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Systematic Review

Impact of Prolonged Sitting Interruption on Blood Glucose, Insulin and Triacylglycerol in Adults: A Systematic Review and Meta-Analysis

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Abstract: Background: Physical activity (PA) and/or exercise improves postprandial cardiometabolic risk markers; however, the optimal exercise intensity, frequency, and dose remain unclear. We aimed to (1) compare the acute metabolic effects of interrupted prolonged sitting with PA bouts of different frequencies and durations on blood glucose, insulin, and triacylglycerol responses, and (2) compare the effects of the different types and different times of PA breaks on these measures. Methods: A literature search was carried out using four databases. Network meta-analysis (NMA) and paired meta-analysis were performed to estimate the total standardized mean differences (SMDs) with 95% confidence intervals (95%CI). Results: According to the NMA, compared to prolonged sitting, every 30 min interruption had the highest probability (SUCRA) of being the best intervention for improving blood glucose (SUCRA = 81.8%, SMD = −1.18, 95%CI: −1.72, −0.64) and insulin (SUCRA = 77.5%, SMD = −0.98, 95%CI: −1.36, −0.60). Additionally, every 20 min interruption also significantly lowered blood glucose (SMD = −0.89, 95%CI: −1.52, −0.27) and insulin (SMD = −0.94, 95%CI: −1.41, −0.46). Pairwise meta-analysis suggested that frequent breaks by light-intensity PA significantly lowered glucose (SMD = −1.45, 95%CI: −2.32, −0.57) and insulin (SMD = −1.04, 95%CI: −1.53, −0.55). The same was found for frequent breaks by moderate-to-vigorous PA, which also significantly lowered glucose (SMD = −0.6, 95%CI: −0.83, −0.37) and insulin (SMD = −0.53, 95%CI: −0.73, −0.32). Conclusions: According to the NMA, performing short bouts of PA every 30 min is the most effective prolonged sitting intervention for improving blood glucose and insulin. More evidence is needed to determine the optimal type and time of PA breaks for braking sedentary sitting. PROSPERO Registration: CRD42022340036.

Keywords: physical activity; sedentary; glucose; insulin; triacylglycerol

Citation: Dong, Y.; Pan, Y.; Zhang, X.; He, Q.; Chen, S.; Du, L.; Yin, S. Impact of Prolonged Sitting Interruption on Blood Glucose, Insulin and Triacylglycerol in Adults: A Systematic Review and Meta-Analysis. *Appl. Sci.* **2024**, *14*, 3201. https://doi.org/10.3390/app14083201

Academic Editors: Nikolaos Zaras and Spyridon Methenitis

Received: 12 March 2024
Revised: 8 April 2024
Accepted: 9 April 2024
Published: 10 April 2024

1. Introduction

Physical activity (PA) and/or exercise are essential for improving glucose levels and other cardiometabolic risk factors [1]. Prolonged time spent engaging in sedentary behaviors is associated with negative metabolic outcomes [2], which contribute to the occurrence and development of cardiovascular disease and type 2 diabetes mellitus (T2DM) [3]. Light-intensity physical activity (LPA) and moderate-to-vigorous physical activity (MVPA) are beneficially associated with markers of glucose and lipid metabolism, especially in obesity [4,5]. Exercise induces metabolic improvements by optimizing energy substrate oxidation, enhancing lipid and glucose metabolism, promoting the secretion of anti-inflammatory muscle-derived biomolecules, and improving systemic insulin sensitivity and cardiometabolic health [6]. Untrained and dysfunctional muscles exacerbate the whole-body inflammatory status in obese and inactive people by reducing glucose metabolism and limiting lipid clearance [7]. Exercise can moderately improve inflammation

in obesity and restore insulin sensitivity, and it has a positive effect on body weight [8]. In addition, exercise has positive mental effects such as improved memory, sleep, and mood, and reduced stress [9].

Previous research has shown that activities contributing to glucose control include taking breaks during prolonged sitting, scheduling post-meal workouts to prevent hyperglycemia, and performing aerobic and/or resistance exercise (RE) [1]. One review [10] found that PA breaks (proving better than energy-matched continuous exercise) moderately attenuated glucose, insulin, and triacylglycerol, with greater glycemic attenuation in people with a higher body mass index. Transient exaggerated spikes in glucose and lipids after meals may promote oxidative stress, triggering a biochemical inflammatory cascade that creates an environment conducive to the development of cardiovascular disease [11]. There are many randomized controlled trials (RCTs) studying the acute metabolic response of PA interruption, but there are few reviews on the optimal type, frequency, intensity, and duration of exercise required to reduce glucose and other metabolic markers; therefore, the optimal mode of exercise remains unclear [1]. Overall, the most important factors are those that influence exercise fuel metabolism, as well as the intensity and duration of PA [8]. Therefore, in an attempt to integrate multiple factors, we performed network and pairwise meta-analyses to (1) compare the acute metabolic effects of interrupted prolonged sitting with PA bouts of different frequencies and durations on blood glucose, insulin, and triacylglycerol responses, and (2) compare the effects of the different types and different times of PA breaks on these measures in adults.

2. Methods

The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12] and was registered in PROSPERO (CRD42022340036).

2.1. Search Strategy

A search was conducted in PubMed, Scopus, Web of Science, Embase and CINAHL up to 1 January 2023. The following keywords were employed: ("physical activity" OR exercise) AND (sedentary OR sitting) AND (randomize OR break OR interrupt) AND (glucose OR insulin OR metabolic OR triglyceride OR triacylglycerol). A second search was conducted by screening the relevant articles through references. The results were downloaded and reviewed using the software EndNote X9.3.2 (Clarivate Analytics, New York, NY, USA). The full search strategy for each database is detailed in Supplementary File S1.

