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FULL RESEARCH PAPER
Physical activity

Optimizing physical activity bouts to interrupt sedentary behaviour for cardiometabolic health: a systematic review and meta-analyses of randomized controlled trials

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Aims Chronic diseases such as type 2 diabetes mellitus and cardiovascular diseases are leading causes of mortality worldwide, with sedentary behaviour (SB) and physical inactivity recognized as major interrelated risk factors. Prolonged SB, particularly when combined with insufficient physical activity, adversely affects cardiometabolic health. This systematic review aimed to evaluate which characteristics of physical activity (PA) bouts, in terms of frequency, duration, and intensity, are associated with improvements in cardiometabolic outcomes.

Methods and results Studies assessing physical activity interventions compared with sedentary control conditions were included. Eligible studies involved adults aged 18–65 years, with or without cardiometabolic conditions. PubMed, Cochrane Central, Embase, and Web of Science were searched to February 2025. Random-effects models were used to calculate pooled standardized mean differences (SMD) with 95% confidence interval (CI). Subgroup and meta-regression analyses explored potential moderators. A total of 144 studies (247 intervention arms; 2216 participants) were included. Frequent PA bouts reduced blood glucose [SMD −0.22 (95% CI −0.27 to −0.16)]. Longer and/or more intense PA bouts decreased triglycerides [SMD −0.27 (−0.34 to −0.19)], with significant duration × intensity interactions for glucose ($P = 0.032$) and triglycerides ($P < 0.001$). Moderate-to-vigorous PA bouts improved endothelial function [flow-mediated dilation SMD 0.88 (0.47–2.24); shear rate SMD 0.54 (0.31–0.78)]. PA bouts also lowered insulin [SMD −0.26 (−0.32 to −0.19)], systolic BP [SMD −0.29 (−0.39 to −0.19)], and diastolic BP [SMD −0.16 (−0.26 to −0.05)].

Conclusion In acute experimental settings, glucose regulation appears to benefit more from frequent PA bouts, while triglyceride responses are more closely related to greater duration and/or intensity. Blood pressure shows favourable acute responses across PA types, whereas higher PA intensity is associated with improved endothelial function. Tailoring strategies to interrupt SB with PA bouts may help inform approaches to improve cardiometabolic health.

Lay summary This study identifies how the frequency, duration, and intensity of physical activity bouts produce distinct short-term benefits for blood sugar, blood lipids, blood pressure, and vascular function when used to interrupt prolonged sitting.

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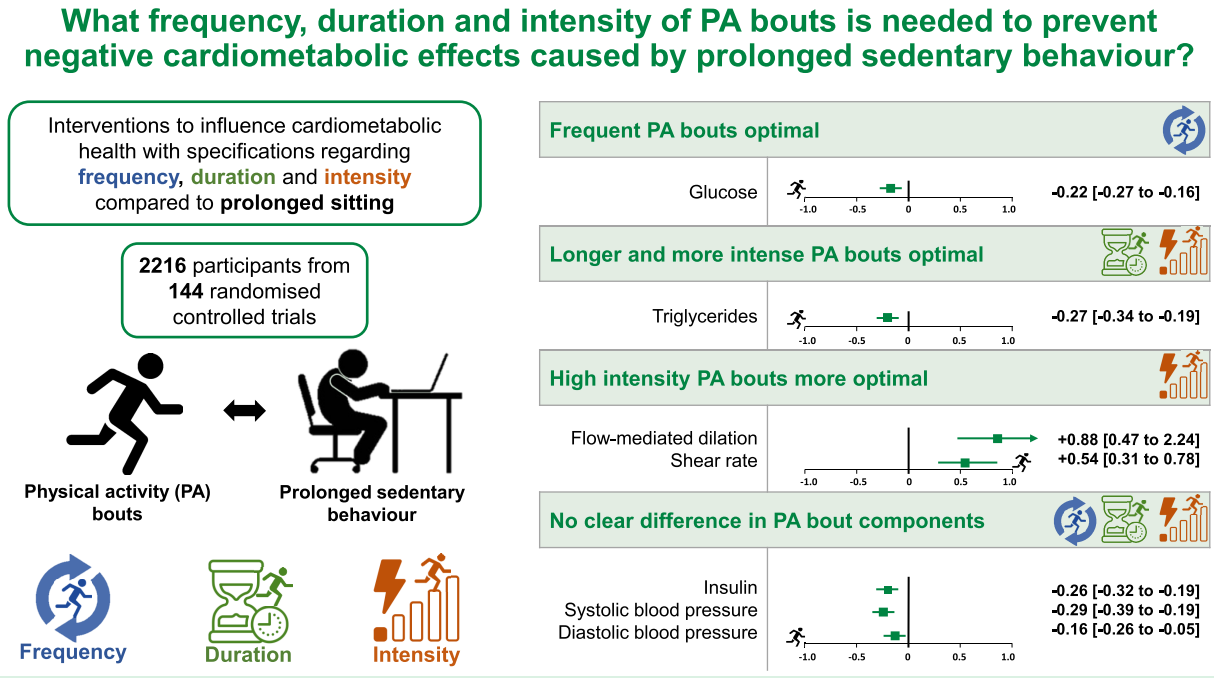
Key findings

- Frequent physical activity bouts most effectively improve blood sugar, while longer or more intense bouts are needed to reduce blood lipids.
- Blood pressure improves with a wide range of physical activity bouts, whereas vascular function benefits mainly from higher-intensity activity.

Registration PROSPERO 2023 CRD42023495310

Graphical Abstract



Keywords Sedentary behaviour • Physical activity • lipids • Glucose metabolism • Vascular function

Summary boxes

What is already known on this topic

- Prolonged sedentary behaviour is associated with detrimental health effects and increased risk for developing chronic diseases.
- Interrupting sedentary behaviour with physical activity bouts is known to benefit metabolic and cardiovascular health.
- Current guidelines recommend limiting and interrupting sedentary behaviour for health promotion, but remain vague regarding the modality of physical activity bouts.

What this study adds

- Frequent physical activity bouts to interrupt sedentary behaviour significantly improve glycaemic control.
- Longer and more intense physical activity bouts are linked to improved lipid profiles.
- High-intensity physical activity bouts provide the greatest benefit to endothelial function.
- These findings highlight the need for tailored components of physical activity to target specific cardiometabolic outcomes.

Introduction

According to the World Health Organisation (WHO), chronic diseases are a major global public health concern and the leading cause of mortality worldwide.[1] In the absence of evidence-based actions, the global annual deaths from chronic diseases are projected to rise to 55 million deaths in 2030, accompanied by a substantial increase in socio-economic costs.[1] In this

context, the WHO identifies type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) as key chronic conditions of concern related to cardiometabolic health.

Both sedentary behaviour (SB) and physical inactivity have been recognized as interdependent risk factors for the development of T2DM and CVD.[2,3] SB refers to any waking behaviour, characterized by a low energy expenditure, while being in a sitting or reclining posture,[4] whereas physical inactivity denotes insufficient levels (<150 min per week) of moderate-to-vigorous physical activity (MVPA). Studies using objective measures have demonstrated that, on average, Western adults spend 8–12 h in SB per day, of which the majority is spent in prolonged sedentary bouts (lasting ≥30 min).[2] In addition, up to 30% of adults worldwide are physically inactive, with higher levels of inactivity in high-income countries.[5] Within this context, it has become evident that excessive prolonged SB, often in combination with physical inactivity, negatively impacts cardiometabolic health, contributing to insulin resistance, increased adiposity, poor lipid profiles and endothelial dysfunction.[6–8] Given their detrimental effects on T2DM and CVD, strategies aimed at reducing SB and promoting physical activity (PA) warrant further investigation.

