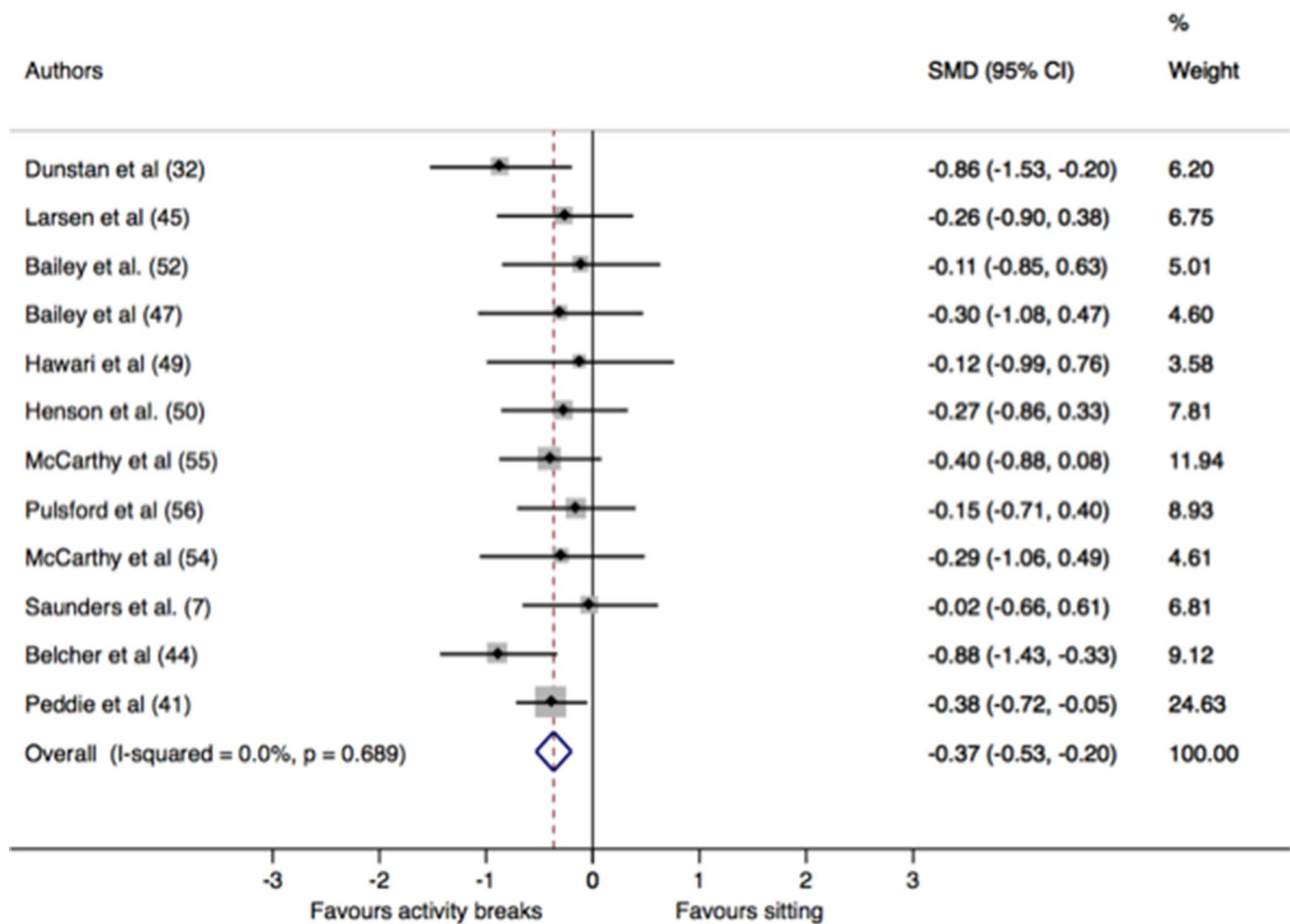
Fig. 4 Effect (Cohen's *d*) of regular activity breaks (< 10 min in duration) compared to prolonged sitting on postprandial insulin responses. Studies are sorted by carbohydrate content of the test meal. The *diamond* indicates the standardized mean difference (SMD) with associated 95% confidence interval for each subgroup. *Shaded* area represents weighting of individual studies

observed when measured the day following the activity intervention. The small number of studies measuring triglyceride response and an even smaller number of studies measuring postprandial responses the day following the intervention may indicate these results should be interpreted with caution. However, the results are compatible with documented effects of more prolonged bouts of activity on postprandial responses, which occur the day following exposure to intermitted or sustained bouts of activity. The delayed response may be related to the upregulation of lipoprotein lipase activity, which peaks 8–16 h after a bout of activity [64]. Further research on this topic is clearly warranted.