2.2. Study Selection

To be included, studies had to (1) include adult participants who were healthy or with T2DM/prediabetes, had impaired fasting glucose, and were overweight/obese; (2) assess interrupted prolonged sitting with PA bouts (continuous exercise or PA breaks); (3) attempt to control for sitting and PA break conditions, with the corresponding protocols clearly reported; (4) consider carryover effects in a cross-over design; and (5) include at least one short-term outcome regarding blood glucose, insulin, or triacylglycerol. Exclusion criteria were as follows: (1) repetitive studies; (2) studies involving less than 10 participants; (3) patients who were hospitalized or diagnosed with peripheral arterial disease or chronic obstructive pulmonary disease; (4) data not available; (5) commentaries, letters, reviews, conference abstracts, or dissertations; and (6) non-English articles.

2.3. Data Extraction and Risk-of-Bias Assessment

Two authors used a standardized data extraction sheet in parallel to obtain information about the first author, publication year, country, participant characteristics, and study design, alongside a detailed description of the interventions and outcomes of interest (blood glucose, insulin, and triacylglycerol measures data from the intervention day). The PA intensity of the intervention was reported in the original studies using LPA 1.5–3.99 metabolic

equivalents (accelerometer, 100–1951 counts/min) and MVPA $\geq$ 4 metabolic equivalents (accelerometer $\geq$ 1952 counts/min) [11,13]. Studies that did not report intensity were classified according to the above criteria. The duration, frequency, and type were reported in the original studies.

Risk-of-bias assessment was assessed using The Cochrane Collaboration's risk of bias (RoB 2) tool for RCTs [14]. Any disagreements arising during the processes were resolved by discussion, and a third reviewer was consulted in the event of persistent disagreement. The washout period for the cross-over studies was used for the other sources of bias domain. Each domain rated was as "high risk", "low risk", or "unclear".

2.4. Statistical Analysis

Network meta-analyses and pairwise meta-analyses were conducted using Stata17 (Stata Corp, College Station, TX, USA) to compare the effects of different PA interruptions, with prolonged sitting serving as the reference. The significance level was set to $p < 0.05$ (two-tailed). Given the multiple intervention arms in the RCTs, we compared different interventions targeting prolonged sitting via a network meta-analysis and then a pairwise meta-analysis of subgroups. A continuous glucose monitoring system (CGMS) was first used to assess the outcome measures, followed by the incremental area under the curve (iAUC) [15], and, finally, the total area under the curve (tAUC) [16].

Interventions were considered beneficial for glycemic or triacylglycerol responses if the corresponding standardized mean difference (SMD) estimate was negative and the 95% confidence interval (CI) did not include zero. All relationships between interventions were illustrated using a network plot. Nodal sizes and line widths in the plot represent sample sizes and recorded comparisons, respectively. Global tests were performed comparing deviance and deviance information criterion statistics between consistency and inconsistency models [17], as well as to assess the local inconsistency of all closed triangle and quadrangle loops in the network via a loop-specific approach [18]. Node splitting was used to assess model inconsistency. In addition, we plotted funnel plots to assess potential publication bias. The area under the cumulative rating curve (SUCRA) was estimated to rank the probabilities, where interventions with higher values of SUCRA (ranging between 0 and 1) were deemed to have greater effectiveness.

Pairwise pooled meta-analysis effects were estimated primarily using fixed effects (inverse-variance) meta-analysis models. Random effects results were also reported, and SMDs were interpreted according to Hedges's g. In cases where more than two arms were categorized into the same class, the control group was split and used twice in the meta-analysis. Heterogeneity and consistency tests were conducted utilizing the Q and I^2 statistics, respectively. Since visual observations of funnel plots are subjective and can be misinterpreted [19], there may be publication bias or selective reporting of results or analyses, not only for glucose but also for insulin and triacylglycerol measurements. We tested publication bias in a paired meta-analysis using the pairwise Egger test and Begg's rank correlation test.

3. Results

3.1. Literature Search and Study Characteristics

The literature review yielded 2930 articles. After applying selection criteria, 38 studies, including 763 participants, were included in the meta-analyses. A flow diagram of the study selection process is depicted in Figure 1.

The characteristics of the included studies are described in Table 1. A total of 38 studies were included in the network meta-analysis. Fifteen studies [4,11,13,20–31] reported overweight/obese adults, two [32,33] reported central obesity, and nine [34–42] reported non-obese or normal-weight adults. Five studies [43–47] reported inactive adults, six studies [26,45,48–51] reported prediabetes and/or T2DM, and three [25,27,52] reported postmenopausal women. Participants ranged in age from 18 to 75, and sample sizes ranged from 10 to 70. The publication data of the included studies were from 2010 to 2022.

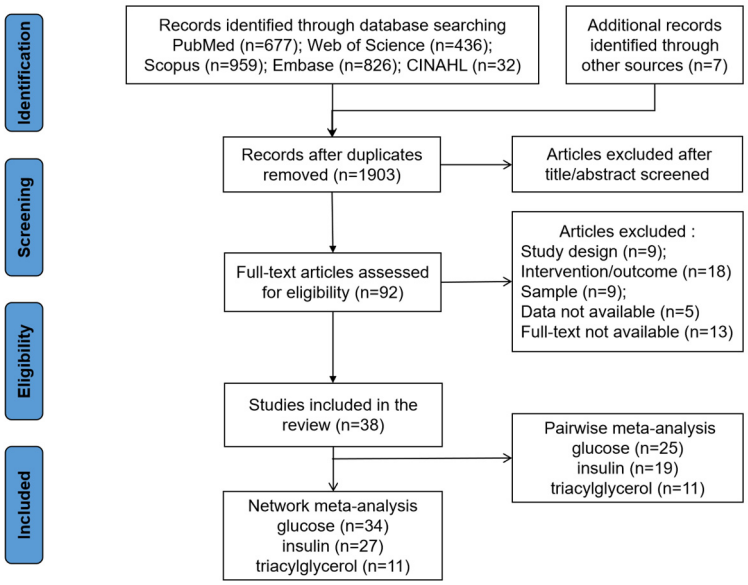

Figure 1. PRISMA flow diagram.