Reducing and regularly interrupting SB, even with low-intensity PA bouts, alongside sufficient MVPA, is crucial for maintaining a healthy cardiometabolic profile.[9,10] Reflecting this, the WHO guidelines advise individuals to engage in 150–300 min of moderate-intensity PA, 75–150 min of vigorous-intensity PA, or an equivalent combination each week.[10] Notably, the 2020 WHO guidelines also included recommendations on SB for the first time, emphasising the importance of limiting sedentary time. The WHO states that replacing SB with PA of any intensity can yield health benefits. However, these recommendations remain non-prescriptive and somewhat vague, primarily due to a lack of robust scientific evidence on the optimal frequency, intensity, and duration of PA bouts needed to reduce and interrupt sedentary time. To date, it remains unclear whether standing, light-intensity PA, or moderate-to-vigorous intensity PA is most beneficial for cardiometabolic health, and whether repeated short PA bouts to interrupt SB are superior to a single continuous PA bout (resembling structured exercise) to replace time spent in SB. The absence of specificity in the guidelines on prolonged SB reflects this evidence gap. To support policy development, well-designed randomized controlled trials are needed to evaluate effective and practical strategies for reducing sedentary time.

Many acute experimental studies have demonstrated the beneficial effects of interrupting SB on cardiometabolic health. Although these effects have been explored in meta-analyses, focusing on both metabolic[9,11,12] and cardiovascular[13] outcomes, they primarily examined the frequency of PA bouts in isolation (e.g. continuous PA vs. frequent PA bouts). To date, only one systematic review has included a network meta-analysis evaluating the effects of PA bouts based on both intensity and frequency.[14] However, reported outcomes of this review were limited to postprandial glycemia and insulin responses. A better understanding of how specific components of PA bouts, namely duration, intensity, and frequency, acutely influence cardiometabolic responses when used to interrupt SB is essential for designing effective long-term strategies. Because these components typically change simultaneously in free-living settings, laboratory-based studies are ideal to precisely control and modulate components in isolation, ensuring accurate assessment of their individual contributions.

Therefore, the aim of this systematic review is to evaluate the acute effects of different PA interventions designed to reduce SB, specifically varying in duration, frequency and intensity, on (postprandial) metabolic and vascular responses in sedentary healthy adults and individuals with cardiometabolic health-related disorders. By synthesising this evidence, the review will offer practical recommendations on the optimal characteristics of PA bouts in both healthy adults and individuals with chronic diseases, addressing the urgent global challenge of cardiometabolic disease prevention.

Methods

This systematic review and meta-analysis were registered in the PROSPERO international prospective register of systematic reviews (CRD42023495310) and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines.

Eligibility criteria

The eligibility criteria were based on the PICOS (population, intervention, comparison, outcomes and study type) framework and defined as follows: 1) study population: healthy adults (18–65 years of age) and adults with cardiometabolic health related diseases including prediabetes/T2DM, obesity, CVD, (pre)hypertension and the metabolic syndrome; 2) intervention: laboratory-based aerobic PA interventions aimed at reducing and interrupting SB in terms of frequency, intensity and duration. Studies were excluded if only the combined effects of frequency, duration and/or intensity were reported, the PA bouts were not controlled or when no wash-out period was included; 3) Comparison group: uninterrupted sitting control group; 4) Outcome variables: metabolic outcomes including glucose, insulin, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, glycerol, non-esterified fatty acids and cardiovascular function outcomes including systolic blood pressure, diastolic blood pressure, flow-mediated-dilation, shear rate, blood flow, augmentation index and pulse wave velocity. Outcomes for metabolic status were registered after fasting or after a standardized meal (postprandial); 5) study type: acute (1–7 days) randomized controlled trials (RCTs) and randomized cross-over trials.

Information sources and search strategy

The computer-based searches were performed in the electronic databases PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Embase and Web of Science for studies published from inception until February 2025. To retrieve the eligible studies database, specific search strategies were designed in consultation with an experienced professional clinical librarian (G.H.L.M.F.) and consisted of four main concepts: 1) SB, 2) PA interventions to reduce SB, 3) cardiometabolic health-related outcomes, and 4) randomized (cross-over) controlled trials. Relevant keywords and search terms were included in a sensitive search (see Supplementary material online, *Appendix I*). The systematic search was restricted to the English, Dutch, German or French language.

Selection process

Database search results were imported into EndNote (EndNote 21.5, Clarivate, Philadelphia, PA, USA), where duplicates were

removed using the deduplication method from Bramer *et al.*[15] Results were then exported to Rayyan[16] and two reviewers (W.M.A.F. and J.L.P.V.) independently assessed if studies met the pre-specified inclusion criteria, based on title and abstract screening. Disagreements were resolved by consensus with a third reviewer (B.O.E.). Following the title and abstract screening, full-texts were retrieved for in-depth eligibility assessment.

Data extraction

Data were independently extracted by reviewers (W.M.A.F. and J.L.P.V.) with the aid of a predesigned, pilot-tested data collection file, adapted from the extraction form provided by the Cochrane Collaboration. For each study, reviewers extracted information regarding the study information (author, year of publication, language, location, data availability), study characteristics (study aim, study design, study population, country where the study was conducted and study duration), study participants (sample size, demographics, disease status, medication use and baseline PA level), study methods (intervention arms, intervention duration, intensity and/or frequency of PA bouts, number of bouts, timing of PA, time between intervention and measurements, caloric intake, meal composition, meal timing, number of included participants per intervention arm, dropouts and the number of participants that were randomized and analysed) and the outcome variables (outcome definition, unit of measurement, time points measured and reported, statistical methods used).

If a study consisted of multiple intervention arms, data were only extracted from the intervention arms that met the inclusion criteria. In case insufficient details could be retrieved from the studies, corresponding authors were contacted for additional information, or data were estimated from figures and graphs. After data extraction, discrepancies were evaluated and resolved through discussion. For postprandial responses, total and incremental area under the curve (tAUC and iAUC) were extracted. In case postprandial responses were not reported as tAUC and/or iAUC, corresponding authors were contacted, or values were calculated by means of a software package provided in GraphPad Prism version 10. Studies where data could not be retrieved were still excluded.

Risk of Bias (RoB) assessment

Two independent reviewers (W.M.A.F. and J.L.P.V.) were responsible for the risk of bias assessment as recommended by Chandler *et al*. (Cochrane 'Risk of Bias' [RoB] assessment tool, the Cochrane Collaboration).[17] The RoB 2 tool was used to assess the following methodological domains: randomisation process, deviation from intended interventions, missing outcome data, measurement of the outcome and selection of the reported outcome. For studies with a cross-over design, the adapted version of the RoB 2 tool was used to assess the risk of bias arising from period and carryover effects. Each of these domains was judged, and RoB was classified as 'low risk', 'some concerns' or 'high risk'. Disagreements between reviewers were resolved through discussion. Based on the subdomains, one global RoB was attributed to all studies following the same classification.

Reporting bias assessment

To assess publication bias, funnel plots were generated for the meta-analyses. If asymmetry was detected, studies were reviewed for explanations other than publication bias, such as methodological differences or population heterogeneity. In addition, Egger's test was performed to quantitatively assess publication bias for each outcome, with a P-value < 0.05 indicating significant publication bias.

Certainty assessment

Certainty of the evidence was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) approach. This method evaluates the quality of evidence based on factors such as study design, risk of bias, consistency of results, directness of evidence, precision of estimates, and potential publication bias. Certainty of the evidence was classified into four levels: high, moderate, low, or very low, reflecting the degree of confidence in the effect estimates. This systematic assessment ensured a transparent and structured evaluation of the certainty of the evidence supporting the review's conclusions. An overview of the results with a reflection on clinical significance and level of certainty is provided in a GRADE summary of findings table.