At present there is insufficient evidence to draw strong conclusions on the impact of prolonged sitting on blood pressure or vascular form and function, suggesting that further research on this topic is clearly needed. Although not the focus of the current review, there has been relatively little experimental research on the relationship between prolonged sitting and numerous other important health outcomes,

including coagulatory factors, regional blood flow, autonomic nervous system balance, stress hormone levels, and cognition, to name a few. Given that the impact of prolonged sitting on postprandial glucose and insulin is now relatively well-established, more research is needed to better understand the relationship between sitting and a wider range of health outcomes.

Several physiological mechanisms have been suggested which would link bouts of prolonged sitting with postprandial insulin, glucose and triglyceride levels [65, 66]. Periods of inactivity have been shown to result in insulin resistance in skeletal muscle [65], whereas light-intensity activity breaks have been shown to stimulate metabolic pathways related to glucose uptake [66, 67]. Less research has examined the mechanisms linking prolonged sitting with triglyceride levels. Although research in animal models suggests that muscle inactivity may result in reductions in lipoprotein lipase activity [68], work in humans has failed to detect changes in response to prolonged sitting [25]. Given
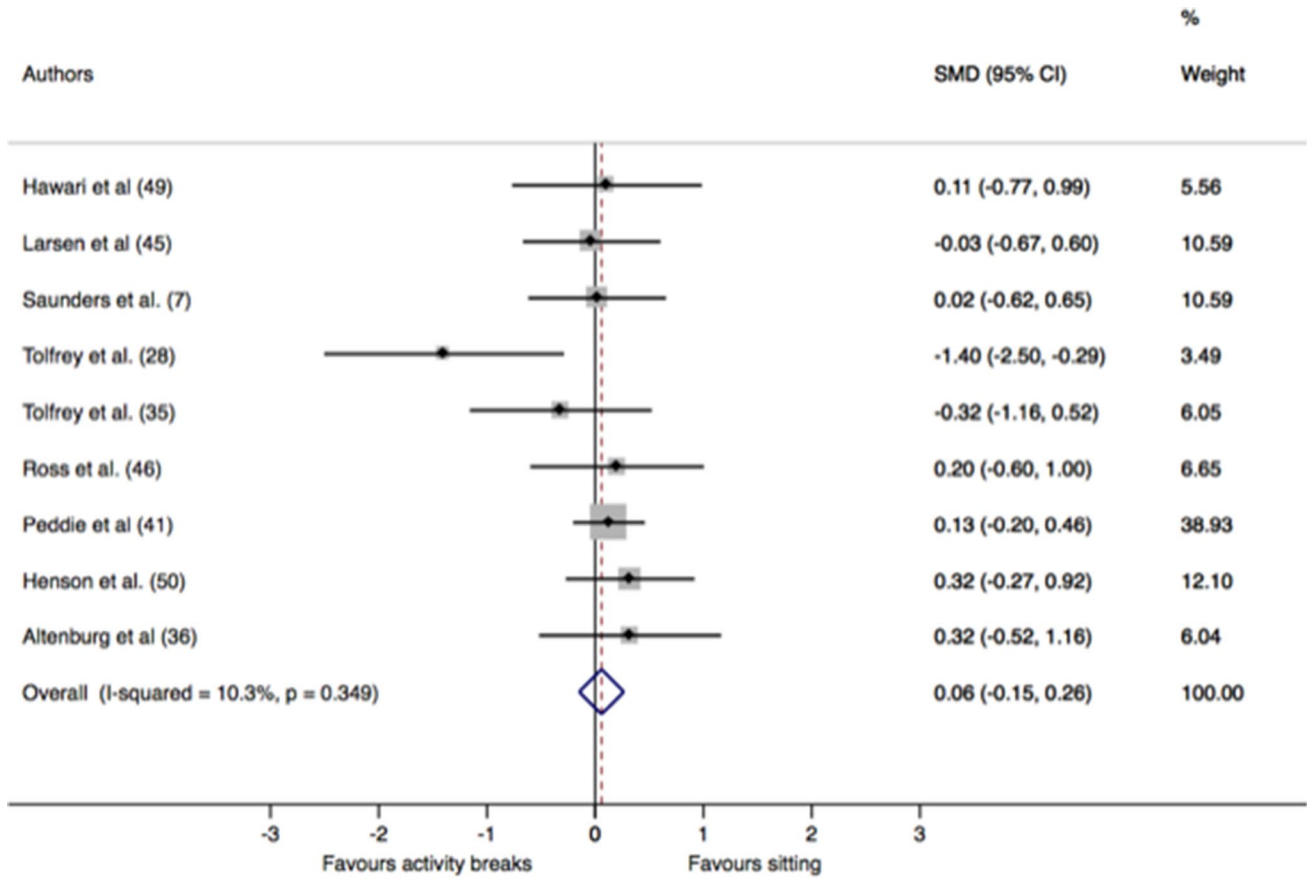
Fig. 5 Effect (Cohen's *d*) of regular activity breaks (<10 min in duration) compared to prolonged sitting on postprandial triglyceride responses. Studies are sorted by fat content of the test meal. The *dia-mond* indicates the standardized mean difference (SMD) with associated 95% confidence interval for each subgroup. *Shaded* area represents weighting of individual studies