Table 1. Descriptive characteristics of the included studies.

Study	Participants	Age	Arms	Outcomes
Altenburg et al. [34] 2019, The Netherlands	20 healthy-weight males	19.2 ± 0.6	Sitting 300 min Interrupted with 10 min standing every 60 min	Insulin AUC
Bailey et al. [36] 2015, UK	10 non-obese healthy adults	24 ± 3	Sitting 300 min Interrupted with 2 min bouts of standing every 20 min 2 min bouts of light-intensity walking (3.2 km/h) every 20 min	Glucose AUC
Bailey et al. [35] 2016, UK	13 healthy adults	26.6 ± 8.5	Sitting 300 min 2 min bouts of light-intensity walking (3.25km/h) every 20 min 2 min bouts of moderate walking (5.8–7.95km/h) every 20 min	Glucose iAUC; Insulin iAUC
Bailey et al. [20] 2022, UK	12 over-weight/obese adults	48 ± 10	Uninterrupted sitting ≥10 h Interrupted with 6–10 min of activity accrued in each hour	Glucose iAUC
Benatti et al. [43] 2017, Denmark	14 inactive, healthy males	30.1 ± 8.8	Sitting 9 h Interrupted by 15 min of standing every 30 min A single 30 min bout of moderate-intensity exercise on treadmill	Glucose iAUC; Insulin iAUC; TAG iAUC
Bhammar et al. [13] 2017, USA	10 over-weight/obese adults	32 ± 5	Sitting 540 min Sitting and a single 60 min bout of moderate walking Interrupted with 2 min moderate walking every 20 min Interrupted with 2 min vigorous walking every 60 min	Glucose time-averaged CGMS
Blankenship et al. [21] 2014, USA	10 overweight/obese	51.9 ± 15.4	Sitting 6 h, 30 min walking, ~300 kcal before lunch Frequent breaks (every 20 min), ~300 kcal	Glucose AUC; Insulin AUC

Table 1. *Cont.*

Study	Participants	Age	Arms	Outcomes
Champion et al. [44] 2018, UK	24 inactive adults	35.8 ± 10.9	Sitting 390 min Interrupted with 20 min of light-intensity walking every 60 min	Glucose iAUC; Insulin iAUC; TAG iAUC
Charlett et al. [37] 2021, UK	12 normal-weight	25 ± 6	Sitting 300 min 3 min of bodyweight resistance exercise every 30 min	Glucose iAUC
Chen et al. [32] 2018, UK	11 centra overweight	50 ± 5	Sitting 315 min 2 min walking (6.4 km/h) every 20 min over 315 min, 30 min total	Glucose iAUC; Insulin iAUC; TAG iAUC
Chrismas et al. [22] 2019, Qatar	11 obese females	21–44	Sitting 300 min Interrupted with 3 min of moderate-intensity walking every 30 min	Glucose iAUC; Insulin iAUC; TAG iAUC
Dunstan et al. [11] 2012, Australia	19 overweight/obese	53.8 ± 4.9	Sitting 420 min Interrupted with 2 min of light-intensity walking every 20 min 2 min bouts of moderate-intensity walking every 20 min	Glucose iAUC; Insulin iAUC
Duvivier et al. [38] 2013, The Netherlands	18 healthy adults	21 ± 2	Sitting 840 min Sitting 780 min/day and 60 min of vigorous exercise	Glucose AUC; Insulin AUC
Duvivier et al. [23] 2017, The Netherlands	24 overweight/obese	64 ± 7	Sitting 13.5 h Interrupted every 30 min with standing/walking bouts	Glucose iAUC; Insulin iAUC
Hansen et al. [39] 2016, Denmark	14 healthy normal weight	20–23	Sitting 150 min 2 min bouts of light-intensity walking (3.5–4.5 km/h) every 20 min	Glucose iAUC
Hawari et al. [24] 2019, UK	14 overweight/obese	37 ± 16	Sitting 390 min Interrupted with 30 s of 10 chair squats every 20 min	Insulin time-averaged AUC
Kashiwabara et al. [53] 2018, Japan	12 older women with hypertriglyceridemia, inactive	70.5 ± 4.6	Sitting 8 h Moderate walking in one 30 min bout in the morning Light walking in twenty 90-s bouts (every 20 min)	Glucose iAUC; Insulin iAUC; TAG iAUC
Kerr et al. [27] 2017, USA	10 overweight/ obese postmenopausal women	66 ± 9	Sitting 300 min 2 min of standing every 20 min 2 min of light-intensity walking every 60 min	Glucose iAUC; Insulin iAUC
Larsen et al. [4] 2015, Australia	19 overweight/obese	56.7 ± 1.5	Sitting 420 min 2 min bouts of walking every 20 min (3.2 km/h)	Glucose iAUC; Insulin iAUC; TAG iAUC
Ma et al. [54] 2020, China	16 non-obese, inactive, healthy	24 ± 3	Sitting 540 min 3 min bouts of moderate walking (60%VO2max) every 30 min 5 min bouts of moderate walking (60%VO2max) every 45 min 8 min bouts of moderate walking (60%VO2max) every 60 min	Glucose iAUC
Maylor et al. [46] 2019, UK	14 inactive females	33.8 ± 13.4	Sitting 450 min 2 min of moderate treadmill physical activity every 30 min	Insulin iAUC