Synthesis methods and statistical analysis

Intensity of PA was based on percentage heart rate reserve, percentage peak oxygen uptake, percentage maximal heart rate and metabolic equivalents, and categorized as standing, light-intensity PA (1.5–3.0 Metabolic Equivalent of Task [MET]), moderate-intensity PA (3.0–6.0 MET) and vigorous-intensity PA (>6.0 MET).[18] Frequency was defined based on sedentary time between two PA bouts, and duration was defined based on the duration of one single PA bout. Furthermore, a distinction was made between interventions with one continuous PA bout (only one PA bout per day) and interventions in which multiple PA bouts were accumulated. Blood parameters, in terms of group mean and standard deviation, were converted to the same unit (from mg/dL to mmol/L), including triglycerides (multiply by 0.0112), total cholesterol, HDL cholesterol, LDL cholesterol (multiply by 0.02586), glucose (multiply by 0.05551) and insulin concentration (μIU to pmol; multiply by 6.9444).[19]

Aggregated data were used for both quantitative and narrative synthesis. Statistical analyses were performed using R version 3.6.0 (The R Foundation for Statistical Computing, Vienna, Austria) and RevMan version 5.4.1. Mean tAUC or iAUC and mean differences with 95% confidence intervals were calculated, and pooled effect estimates were obtained using a random-effects model due to the large heterogeneity among the studies (differences in population, age and intervention characteristics). When mean differences were not available, authors of the included studies were contacted to request additional data. In case standard deviations of mean differences within a study were still missing, the averaged intraclass correlation coefficient (ICC) of similar included studies was used to calculate the SD of the mean difference as recommended in the Cochrane Handbook for Systematic Reviews of Interventions.[17] Finally, when data were presented as median and interquartile range, the mean and standard deviation were estimated using the formula from Hozo *et al*.[20] In addition, because various measurement scales were used, a standardized mean difference (SMD; Hedges' g) and 95% confidence interval ([95%CI]) were used to analyse continuous outcomes. SMDs of 0.2, 0.5 and 0.8 were considered as small, moderate and large, respectively.[21]

Interaction effects between intensity, frequency and duration of PA bouts were tested using mixed effects models. Heterogeneity of each summary effect size was quantified using the Chi^2 test and I^2 statistic, in which the boundary limits 25%, 50%, and 75% were designated as low, moderate, and high heterogeneity values, respectively. Subgroup analyses were performed to investigate differences in PA intensity, duration and frequency using a test of interaction based on Cochran's Q test. Potential moderators, including population characteristics (age, sex proportion [% male], BMI and health status) and intervention characteristics (PA volume [frequency × duration], time between PA and measurement and the timing of PA), that may influence

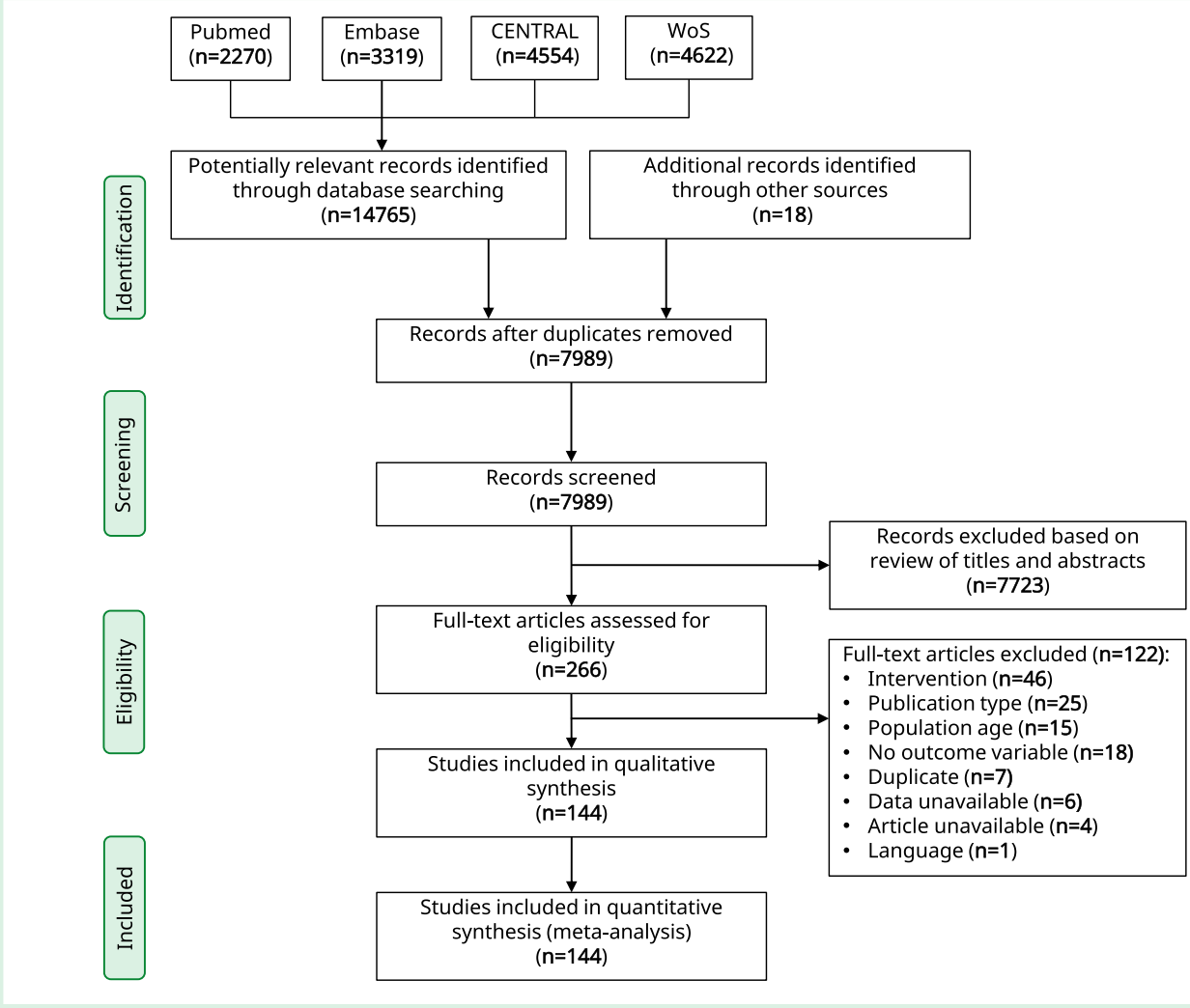


Figure 1 PRISMA flow diagram of the study selection process. CENTRAL, Cochrane Central Register of Controlled Trials, WoS, Web of Science.

heterogeneity and intervention effect size were explored using mixed effects meta-regression analysis and using subgroup analysis (Cochran's Q test). Sensitivity analyses were performed to evaluate the robustness of the results. Here, studies at high risk of bias were removed to evaluate the effect of those studies on the summary estimates.

Results

The search strategy identified 14 765 potentially relevant studies and an additional 18 studies by hand searching, of which 7992 remained after deduplication (*Figure 1*). Seven authors were contacted to obtain the full text, protocol data or for sharing relevant data. In total, 144 studies with 247 intervention arms were included in the systematic review and meta-analyses. The main reasons for exclusion were related to intervention characteristics ($n = 46$) or population ($n = 25$). Included studies were published over a 31-year period (from 1994 to 2025), all written in the English language and performed in twenty different countries, predominantly originating from the United States ($n = 43$).