Table 2 Association between macronutrient composition of the meal challenge(s) and postprandial insulin, glucose, triglyceride levels in meta-regression

	β	95% CI	*p*
Glucose	−0.002	−0.004 to 0.001	0.22
Insulin	−0.0005	−0.004 to 0.003	0.72
Triglycerides	0.005	−0.005 to 0.015	0.29

β represent the impact of a change of 100 g of carbohydrate in the test meal(s) on the effect size—the difference between prolonged sitting and regular activity breaks interventions—for glucose and insulin, and the impact of a change of 100 g of fat on the effect size for postprandial triglyceride response

CI confidence interval

Table 3 Association between BMI and postprandial insulin, glucose, triglyceride levels in meta-regression

	β	95% CI	*p*
Glucose	−0.008	−0.042 to 0.027	0.65
Insulin	0.010	−0.027 to 0.047	0.56
Triglycerides	0.024	−0.027 to 0.075	0.30

β represent the impact of a 1-kg/m^2 change in BMI on postprandial insulin, glucose and triglycerides

BMI body mass index, *CI* confidence interval

that available evidence suggests a strong and consistent link between sitting and important markers of cardiometabolic risk, more research is needed to better elucidate the mechanisms underpinning these relationships.

4.1 Strengths and Limitations

The present study used a systematic search methodology and identified a large number of experimental studies (*n* = 44) and a wider age range than previous meta-analyses in this field. This allowed us to investigate the impact of age, meal composition, and the timing of the test-meal, which have not been examined in previous reviews on this topic. Our review also included studies measuring blood pressure and vascular

parameters, although there was not sufficient evidence available on these topics to perform meta-analyses. This review was limited by the exclusion of non-English language papers and unpublished literature, all of which may have resulted in the omission of relevant findings. However, the funnel plots did not indicate evidence of publication bias in favor of large effect sizes in smaller studies. The meta-analysis performed in the current study included interventions which employed venous, capillary and interstitial blood samples. While it is recognized that these methods do not provide identical results, they are strongly correlated with each other [69, 70], and it was felt that combining the methods was therefore justified to maximize the available data. Further, our analyses were confined to apparently healthy individuals and therefore excluded studies on individuals with diabetes and cardiovascular disease, who are most likely to benefit from any reductions in cardiometabolic risk factors. It is possible that this may have diluted the observed relationship between activity breaks and reductions in postprandial insulin and glucose levels, thus making the reported effects more conservative. Given that research is now beginning to examine individuals with these chronic conditions [71, 72], future reviews should focus on these populations. Finally, the majority of the studies included in the current review exposed participants to > 3 h of uninterrupted sitting, and it is currently unclear if, or how frequently, adults in the general population accumulate sedentary bouts of this duration. Although this is a relatively long period of uninterrupted sitting, findings from the REGARDS study suggest that American adults accumulate 14% of their daily sedentary time in bouts of ≥ 90 min, a proportion which increases consistently with age [73]. Further research is therefore needed both to understand the frequency of prolonged sitting in the general population and to identify the minimum amount of uninterrupted sitting which results in clinically relevant changes in health outcomes.

5 Conclusions

Our findings suggest that acute periods of uninterrupted sitting result in significant increases in postprandial insulin and glucose levels, when compared to periods of sitting interrupted with light- or moderate-intensity physical activity. Breaking up sitting time may have benefits for postprandial triglyceride levels, but these are only seen the day following the intervention. There was insufficient data to quantitatively assess the effect of sitting with or without activity breaks on blood pressure or vascular function. It would be valuable for future research investigating the effects of sedentary behavior on cardiometabolic health to include blood pressure and vascular form and function measures as endpoints

now that the weight of evidence clearly shows that regularly interrupting prolonged sitting with activity breaks produces marked and meaningful improvements in postprandial glucose metabolism.

Compliance with Ethical Standards

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