Table 1. *Cont.*

Study	Participants	Age	Arms	Outcomes
McCarthy et al. [28] 2017, UK	13 obese adults	66 ± 6	Sitting 7.5 h 5 min arm ergometry every 30 min, total 1 h	Glucose iAUC; Insulin iAUC
McCarthy et al. [40] 2017, UK	34 healthy adults	40 ± 9	Sitting 7.5 h 5 min light walking bouts every 30 min, total 1 h	Glucose iAUC; Insulin iAUC
Miyashita et al. [52] 2016, Japan	15 postmenopausal women	68.8 ± 3.2	Sitting 8 h Sitting 1 h, 20 × 1.5 min walking every 15 min (3.7 km/h) Sitting 1 h, 30 min walking (3.7 km/h), 6.5 h sitting	Glucose iAUC; Insulin iAUC
Newsom et al. [29] 2013, USA	11 obese adults	28 ± 2	Sitting 480 min Sitting and a single bout of exercise (~55 min, 65%VO2max)	Glucose AUC; Insulin AUC
Peddie et al. [41] 2013, New Zealand	70 normal-weight adults	25.9 ± 5.3	Sitting 9 h Sitting 8.5 h and 100-s bouts of brisk walking (60% of VO2max) every 30 min Sitting 0.25 h, 30 min treadmill walking @60% VO2max, 8.25 h sitting	Glucose iAUC; Insulin iAUC; TAG iAUC
Peddie et al. [42] 2021, New Zealand	18 healthy, normal weight	23.5 ± 5	Sitting 6 h 2 min walking (5 km/h, 10% incline) every 30 min	Glucose iAUC; Insulin iAUC
Pulsford et al. [47] 2017, UK	25 inactive males	40.2 ± 12.2	Sitting 420 min 2 min bouts of light-intensity walking (3.2 km/h) every 20 min 2 min bouts of standing every 20 min	Glucose AUC; Insulin AUC
Wheeler et al. [30] 2020, Australia	67 overweight/obese	67 ± 7	Sitting 8 h sitting 1 h, moderate-intensity walking (30 min), uninterrupted sitting 6.5 h	Glucose AUC; Insulin AUC
Wong et al. [33] 2021, China	21 young centrally obese males	23 ± 4	Sitting 360 min 2 min bouts of light-intensity walking (3.2 km/h) every 30 min 6 min bouts of light-intensity walking (3.2 km/h) every 60 min	Glucose iAUC; Insulin iAUC; TAG iAUC
Yates et al. [31] 2020, UK	60 overweight/obese	67–75	Sitting 7.5 h 5 min of self-paced light walking every 30 min	Time-averaged AUC for Glucose, Insulin, TAG
Henson et al. [25] 2016, UK	22 overweight/obese postmenopausal women	66.6 ± 4.7	Sitting 7.5 h 5 min bouts of standing every 30 min 5 min bouts of light-intensity walking every 30 min	Insulin iAUC; TAG iAUC
Di Pietro et al. [45] 2013, USA	10 Inactive older impaired fasting glucose	69 ± 6	Sitting One bout of 45 min morning walking (moderate intensity) Three 15 min bouts of moderate postmeal walking	Glucose time-averaged CGMS
Duvivier et al. [49] 2017, The Netherlands	19 T2DM	63 ± 9	Sitting 14 h Sitting 13 h + 1 h moderate cycling (5.9 METs) Interrupted with light-intensity walking and standing every 30 min	Glucose time-averaged CGMS

Table 1. *Cont.*

Study	Participants	Age	Arms	Outcomes
Dempsey et al. [55] 2016, Australia	24 T2DM	62 ± 6	Sitting 7 h 3 min bouts of light-intensity walking at 3.2 km/h every 30 min 3 min bouts of simple resistance activities every 30 min	Glucose time-averaged CGMS; Insulin iAUC; TAG iAUC
Honda et al. [50] 2016, Japan	16 T2DM	65.4 ± 1.1	Sitting 3 min bouts of stair climbing up and down (80–110 steps/min) at 60 and 120 min	Glucose AUC
van Dijk et al. [51] 2013, The Netherlands	20 T2DM males	64 ± 1	Sitting 11 h A single 45 min cycling at 50% max workload capacity (6 METs) Sitting and 3 × 15 bouts of walking after each 3 meals (3 METs)	Glucose time-averaged CGMS
Holmstrup et al. [26] 2014, USA	11 young, obese, impaired glucose tolerance	25 ± 2.6	Sitting 720 min A single 60 min bout of moderate-intensity exercise 5 min bouts of moderate-intensity exercise every 60 min	Glucose iAUC

The mean ± standard deviation or the mean with the age range in years was reported. Abbreviations: AUC, area under curve; iAUC, incremental area under curve; CGMS, continuous glucose monitoring system; TAG, triacylglycerol; T2DM, type 2 diabetes mellitus; METs, metabolic equivalents.

3.2. Network Meta-Analysis

Blood glucose results were reported in 34 studies and used for the network meta-analysis. The SMDs associated with significant glycemic attenuation were greatest at −1.18 (95%CI −1.72 −0.64) for every 30 min interruption and were −0.89 (95%CI −1.52 −0.27) for every 20 min interruption (Figure 2), while other interruptions did not significantly lower blood glucose. A total of 27 studies provided usable results regarding insulin changes. The SMDs associated with significant insulin lowering were greatest at −0.98 (95%CI −1.36 −0.60) for every 30 min interruption, −0.94 (95%CI −1.41 −0.46) for every 20 min interruption, and −0.89 (95%CI −1.51 −0.27) for a 30 min exercise bout (Figure 2), while other interruptions (every 60 min interruption and 60 min exercise bout) did not significantly lower the insulin level. Eleven studies provided usable results for triacylglycerol measurement. However, the SMDs for every 20 min, 30 min, and 60 min interruption and a 30 min bout were insignificant (Figure 2).

Compared to the overall sample, analyses that excluded people with T2DM found that SMDs (every 20 min and 30 min interruption) were smaller, suggesting that every 20 min and 30 min interruption had greater benefits for blood glucose in T2DM, with glucose attenuation also seen following 60 min interruption. Moreover, every 60 min interruption was found to have a significant beneficial effect on glucose in the sample. The results are presented in Figure 3.