Study characteristics

Most studies used a randomized crossover design ($n = 137$), with six randomized-controlled trials, and one used a controlled study. Study duration ranged from 1 to 7 days (mean 6.9 h, range: 1–36 h). The interval between the PA intervention and cardiometabolic measurements varied and was categorized as 0 to 3 h ($n = 30$), >12 h ($n = 38$) or simultaneously with measurements ($n = 76$). Interventions included standing ($n = 23$), walking ($n = 115$), running ($n = 38$), cycling ($n = 58$) and stair climbing ($n = 13$), with intensity ranging from standing ($n = 23$) to LPA ($n = 54$), MPA ($n = 123$) and VPA ($n = 47$). Mean PA bout duration was 33 ± 70 min (range: 0.3–720 min), and 116 interventions used interval approaches (mean interval 25 ± 46 min, range: 10–240 min). A detailed description of the study interventions is provided in Supplementary material online, *Appendix II*, *Table S1*.

Population characteristics

The included studies evaluated 2216 participants of which 1455 participants were healthy (studies: $n = 98$),[22–117] 515 overweight/obese ($n = 34$),[94,101,102,118–147] 163 (pre)diabetic

Table 1 Confidence in effect estimates in meta-analysis of interventions with sedentary behaviour interruptions for cardiometabolic health outcomes

Outcomes	Illustrative risk	SMD change (95% CI)	No. of participants	Quality of the evidence (GRADE)[a]
Glucose	Normal fasting plasma glucose with postprandial hyperglycemia is associated with a two-fold CVD mortality risk.[163]	−0.22 (−0.27, −0.16)	5556 (177 studies)	High certainty ⊕⊕⊕⊕
Insulin	Preventing insulin resistance could prevent 42% of myocardial infarctions.[164]	−0.26 (−0.32, −0.19)	3810 (121 studies)	High certainty ⊕⊕⊕⊕
Triglycerides	Hazard ratios per 1 mmol/L increase in postprandial triglycerides were 1.16 for all-cause mortality in women and 1.03 in men.[165]	−0.27 (−0.34, −0.19)	3094 (99 studies)	High certainty ⊕⊕⊕⊕
Flow-mediated dilation	A 1% decrease in FMD increases the risk of a cardiovascular event by 13%.[166]	0.88 (0.47, 1.28)	912 (33 studies)	Low certainty ⊕⊕⊖⊖
Shear rate	The reduction in shear rate and its consequent effect on FMD has an important prognostic value. Low FMD has been reported to be an important predictor of cardiovascular risk (RR = 2.66).[167]	0.54 (0.31, 0.78)	638 (23 studies)	Low certainty ⊕⊕⊖⊖
Systolic blood pressure	Every 10 mmHg reduction in SBP reduced the risk of major CVD events (RR = 0.80) and a significant 13% reduction in all-cause mortality (RR = 0.87).[168]	−0.26 (−0.36, −0.16)	1572 (48 studies)	High certainty ⊕⊕⊕⊕
Diastolic blood pressure	Hazard ratio per unit increase in z score for DBP is 1.06 for a composite of myocardial infarction and/or stroke incidence rate.[169]	−0.16 (−0.26, −0.05)	1400 (44 studies)	High certainty ⊕⊕⊕⊕

CI, confidence interval; CVD, cardiovascular disease; FMD, flow-mediated dilation; RR, relative risk; SBP, systolic blood pressure; DBP, diastolic blood pressure; SMD, standardized mean difference.
[a]Grading of Recommendations Assessment and Evaluation (GRADE) Working Group grades of evidence: high certainty (very confident that true effect lies close to estimate of effect); moderate certainty (moderately confident in effect estimate: true effect is likely to be close to estimate of effect, but possibility that it is substantially different exists); low certainty (confidence in effect estimate is limited: true effect may be substantially different from estimate of effect); very low certainty (very little confidence in effect estimate: true effect is likely to be substantially different from estimate of effect).

(*n* = 10),[37,38,148–155] 63 (pre)hypertensive (*n* = 5)[156–160] and 20 the metabolic syndrome (*n* = 2).[161,162] Participants had a mean age of 32.7 ± 5.3 (range: 19.2–64.0 years) and BMI of 26.4 ± 3.3 kg/m^2 (range: 20.0–38.0 kg/m^2). Overall, 51% (range: 9–89%) of the participants were male, with 55 studies including only males and 16 including only females. Forty-three studies included physically active participants, and 50 included only physically inactive participants. Based on 61 studies reporting physical fitness, mean peak oxygen uptake was 40.4 ± 6.3 mL/kg/min (range: 20.0–56.6 mL/kg/min).

Risk of bias/certainty of evidence

Overall risk of bias was low in 109 (21.1%) interventions and high in 32 (6.2%) interventions, with remaining interventions judged to have some concerns (see Supplementary material online, *Appendix III, Figure S1*). An overview of RoB for all different subdomains of the RoB 2 tool is provided in Supplementary material online, *Table S1*. High overall risk could be attributed to problems in the randomisation process (*n* = 10) or inappropriate measurement of the outcome (*n* = 13). Only one study (Rodrigues *et al.*)[158] reported deviations from the intended intervention without proper adjustments in the analysis. In addition, a summary of findings with statements regarding the certainty of the evidence and clinical significance is presented in *Table 1* (GRADE Summary of the Findings).

Publication bias

No publication bias was found for the outcome variables, except for FMD. In this case, asymmetry was identified in the funnel plots (see Supplementary material online, *Appendix IV, Figure S1*) where PA bouts were compared to prolonged SB. Additional statistical analysis (Egger's test) indicated significant publication bias for FMD (Egger's g: −2.94 (95% CI −3.80, −2.08); $P < 0.001$), whereas for all other outcomes, no publication bias was identified. Significant publication bias for FMD was confirmed using selection models ($\chi^2 = 29.95$, $P < 0.001$).

Metabolic health

Glucose metabolism

A total of 177 interventions involving 2778 participants per group were included. Overall, PA bouts significantly reduced glucose concentrations compared to prolonged SB (SMD = −0.22 [−0.27, −0.16]; $P < 0.001$; $I^2 = 11\%$; *Figure 2* and Supplementary material online, *Appendix V, Figures S1–S3*). Subgroup analyses by intensity showed the greatest reductions during LPA (−0.34 [−0.47, −0.22]; $P < 0.001$; $I^2 = 20\%$) and MPA