An inconsistency test based on the network analysis found no significant global inconsistency for glucose (p = 0.995), insulin (p = 0.997), and triacylglycerol (p = 0.73); the same was seen in analyses that excluded people with T2DM of glucose (p = 0.48) and insulin (p = 0.12). In the local inconsistency test, 4 loops out of 15, 1 loop out of 5, and 1 loop out of 3 demonstrated significant differences for glucose, insulin, and triacylglycerol, respectively. Inconsistent testing of the node-splitting model indicated that all comparisons between direct and indirect estimates were consistent for all outcomes. The detailed results for inconsistency are shown in Supplementary File S1 along with network plots for comparisons of different intervention effects on glucose, insulin, and triacylglycerol. The funnel plots for insulin and triacylglycerol are symmetrical, while the funnel plots for glucose show a slight asymmetry (Supplementary File S1).

A

Every 30-min interruption							
− 0.01 (− 1.79, 1.77)	**A 45-min exercise bout**						
− 0.29 (− 1.10, 0.52)	− 0.28 (− 2.08, 1.52)	**Every 20-min interruption**					
− 0.41 (− 1.33, 0.51)	− 0.40 (− 2.28, 1.47)	− 0.12 (− 1.09, 0.84)	**Every 60-min interruption**				
− 0.34 (− 2.38, 1.70)	− 0.33 (− 2.97, 2.31)	− 0.05 (− 2.16, 2.06)	0.07 (− 2.00, 2.14)	**Every 45-min interruption**			
− 0.74 (− 2.51, 1.03)	− 0.73 (− 2.74, 1.28)	− 0.45 (− 2.25, 1.35)	− 0.33 (− 2.20, 1.54)	− 0.40 (− 3.04, 2.24)	**Three 15-min bouts**		
− 0.95 (− 2.08, 0.17)	− 0.94 (− 2.92, 1.04)	− 0.66 (− 1.83, 0.50)	− 0.54 (− 1.75, 0.66)	− 0.61 (− 2.86, 1.63)	− 0.21 (− 2.19, 1.76)	**A 60-min exercise bout**	
− 1.16 (− 2.18, − 0.14)	− 1.15 (− 3.08, 0.78)	− 0.87 (− 1.88, 0.13)	− 0.75 (− 1.96, 0.46)	− 0.82 (− 3.04, 1.39)	− 0.42 (− 2.35, 1.50)	− 0.21 (− 1.58, 1.16)	**A 30-min exercise bout**
− 1.18 (− 1.72, − 0.64)	− 1.17 (− 2.87, 0.52)	**− 0.89 (− 1.52, − 0.27)**	− 0.77 (− 1.57, 0.04)	− 0.84 (− 2.87, 1.18)	− 0.44 (− 2.13, 1.24)	− 0.23 (− 1.25, 0.80)	− 0.02 (− 0.95, 0.91)

B

Every 30-min interruption					
− 0.04 (− 0.64, 0.56)	**Every 20-min interruption**				
− 0.09 (− 0.78, 0.60)	− 0.04 (− 0.71, 0.62)	**A 30-min exercise bout**			
− 0.51 (− 1.79, 0.77)	− 0.47 (− 1.78, 0.84)	− 0.42 (− 1.79, 0.94)	**A 60-min exercise bout**		
− 0.64 (− 1.43, 0.16)	− 0.59 (− 1.43, 0.24)	− 0.55 (− 1.49, 0.39)	− 0.12 (− 1.54, 1.29)	**Every 60-min interruption**	
− 0.98 (− 1.36, − 0.60)	**− 0.94 (− 1.41, − 0.46)**	**− 0.89 (− 1.51, − 0.27)**	− 0.47 (− 1.69, 0.75)	− 0.34 (− 1.06, 0.38)	**Prolonged Sitting**

C

Every 60-min interruption				
− 0.09 (− 0.90, 0.72)	**A 30-min exercise bout**			
− 0.15 (− 1.04, 0.75)	− 0.06 (− 0.80, 0.68)	**Every 20-min interruption**		
− 0.34 (− 0.98, 0.30)	− 0.25 (− 0.76, 0.26)	− 0.19 (− 0.82, 0.43)	**Prolonged Sitting**	
− 0.46 (− 1.13, 0.21)	− 0.37 (− 0.90, 0.16)	− 0.31 (− 0.99, 0.37)	− 0.12 (− 0.41, 0.17)	**Every 30-min interruption**

Figure 2. Comparative effects of different interruptions on glucose (**A**), insulin (**B**), and triacylglycerol (**C**) responses (SMD (95%CI)) using a network meta-analysis. Significant differences are highlighted in bold.

A

Every 30-min interruption								
− 0.02 (− 0.52, 0.47)	**Every 20-min interruption**							
− 0.06 (− 1.63, 1.50)	− 0.04 (− 1.62, 1.54)	**Three 15-min bouts**						
− 0.12 (− 1.30, 1.07)	− 0.09 (− 1.32, 1.14)	− 0.05 (− 1.98, 1.88)	**Every 45-min interruption**					
− 0.21 (− 0.78, 0.36)	− 0.19 (− 0.78, 0.41)	− 0.15 (− 1.76, 1.47)	− 0.09 (− 1.30, 1.11)	**Every 60-min interruption**				
− 0.27 (− 1.82, 1.29)	− 0.24 (− 1.81, 1.33)	− 0.20 (− 2.36, 1.96)	− 0.15 (− 2.07, 1.77)	− 0.06 (− 1.66, 1.55)	**A 45-min exercise bout**			
− 0.72 (− 1.05, − 0.39)	**− 0.69 (− 1.07, − 0.31)**	− 0.65 (− 2.18, 0.88)	− 0.60 (− 1.78, 0.58)	**− 0.51 (− 1.01, − 0.01)**	− 0.45 (− 1.97, 1.07)	**Prolonged sitting**		
− 0.85 (− 1.44, − 0.27)	**− 0.83 (− 1.42, − 0.24)**	− 0.79 (− 2.41, 0.83)	− 0.74 (− 2.02, 0.55)	− 0.64 (− 1.36, 0.08)	− 0.59 (− 2.20, 1.03)	− 0.14 (− 0.67, 0.40)	**A 30-min exercise bout**	
− 0.91 (− 1.69, − 0.13)	**− 0.89 (− 1.67, − 0.10)**	− 0.84 (− 2.53, 0.84)	− 0.79 (− 2.15, 0.57)	− 0.70 (− 1.51, 0.11)	− 0.64 (− 2.32, 1.04)	− 0.19 (− 0.90, 0.52)	− 0.06 (− 0.94, 0.83)	**A 60-min exercise bout**

B

Every 30-min interruption					
− 0.02 (− 0.64, 0.61)	**Every 20-min interruption**				
− 0.07 (− 0.78, 0.65)	− 0.05 (− 0.73, 0.63)	**A 30-min exercise bout**			
− 0.48 (− 1.80, 0.83)	− 0.47 (− 1.81, 0.87)	− 0.42 (− 1.82, 0.98)	**A 60-min exercise bout**		
− 0.61 (− 1.43, 0.21)	− 0.60 (− 1.45, 0.26)	− 0.55 (− 1.51, 0.41)	− 0.13 (− 1.58, 1.32)	**Every 60-min interruption**	
− 0.95 (− 1.37, − 0.54)	**− 0.94 (− 1.42, − 0.45)**	**− 0.89 (− 1.52, − 0.25)**	− 0.47 (− 1.72, 0.78)	− 0.34 (− 1.08, 0.40)	**Prolonged sitting**

Figure 3. Comparative effects of different interruptions on glucose (**A**) and insulin (**B**) responses (SMD (95%CI)) using a network meta-analysis, which excluded participants with T2DM. Significant differences are highlighted in bold.

3.3. Pairwise Meta-Analysis

Based on studies assessing frequent interruptions, we calculated SMDs and 95%CIs for different types of PA breaks and different times of PA breaks and their effects on glucose, insulin, and triacylglycerol. An inconsistency test based on the network analysis found significant global inconsistency for glucose ($p < 0.001$), insulin ($p < 0.001$) and triacylglycerol ($p < 0.05$). We conducted pairwise meta-analysis.

A pooled analysis of MVPA showed a significant decrease in both glucose (SMD = −0.6, 95%CI: −0.83, −0.37) and insulin (SMD = −0.53, 95%CI: −0.73, −0.32) compared to prolonged sitting. Although the SMDs of LPA were larger, −1.04 (95%CI −1.53 −0.55) for insulin and −1.45 (95%CI −2.32 −0.57) for glucose, significant heterogeneity was present ($I^2 > 75\%$, $p < 0.05$) (Table 2). In the case of LPA interruption, neither Begg's rank correlation (Kendall $\tau = -5.00$, $p \geq 0.84$) nor Egger's regression (intercept = −5.69, SE = 5.074, $p \geq 0.26$) indicated a bias in the insulin results. Although Begg's rank correlation (Kendall $\tau = -27.00$, $p > 0.32$) lacked statistical significance, Egger's regression (intercept = −9.98, SE = 1.56, $p \leq 0.001$) hinted at a potential publication bias related to glucose. For triacylglycerol, both Begg's (Kendall $\tau = -31.00$, $p < 0.05$) and Egger's regression (intercept = −10.65, SE = 4.1, $p < 0.05$) were suggestive of publication bias. Subgroup analysis of frequent standing interruptions demonstrated a significant moderate decrease in glucose, but triacylglycerol exceeded expectations and was significantly negative, with SMDs being 0.42 and the 95%CI being 0.17 to 0.68 (Table 2). Finally, although a comprehensive analysis of RE showed significant declines regarding all three outcomes, the number of included studies and participants was small.

Table 2. Physical activity break interruption via a comparison of pooled estimates.

Outcome	Interruption (vs. Prolonged Sitting)	N of Studies	N of People	Effect Estimates	I^2 (%)
Type/intensity					
				SMD (95%CI)	
Blood glucose	MVPA	7	147	**−0.6 (−0.83, −0.37)**	30.91
	LPA	18	339	**−1.45 (−2.32, −0.57)**	96.4
	Standing	8	133	**−0.65 (−1.21, −0.09)**	81.24
	RE	3	49	**−1.04 (−1.58, −0.49)**	97.65
Insulin	MVPA	9	175	**−0.53 (−0.73, −0.32)**	0
	LPA	15	244	**−1.04 (−1.53, −0.55)**	85.99
	Standing	8	151	−0.45 (−0.97, 0.06)	80.37
	RE	2	37	**−0.86 (−1.34, −0.39)**	74.51
Triacylglycerol	MVPA	3	90	0.22 (−0.07, 0.52)	75.46
	LPA	8	182	−0.39 (−0.85, 0.06)	81.46
	Standing	5	118	**0.42 (0.17, 0.68)**	0
	RE	1	24	**−0.67 (−1.24, −0.1)**	/
Duration of breaks					
				SMD (95%CI)	
Blood glucose	More than 5 min	3	57	**−1.12 (−1.51, −0.73)**	32.82
	5 min	4	129	**−0.99 (−1.53, −0.45)**	83.49
	3 min	5	87	**−0.88 (−1.31, −0.46)**	96.69
	2 min	15	170	**−0.85 (−1.31, −0.39)**	78.82
Insulin	More than 5 min	4	79	0.04 (−0.27, 0.34)	0
	5 min	4	129	**−1.07 (−1.66, −0.49)**	85.87
	3 min	3	35	**−0.91 (−1.35, −0.48)**	58.32
	2 min	14	215	**−0.87 (−1.25, −0.50)**	72.66
Triacylglycerol	More than 5 min	3	59	−0.24 (−0.6, 0.12)	50.38
	5 min	2	82	−0.02 (−0.3, 0.26)	91.81
	3 min	2	35	−0.39 (−0.81, 0.02)	0
	2 min	5	131	−0.1 (−0.35, 0.14)	82.63

SMD (95%CI), standardized mean difference (95% confidence interval). Bold results indicate statistical significance.