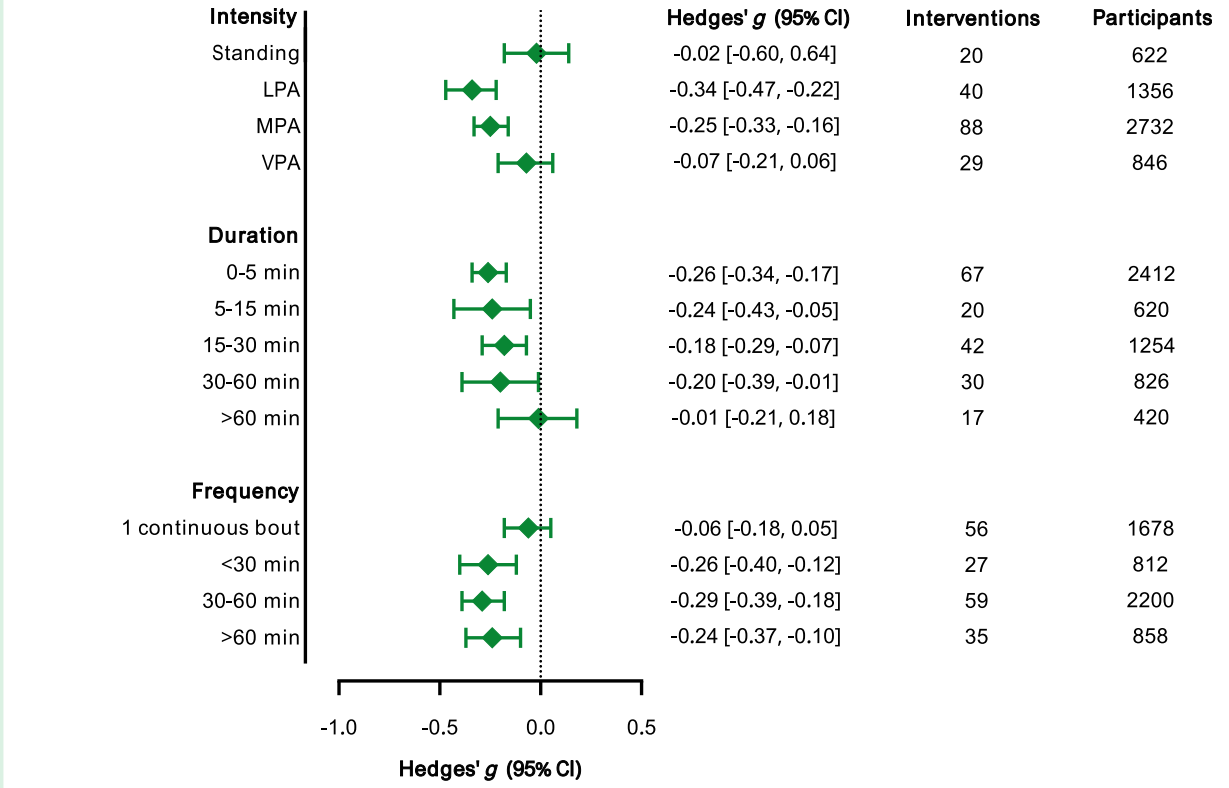


Figure 2 Random effects meta-analysis adjusted to Hedges' g on the effect of physical activity intensity, duration and frequency on glucose concentrations, compared to prolonged sitting control groups. CI, confidence interval.

(−0.25 [−0.33, −0.16]; $P < 0.001$; $I^2 = 15\%$), whereas standing showed no effect (−0.02 [−0.18, 0.14]; $P = 0.78$; $I^2 = 0\%$; $\chi^2 = 14.17$; $P = 0.002$). PA bouts up to 60 min reduced glucose, while longer PA bouts (> 60 min) had no significant effect (−0.01 [−0.21, 0.18]; $P = 0.88$; $I^2 = 0\%$). Frequency alone showed no effect for single continuous bouts, but a significant interaction between bout duration and frequency ($P = 0.032$) indicated that higher frequency was associated with shorter bout duration.

Insulin sensitivity

A total of 121 interventions were included, with 1951 participants per group. Overall, PA bouts significantly reduced insulin concentrations (−0.26 [−0.32, −0.19]; $P < 0.001$; $I^2 = 35\%$). Reductions were observed across all intensities of PA (LPA: −0.25 [−0.41, −0.10]; $P = 0.001$; $I^2 = 0\%$, MPA: −0.29 [−0.37, −0.20]; $P < 0.001$; $I^2 = 0\%$, VPA: −0.28 [−0.43, −0.13]; $P < 0.009$; $I^2 = 0\%$), except for standing ($P = 0.65$). Additionally, no statistically significant differences were found between the various frequencies or durations of PA bouts, meaning that different interruption patterns were equally effective in reducing insulin concentrations (see Supplementary material online, *Appendix V, Figures S4–S6*).

Lipid metabolism

In total, 99 interventions were included with 1547 study participants per group. Overall, PA bouts significantly reduced triglyceride concentrations (−0.27 [−0.34, −0.19]; $P < 0.001$; $I^2 = 1\%$; *Figure 3* and Supplementary material online, *Appendix V, Figures S7–S9*). Reductions increased with higher PA intensity ($\chi^2 = 7.05$; $P = 0.030$), with no effects from standing bouts and the largest effects following vigorous-intensity PA bouts (−0.40 [−0.57, −0.23]; $P < 0.001$; $I^2 = 0\%$). Longer bouts (>30 min) also produced greater reductions ($\chi^2 = 14.04$; $P = 0.007$). A single continuous daily PA bout significantly lowered triglycerides (−0.45 [−0.57, −0.33]; $P < 0.001$; $I^2 = 13\%$), whereas increasing bout frequency did not. Duration and intensity showed a significant interaction ($P < 0.001$), indicating that shorter bouts were typically higher in intensity. Cholesterol-related outcomes were not included in the meta-analyses due to insufficient data.

Cardiovascular health

Mean blood pressure

Studies assessing mean systolic (49 interventions, 803 participants per group) and diastolic (44 interventions, 700 participants per group) blood pressure were included. For systolic blood pressure, all intensities except standing produced comparable reductions (LPA: −0.31 [−0.51, −0.12]; $P = 0.002$; $I^2 = 0\%$, MPA: −0.27 [−0.42, −0.11]; $P < 0.001$; $I^2 = 0\%$, VPA: −0.33 [−0.42, −0.11]; $P = 0.009$; $I^2 = 17\%$, *Figure 4* and Supplementary material online, *Appendix V, Figures S10–S12*). Similar reductions were observed across all bout frequencies and durations (−0.29 [−0.39, −0.19]; $P < 0.001$; $I^2 = 0\%$). For diastolic blood pressure, an overall significant reduction was

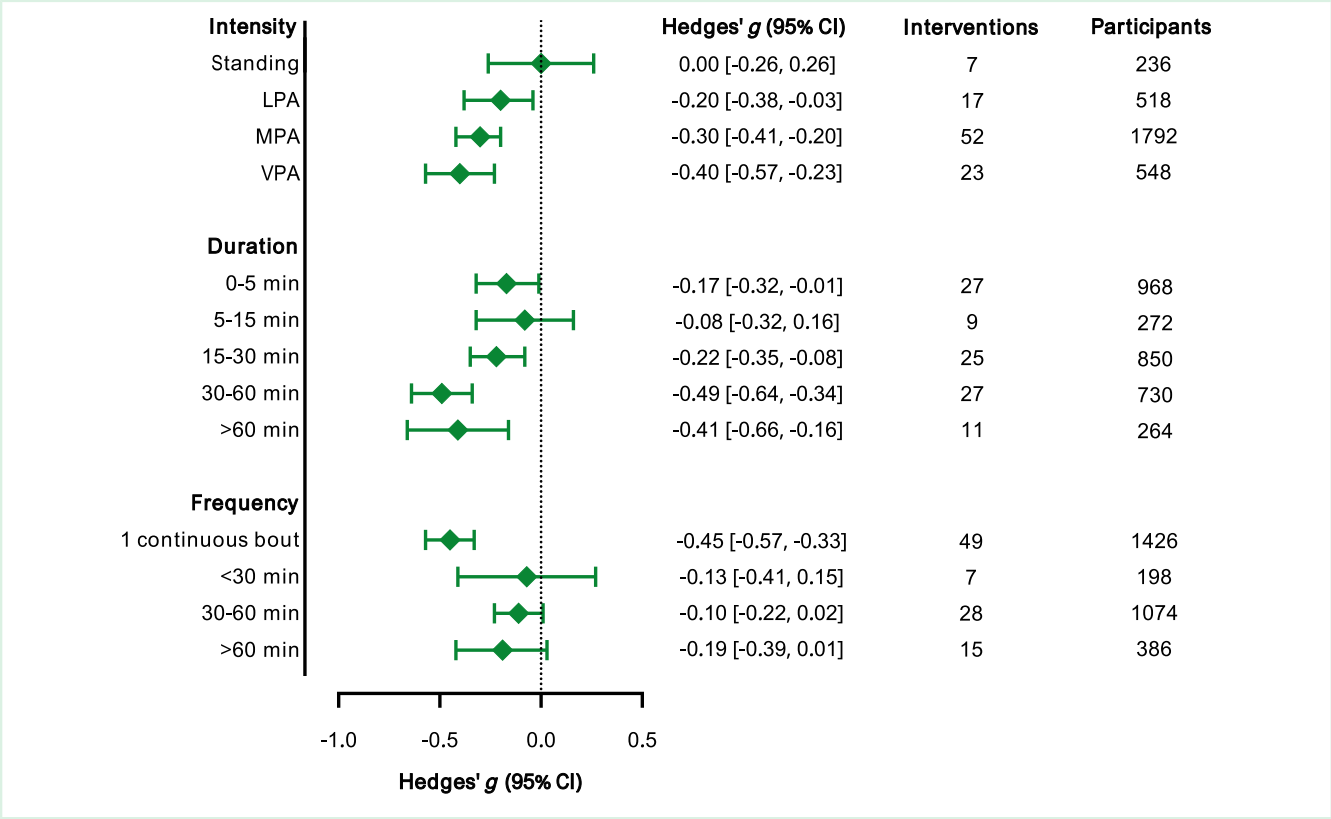


Figure 3 Random effects meta-analysis adjusted to Hedges' g on the effect of physical activity intensity, duration and frequency on triglyceride concentrations, compared to prolonged sitting control groups. CI, confidence interval.