An interruption greater than 5 min resulted in a significant decrease in glucose but not insulin or triacylglycerol (Table 2). The pooled analysis of 5 min interruption showed significant attenuations of both glycemia and insulin, and there was significant heterogeneity ($I^2 > 75\%$, $p < 0.05$). Regarding glycemia, both Begg's rank correlation (Kendall $\tau = -25.00$, $p < 0.05$) and Egger's regression (intercept = −9.37, SE = 4.06, $p < 0.05$) were suggestive of publication bias. Additionally, for 5 min interruption effects on insulin, though Begg's rank correlation (Kendall $\tau = -21.00$, $p > 0.07$) did not suggest statistical significance, Egger's regression (intercept = −9.79, SE = 4.531, $p < 0.05$) indicated the presence of publication bias. A comprehensive analysis of 3 min interruptions showed significant declines in blood glucose and insulin outcomes. The SMDs of 2 min PA were found to be significant, −0.87 (95%CI: −1.25 −0.50) for insulin and −0.85 (95%CI: −1.31 −0.39) for glucose.

3.4. Quality Assessment

The risk of bias is shown in Figure 4. The majority of studies (21/38) were rated as being at a low risk of bias in the field of randomized sequence generation. With regard to allocation concealment, 15/38 studies were at a low risk of bias. However, it is not surprising that all studies were rated as being at a high risk of bias for participant and staff blinding because it was not possible to blind them to the different interventions and interruptions. In terms of outcome assessment blinding, only five studies masked their outcome assessors to treatment allocation. Regarding incomplete outcome data and selective reporting, 35 and 22 studies had a low risk of bias, respectively. Finally, 23/38 studies were categorized as having an unclear risk of bias for other areas of bias.

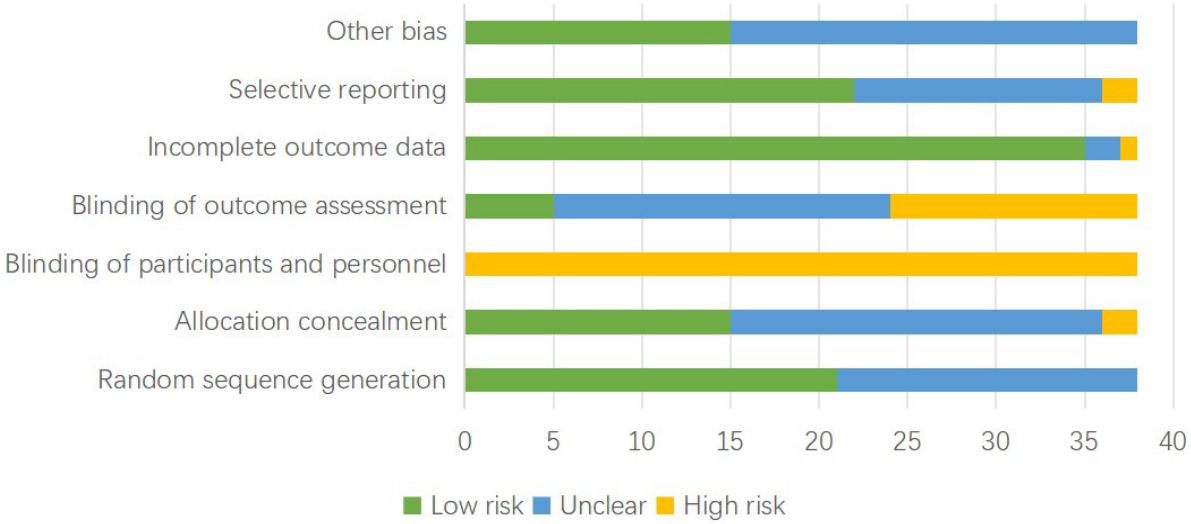

Figure 4. Quality of included studies.

4. Discussion

Several reviews [10,56–58] have reported on the association of prolonged sitting interruptions with biomarkers of cardiometabolic health and found them to be effective to varying degrees. These studies have indicated that frequent short interruptions, including standing, LPA, and MVPA, significantly lower postprandial glucose compared to a single interruption of exercise. In the current systematic review with meta-analyses, the effects of these PA interventions on glucose and triacylglycerol metabolism were considered from the perspective of frequency, duration, type, and intensity, and a small body of evidence was identified. A total of 38 studies were included, of which 4–8 control interventions were eventually incorporated into network meta-analyses of glucose, insulin, and triacylglycerol outcomes.

Overall, the pooled findings provided some support for modest-to-high improvements in glycemic control with PA intervention but not for triacylglycerol. It was previously re-

ported that there were no significant triacylglycerol responses to regular activity breaks [58]. Some results were fairly consistent, while others varied widely between studies, particularly with regard to the LPA interval and 5 min interruption. This may be because some interventions are more effective in T2DM and obesity than others. There was also a wide range of prolonged sitting settings, components of behavior change, methods of outcome measurement, and degrees of outcome focus. In some cases, a single study that differed from the overall model seemed problematic, and differences in each outcome were often driven by participants' age, gender, body weight, health status, as well as bias risks. Because of the small number of samples and studies, we did not conduct stratified analyses to assess the effectiveness of resistance exercise for particular populations.

Our findings regarding the pooled analysis of interval interventions noted attenuations in blood glucose and insulin responses which were consistent with the results of Loh et al. [10] and Buffey et al. [59]. However, they were slightly different to those of Quan et al. [57] who found that the interval intervention with MPA was slightly superior to LPA in lowering postprandial glycemia and insulin responses in adults with no chronic diseases. Our findings suggest that LPA works better than MVPA. The proposed mechanisms are as follows. The increased glucose uptake during interrupted sitting is preferentially regulated by the muscle contraction-mediated pathway, which is independent of insulin. Increased insulin sensitivity is responsible for the increased activity of glycogen synthase and hexokinase, increasing fat oxidation capacity, reducing the concentration of diacylglycerol and ceramide in cells, and changing the fatty acid composition of skeletal muscle phospholipids [60,61]. Buffey et al. [59] reported that the act of standing as a pause in sitting markedly lowered glucose levels after eating, yet it did not markedly impact insulin levels, whereas light walking breaks showed a significant and superior effect on both. Due to the higher intensity and frequency of muscle activity and greater glucose uptake mediated by muscle contractions, the acute benefits of light-intensity walking on postprandial glucose and insulin are more pronounced than with standing. Similarly, Loh et al. [10] reported a decreased level of both, with frequent breaks, in 37 studies. Our network and pairwise analyses revealed the same directionality of these effect estimates, with a slightly larger effect size. The most likely explanations for this are the participant attributes, sitting duration, and methodological differences.

In research by Dempsey et al. [48], McCarthy et al. [28], and Henson et al. [25], the glucose- and insulin-level lowering effects were significantly greater than those in other studies when break durations were studied. In the study by Dempsey et al. [48], subjects had T2DM and the intervention was in the form of 3 min sessions of simple resistance activities after every 30 min of interrupted sitting. McCarthy et al. [28] studied the effects of interrupted sitting with 5 min of arm ergometry every 30 min in 34 healthy adults. These results remind us of the importance of RE. Therefore, it can be inferred that RE has a significant effect on prandial glucose management; however, more research is needed to confirm this hypothesis. The glucose- and insulin-level lowering effects were also relatively clear in the study by Henson et al. [25], in which subjects were 22 overweight or obese postmenopausal women. In our subgroup analyses of more than a 5 min interruption and its effects on glycemia and insulin, we found different effect estimates, without significant heterogeneity between studies. This is most likely due to the different samples included. For example, of the three studies that included blood glucose, two had an average participant age of 60 or older, and one had a sample of patients with T2DM. The participants in the four insulin studies were young and healthy.

No significant reduction in glucose and insulin levels was observed with 45 min, 60 min, and three 15 min exercise sessions. A 30 min exercise session showed an SMD of −0.89 (95%CI: −1.51 −0.27) for insulin. Our review shows that sitting with activity breaks every 20 and 30 min is beneficial for blood glucose and insulin levels in a sample including healthy, overweight, obese, and inactive adults, as well as those with impaired glucose tolerance and diabetes. The activity breaks in the studies usually involved walking

or simple weightlifting. Durations of 5, 3, and 2 min showed significant effects on both glucose and insulin.

Overall, our study has some strengths. First, every study incorporated in our meta-analysis employed a randomized, controlled, cross-over methodology. In addition, a network meta-analysis was used to simultaneously compare the effects of multiple physical activity interventions with greater accuracy [62]. However, our study also has some limitations. Firstly, the small sample size of the included studies and the heterogeneity of the measurement methods—as well as the heterogeneity of the interventions in the control for duration, frequency, and intensity—were potential confounding factors for the reported results. This study was limited by the acute nature of metabolism, and, thus, the validity of long-term results cannot be determined. In the future, the long-term longitudinal-effect RCTs of PA breaks should be carried out to investigate the long-term metabolic effects of these interventions, as well as their effectiveness and feasibility in life, especially for patients with, or at high risk of, T2DM. In addition, there was a small number of RE intervention studies with prediabetes/diabetes participants, so results were unclear for these subgroups. Consequently, additional studies are required to comprehend the possible immediate and delayed impacts of these interventions on postprandial metabolism. Although we were not able to resolve queries about the potential sources of bias, the experimental design and PA interventions were well controlled, with the washout period removing any potential carryover effects from the previous trial.

5. Conclusions

According to the network meta-analysis, performing short bouts of PA every 30 min is the most effective prolonged sitting intervention for improving blood glucose and insulin. More evidence is needed to determine the optimal type and time of PA breaks. Future research should investigate the metabolic effects of different types and intensity levels of PA interruption and the long-term metabolic effects of every 30 min interruption, as well as their effectiveness and feasibility in daily life.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/app14083201/s1. Table S1 Search strategy, Figure S1 Network plots for comparisons of different interventions on glucose, insulin, and triacylglycerol, Figure S2 Forest plots of network meta-analyses for glucose and insulin compared with prolonged sitting, Figure S3 Local inconsistency test results for glucose, insulin and triacylglycerol responses, Table S2 The ranking of interventions for glucose and insulin in the network meta-analysis, Figure S4 Funnel plots for each outcome in the network meta-analysis for glucose, insulin and triacylglycerol, Table S3 The risk of bias assessment of included studies.

Author Contributions: Conceptualization, Y.P. and X.Z.; methodology, S.C.; software, Q.H.; validation, X.Z., S.C. and Y.P.; formal analysis, Y.D. and L.D.; resources, X.Z.; data curation, S.Y.; writing—original draft preparation, Y.D.; writing—review and editing, Q.H.; visualization, L.D.; supervision, X.Z.; project administration, Y.P.; funding acquisition, Y.P. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: All relevant data are present in the paper and its Supporting Information Files.

Conflicts of Interest: The authors declare that they have no conflicts of interest relevant to this review.

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