observed (−0.16 [−0.26, −0.05]; $P = 0.003$; $I^2 = 0\%$), driven primarily by LPA, which was the only intensity with a statistically significant decrease (−0.37 [−0.59, −0.15]; $P < 0.001$; $I^2 = 0\%$, Supplementary material online, *Appendix V, Figures S13–S15*).

Vascular endothelial function

Due to the limited number of studies on vascular endothelial function (FMD: $n = 33$ interventions, 456 participants; shear rate: $n = 23$ interventions, 319 participants), only PA intensity was included in the meta-analysis. A significant overall effect was observed for both FMD (0.88 [0.47, 2.24]; $P < 0.001$; $I^2 = 0\%$) and shear rate (0.54 [0.31, 0.78]; $P < 0.001$; $I^2 = 52\%$; *Figure 5* and Supplementary material online, *Appendix V, Figures S16* and *S17*). Improvements were significant only after moderate- (MPA; FMD: 0.85 [0.17, 1.53]; $P < 0.001$; $I^2 = 88\%$, shear rate: 0.77 [0.18, 1.37]; $P < 0.001$; $I^2 = 75\%$) and vigorous-intensity PA (VPA; FMD: 1.39 [0.54, 2.24]; $P < 0.001$; $I^2 = 89\%$, shear rate: 0.77 [0.37, 1.17]; $P < 0.001$; $I^2 = 35\%$). Blood flow and arterial stiffness outcomes were not included in the meta-analyses due to limited data availability.

Moderator and subgroup analysis

Meta-regression analyses showed that the effect of PA bouts on triglyceride concentrations was significantly moderated by health status ($\beta = -0.169$ [−0.301, −0.038]; $P = 0.012$) and the interval between the PA bout and measurement ($\beta = -0.130$ [−0.247, −0.012]; $P = 0.031$). Subgroup analyses confirmed greater triglyceride reductions when the interval exceeded 12 h ($\chi^2 = 6.15$; $P = 0.010$) (see Supplementary material online, *Appendix VI, Figures S1–S7*) in individuals with Metabolic Syndrome compared to healthy participants ($\chi^2 = 5.88$; $P = 0.020$) or those with overweight/obesity ($\chi^2 = 7.77$; $P = 0.005$).

For glucose, effects were moderated by both timing ($\beta = 0.124$ [0.045, 0.204]; $P = 0.002$) and health status ($\beta = -0.175$ [−0.315, −0.034]; $P = 0.015$). Participants with (pre)-T2DM showed greater reductions than healthy participants ($\chi^2 = 14.64$; $P < 0.001$) or those with overweight/obesity ($\chi^2 = 15.00$; $P < 0.001$). Effects were strongest when PA bouts occurred 0–3 h before ($\chi^2 = 7.60$; $P = 0.006$) or during glucose measurements ($\chi^2 = 5.49$; $P = 0.020$), with no significant effects for bouts performed 12 h prior.

Discussion

This systematic review and meta-analysis provide robust evidence supporting the beneficial effects of interrupting SB with PA bouts on metabolic and cardiovascular health in an acute setting. A total of 144 studies, encompassing 247 interventions with a wide range of intensities, frequencies, and durations of PA bouts, were summarized. Results indicated that glucose homeostasis benefits most from an increased frequency, while improvements in (postprandial) triglyceride concentrations depend on greater duration and/or intensity of PA bouts. Furthermore, the results for cardiovascular health outcomes

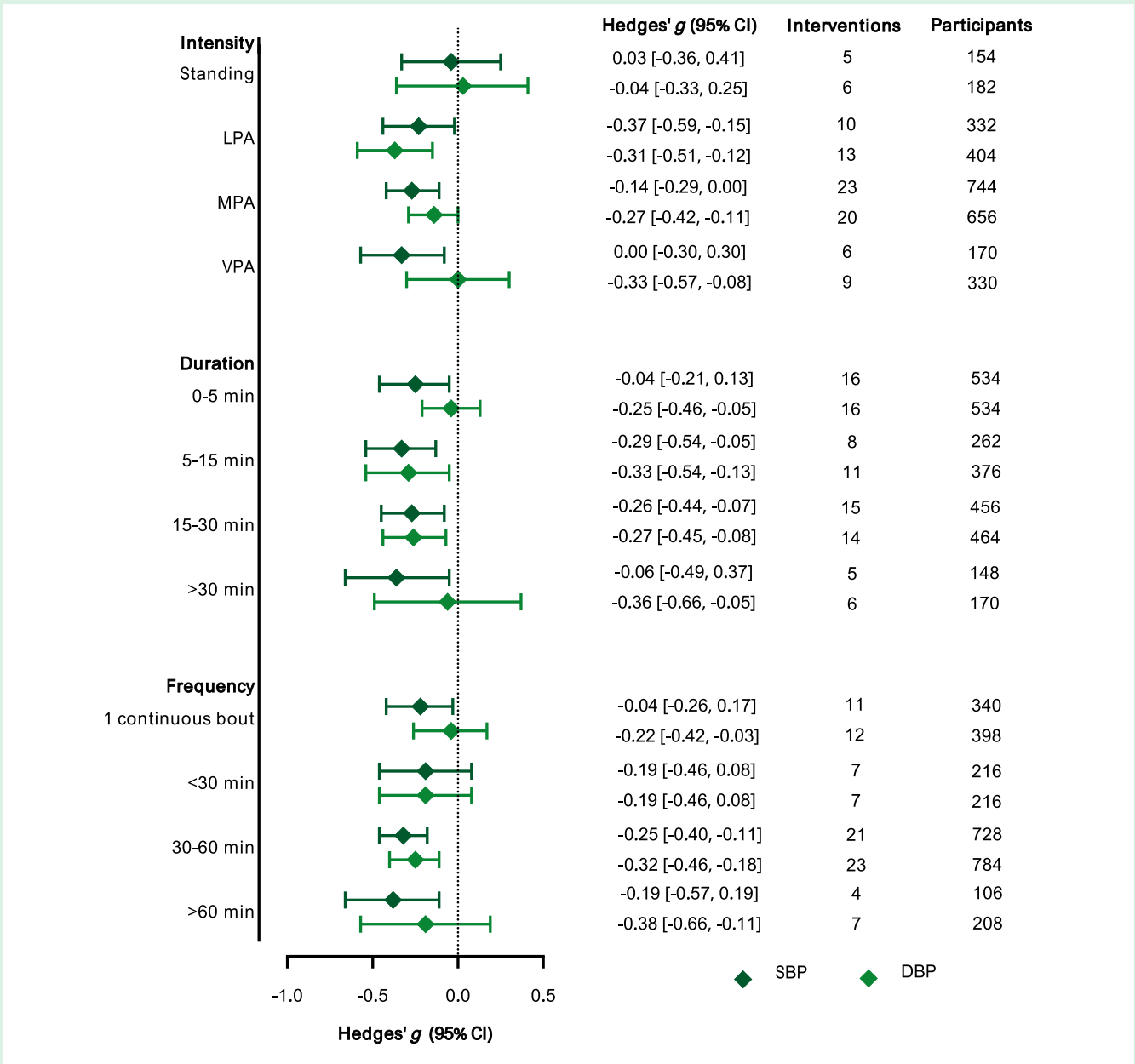


Figure 4 Random effects meta-analysis adjusted to Hedges' g on the effect of physical activity intensity, duration and frequency on both systolic and diastolic blood pressure, compared to prolonged sitting control groups. CI, confidence interval, SBP, systolic blood pressure, DBP, diastolic blood pressure.

indicate that blood pressure regulation improves regardless of PA components, whereas increased intensity of PA bouts appears to benefit endothelial function, reflected by FMD and shear rate.

Frequent PA bouts, particularly with light- and moderate-intensity PA, were associated with significant reductions in postprandial glucose concentrations. These findings are aligned with and build upon earlier work suggesting that frequent low-to-moderate intensity PA stimulates glucose uptake by skeletal muscle through transient insulin-independent mechanisms (i.e. contraction-induced GLUT 4 translocation) and improved insulin sensitivity post-exercise.[9,11,12,170,171] Results from moderator and subgroup analyses indicate that PA bouts are more effective as a secondary preventive strategy, with greater benefits in obese and (pre)diabetic individuals. The glucose-lowering effects varied by measurement timing, with the most favourable responses observed during or shortly after PA bouts, potentially reflecting greater reliance on carbohydrate metabolism (i.e. glycolysis, glycogenolysis) early after PA onset.[172] Notably, frequent vigorous-intensity PA bouts showed no significant effects on glucose concentrations, possibly due to the acute nature of the interventions, during which increased hepatic endogenous glucose production may blunt the glucose-lowering responses.[173] This interpretation aligns with randomized controlled trials including exercise followed by prolonged sitting.[89,174] Interestingly, the interaction effect observed

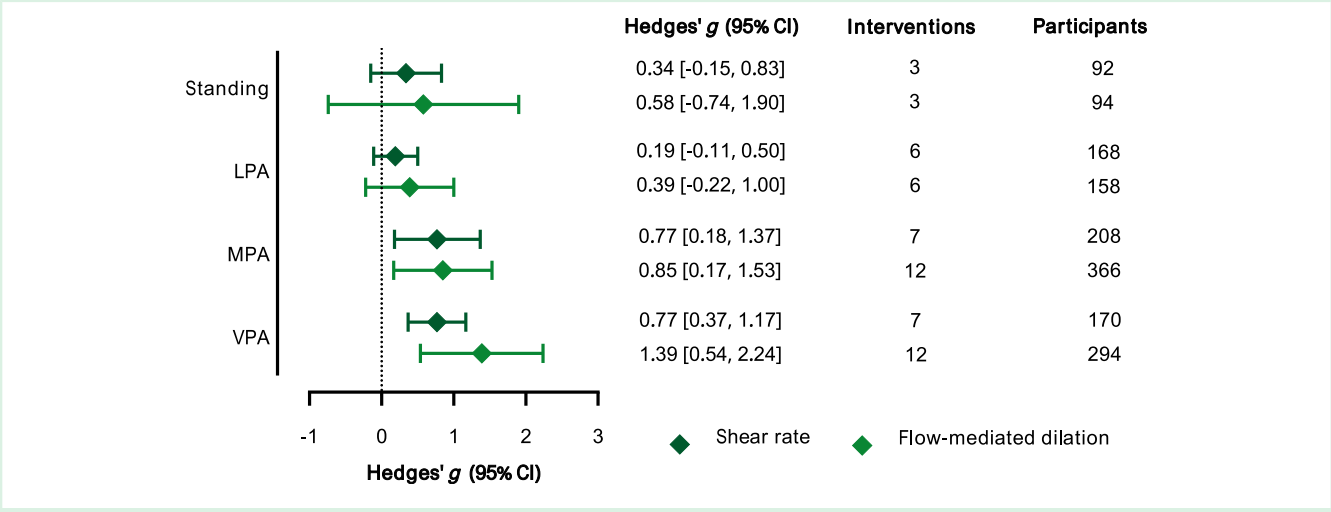


Figure 5 Random effects meta-analysis adjusted to Hedges' g on the effect of physical activity intensity, duration and frequency on endothelial function, compared to prolonged sitting control groups. CI, confidence interval.

between PA frequency and duration suggests that reductions in glucose concentrations are maximized with shorter, more frequent PA bouts, an insight that may prove critical for designing future interventions and public health guidelines. In contrast, insulin concentrations improved regardless of PA components, indicating broadly enhanced insulin sensitivity.

With regard to lipid metabolism, a clear dose-response relationship was observed between PA intensity and improvements in triglyceride tAUC, with the most pronounced effects following vigorous-intensity and PA bouts of longer duration (>30 min). Interestingly, while longer continuous PA bouts proved effective, increasing the frequency of short PA bouts did not yield additional lipid-lowering benefits. Furthermore, shorter bouts were more effective at reducing triglyceride concentrations when combined with higher-intensity activity. These results align with physiological mechanisms suggesting that higher-intensity[175] and longer PA bouts[161] promote increased lipoprotein lipase (LPL) activity[68] and fat oxidation,[175] enhancing triglyceride clearance.[176] This indicates that skeletal muscle LPL-mediated triglyceride clearance is more robust following moderate-to-vigorous PA compared to light-intensity activity, and that longer PA bouts may have cumulative benefits, which is supported by the review of Chastin *et al.*, where sedentary breaks did not result in improvements in triglyceride concentrations as compared to prolonged sitting.[177]

The moderator analysis revealed that intervention effects on postprandial triglycerides were moderated by disease status and timing between PA and the measurement. The timing of PA bouts significantly influenced postprandial triglyceride responses, showing that. PA bouts performed the day before a test meal resulted in greater reductions in triglyceride concentrations compared to activity on the same day. Furthermore, reductions in postprandial triglyceride concentrations were more pronounced in individuals with the metabolic syndrome, likely because they typically exhibit elevated fasting and postprandial triglyceride levels due to insulin resistance and impaired lipoprotein metabolism. These findings have already been described in relation to the effect on postprandial triglyceride concentrations following structured exercise interventions.[176]

Favourable cardiovascular effects were observed, particularly in terms of blood pressure reduction. These effects were evident regardless of PA intensity, duration or frequency, reinforcing previous evidence that even modest PA can acutely improve vascular tone and autonomic regulation,[178] potentially leading to post exercise hypotension.[179,180] However, the observed heterogeneity in study designs and outcome timing (e.g. measurement delays relative to intervention) may have diluted some of these effects. The meta-analysis indicates that higher intensity PA is key to improving FMD and shear rate, both markers of vascular endothelial function. These findings align with those of another meta-analysis, which demonstrated a significant dose-response relationship between both the relative and absolute aerobic PA intensity and FMD.[181] This has important clinical implications as a meta-analysis by Inaba *et al.*, involving over 5000 participants, found that each 1% improvement in FMD is associated with a 13% reduction in cardiovascular event risk.[166] In the present meta-analysis, PA bouts of vigorous intensity increased FMD by 0.6–3.2%, potentially translating into a 12–42% reduction in CVD risk. Moderate-to-vigorous PA produces larger and more sustained increases in blood flow, leading to greater shear stress on the endothelium, a key stimulus for nitric oxide bioavailability. This, in turn, enhances vasodilation and supports endothelial health. While this finding contributes to the understanding of the effects of PA bouts, results should be considered with caution as heterogeneity was high. In this respect, differences in the timing of measurement relative to PA, the interval between tests, the arteries included, and the ultrasound measurement procedures may explain the observed heterogeneity across studies. In addition, existing guidelines on FMD assessment recommend that operators should be experienced in sonography and maintain their level of experience to significantly improve reproducibility.[182] Furthermore, between-study variation with respect to subject-specific factors (e.g. fasted state, medication

and caffeine intake) could explain heterogeneity of the results.[182,183] To translate these findings into a clinical context, incorporating moderate-to-vigorous intermittent lifestyle PA into daily routines may represent a feasible strategy to improve cardiovascular health.[184,185] Notably, as few as four short bouts of VPA totalling 2–3 min per day have been associated with a substantially lower risk of CVD. Moreover, brief intermittent bursts of incidental VPA may help offset cardiovascular risks associated with high SB.[186] Therefore, public health guidelines should emphasize the health benefits of short, intermittent PA bouts. However, since our analysis focused only on intensity in relation to vascular health, further research is needed to clarify the roles of PA duration and frequency.

This meta-analysis also showed that interrupting prolonged SB with standing, as a stand-alone intervention, does not provide sufficient activity intensity to produce acute benefits for any cardiometabolic markers. This review adds to the understanding of cardiometabolic effects of standing breaks, as previous reviews reported contrasting findings.[12,187,188] These results suggest that a simple postural change is insufficient to acutely impact cardiometabolic health outcomes. This may be due to the limited increase in muscle activity and energy expenditure during standing.[189] Nevertheless, the role of standing as an alternative for prolonged SB should be further investigated. In a real-life context, using sit-to-stand desks might lead to spontaneous movement, as already suggested by increased walking time at work in the SMART Work and Life trial[190] where participants were provided with a sit-stand working station to reduce sedentary time. Recognising the possible interaction with other PA modalities might lead to different conclusions than singling outstanding behaviour.

Methodological strengths and limitations

This review represents the most comprehensive analysis to date of the interactive effects of activity bouts to interrupt prolonged SB in terms of frequency, intensity, and duration on acute cardiometabolic responses. Key strengths include a comprehensive and systematic approach to literature selection, the inclusion of only randomized-controlled trials, the large number of interventions included in this review, rigorous risk of bias and certainty assessments using Cochrane and GRADE tools, and the use of robust statistical techniques such as meta-regression and subgroup analyses.

Nevertheless, certain limitations should be noted. First, despite the attempt to homogenize measurement units and statistical methods, the included studies exhibited high heterogeneity in, for example, participant characteristics, food composition, and measurement timing. Therefore, a random effects model was used to account for heterogeneity across study designs, and the results of the meta-analysis were generally equivocal, except for FMD and shear rate, where statistical tests (Cochran's Q and I^2) identified significant heterogeneity in intervention effects. Future studies should consider guidelines for the assessment of endothelial function to improve our understanding of this matter.[182] In addition, many of the studies included in the meta-analyses had relatively small sample sizes. This may have limited the statistical power to detect significant effects of individual studies, potentially contributing to the non-significant findings observed. As such, the absence of statistically significant results in some cases may reflect insufficient sample size rather than a true lack of intervention effect. Third, the results of this review reflect the contribution of PA bout components (frequency, duration, intensity) as reported in well-controlled acute experimental settings. Acute studies were chosen as intervention effects can be better attributed to controlled changes in PA and SB. While understanding the acute physiological responses to different PA bouts is important, the results should be interpreted cautiously and not assumed to translate directly into long-term clinical improvements. Demonstrating the sustainability of these effects in longer-term studies is essential to establishing their clinical relevance. Finally, the review only focused on an adult population. Studies in older populations or children might lead to slightly different results. Future reviews should elaborate on these age groups as guidelines, such as the WHO guideline for PA and SB, which often adjust the recommendations across the lifespan.

Future research and policy implications

These findings highlight the need to translate laboratory evidence into real-world interventions. Long-term studies on the interruption of SB with respect to bout duration, intensity, and/or frequency remain scarce. Workplace sit-to-stand interventions have effectively reduced sedentary time[191] and shown some promise for improving cardiometabolic health,[192] but they typically do not systematically vary or report PA bout characteristics. Consequently, it remains unclear whether the acute benefits reported in this review translate into sustained improvements in glucose homeostasis, lipid profiles, or vascular health. Designing long-term trials is challenging due to adherence and monitoring issues, and most studies focus on total sedentary time[190] or overall MVPA rather than structured interruption patterns. Future research should evaluate the feasibility, adherence, and effectiveness of interrupting SB in free-living environments using well-defined, device-monitored PA bouts. Standardized reporting of bout frequency, duration, and intensity is needed to determine clinically meaningful long-term benefits and to refine the 'minimum effective dose' of activity for high-risk population subgroups.

This review advances understanding how adjustments in PA bout components (frequency, duration and intensity) affect cardiometabolic health markers. However, research on combined patterns of PA and SB remains limited and further work is needed to identify optimal activity patterns for chronic disease prevention. Recent studies indicate that different approaches can improve insulin sensitivity and triglyceride concentrations across populations.[174,193,194] Our findings are restricted to aerobic PA bouts interrupting prolonged SB, but future research should explore other modalities such as resistance exercises, which have shown metabolic[195] and cardiovascular[196] benefits. This will enhance understanding of 24 h movement behaviour and potential complementary or synergistic effects consistent with WHO guidelines emphasising both aerobic and muscle-strengthening activities.[10]

At the policy level, this review supports the inclusion of SB reduction strategies in WHO guidelines and provides specificity regarding their implementation. The findings highlight that even brief (<5 min), frequent light-to-moderate intensity is important for tailoring interventions to populations such as

individuals with dyslipidaemia, T2DM, or hypertension. These insights can help optimize the preventive potential of PA bouts in real-world settings.

Conclusion

This systematic review and meta-analysis suggest that, in acute experimental settings, glucose homeostasis may benefit more from increasing the frequency of PA bouts, whereas acute reductions in postprandial triglyceride concentrations appear to be more closely related to greater PA duration and/or intensity. Findings related to cardiovascular health outcomes indicate that blood pressure responses may improve across different PA components, while a higher PA intensity is associated with more favourable acute changes in endothelial function. Collectively, these acute findings provide insights that may help guide the design of future long-term and free-living interventions aimed at improving cardiometabolic health and tailored prevention strategies for cardiometabolic diseases. Differentiating PA bouts by frequency, duration and intensity remains an important consideration when developing targeted interventions for specific cardiometabolic outcomes and populations with cardiometabolic health-related diseases, such as individuals with dyslipidaemia, T2DM and hypertension.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Author contributions

Jen Vanherle (Conceptualization [supporting]; Formal analysis [supporting]; Investigation [supporting]; Methodology [supporting]; Visualization [supporting]; Writing—original draft [supporting]), Gregor H.L.M. Franssen (Formal analysis [supporting]; Investigation [supporting]; Methodology [supporting]; Supervision [supporting]; Writing—review & editing [supporting]), Anna Ivanova (Formal analysis [supporting]; Investigation [supporting]; Methodology [supporting]; Software [lead]; Writing—review & editing [supporting]), Bert O. Eijnde (PhD (Conceptualization [lead]; Formal analysis [supporting]; Funding acquisition [lead]; Project administration [lead]; Supervision [lead]; Writing—review & editing [equal])), and Wouter M.A. Franssen (PhD (Conceptualization [lead]; Data curation [lead]; Formal analysis [lead]; Investigation [lead]; Methodology [lead]; Project administration [lead]; Supervision [lead]; Visualization [lead]; Writing—original draft [lead]; Writing—review & editing [lead]))

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Ethical approval

Not applicable. All the work was developed using published data.

Conflict of interest: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/and declare: support from the Special Research Fund (BOF) of Hasselt University for the work reported; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Transparency: The lead author (W.M.A.F.) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Data availability

All data generated or analysed during this systematic review are included in this published article [and its supplementary information files].

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