**Table S1: Characteristics of the acute mechanistic studies included in the review**

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| **Author****Year****Reference****Country** | **Population characteristics****Sample size** | **Design****Trial duration** | **LIPA condition**  | **Comparison condition** | **Measurement method of LIPA****LIPA outcome** | **Health outcomes** | **Statistical analyses****Covariates** | **Conclusion** | **Quality Score (%)** |
| Bailey et al. 2015[1]UK | Healthy adults(70.0% men; mean age 24.0 ± 3.0 years; mean BMI 26.5 ±4.3 kg/m²)N=10 | Randomized cross-over trialThree conditions: 1 day for each condition (5 hour testing period) | 2-min walking at 3.2 km/h on a level treadmill every 20 min for 5 hours | Continuous sitting/standing for 2 mins every 20 mins | Borg Rate of Perceived ExertionWalking speed & BRPE | AUC glucose, systolic blood pressure, diastolic blood pressure; triglycerides, total cholesterol, HDL cholesterol | Repeated Measures AnovaCovariate not reported | Interrupting sitting time with frequent brief bouts of light-intensity activity, but not standing, imparts beneficial postprandial responses that may enhance cardio-metabolic heath. No difference in blood pressure or lipid parameters | 46 |
| Crespo et al. 2016[2]USA | Overweight/obese adults (BMI =29±3 kg/m²) N=9 | Randomized cross-over trialFour conditions: 8 hours per condition | Interrupting sitting with: standing, cycling and walking for 10-30 min periods to accumulate 2.5hr throughout 8hr day. Cycling performed at 25-30 rpm and walking performed at 1 mph  | Sitting for 8hr period (excluding 3 toilet breaks and half-hour lunch) | ActivPALGENEAactiv accelerometerTime spent standing, stepping, sittingTime spent in sedentary, light, moderate and vigorous physical activity | Blood glucose | Linear mixed models (LMM) used to test for differences in glucose and HR measurements between treatment. ANOVA used to analyse time spent in sedentary, light, moderate and vigorous PA.Age, gender, BMI, baseline glucose level | 24-hr mean glucose (P<0.001) and cumulative 6-hr postprandial glucose (P<0.001) reduced by 5-12% for stand, walk and cycle compared to sit. Cycle produced lowest 24 hr and cumulative 6-h postprandial mean glucose compared to walk, and stand. Cycle had greatest glucose-lowering effect. Cycle produced 44% lower cumulative 6-h postprandial iUAC compared to sit (p<0.001) and 39% (p<0.01) compared to stand. Walk was 24% lower than sit (P<0.05). | 75 |
| Dempsey et al.2016[3]Australia | Inactive overweight/obese adults with T2D (58.3% men; 62 ± 6 years old)N=24 | Randomized cross-over trial8-hour conditions on three separate days (6-14 days of washout) | Uninterrupted sittingSitting plus 3-min bouts of light-intensity walkingSitting plus 3-min bouts of simple resistance activities | No comparison condition | Indirect calorimetryVO2, VCO2, energy expenditure | Plasma glucoseSerum insulinC-peptide levelsPlasma triglycerides | Generalized linear mixed modelsAge, sex, BMI, preprandial values, period effects (treatment order) | Interrupting prolonged sitting with brief light-intensity walking significantly reduce resting systolic and diastolic blood pressure | 86 |
| Dempsey et al.2016[4]Australia | Inactive overweight/obese adults with T2D (58.3% men; 62 ± 6 years old)N=24 | Randomized cross-over trial8-hour conditions on three separate days (6-14 days of washout) | Uninterrupted sittingSitting plus 3-min bouts of light-intensity walkingSitting plus 3-min bouts of simple resistance activities | No comparison condition | Indirect calorimetryVO2, VCO2, energy expenditure | Plasma glucoseSerum insulinC-peptide levelsPlasma triglycerides | Generalized linear mixed modelsAge, sex, BMI, preprandial values, period effects (treatment order) | Interrupting prolonged sitting with brief light-intensity walking significantly attenuates postprandial glucose, insulin, C-peptide, and triglyceride responses in adults with T2D | 86 |
| Dunstan et al. 2012[5]Australia | Overweight/obese adults (aged 45-65; BMI>25kg/m2)N=19 | Randomized cross-over trialThree conditions: 7 hours per condition | Sitting with 2-min bouts of light intensity walking at 3.2km/h every 20 mins | Uninterrupted sitting and sitting with 2-min bouts of moderate intensity walking at 5.8-6.4km/h every 20 mins | ActiGraph GT1M accelerometer<100 counts/min = sedentaryTime spent sedentary, light, moderate and vigorous | Glucose and insulin incremental area under curves (iAUC) | Generalized estimating equations used to evaluate effects of trial conditions.Age, sex, weight, baseline predrink outcomes values, period effects | Glucose iUAC (p<0.01) and insulin iUAC (p<0.0001) significantly lower after sitting with LIPA compared to uninterrupted sitting. Mean plasma glucose at 2hr postdrink was sig. lower (p>0.05) for LIPA but mean serum insulin at 2hr was not (p=0.4). | 93 |
| Duvivier et al.2013[6]The Netherlands | Men and women (mean age= 21±2 years; predominantly female)N=18 | Counterbalanced randomized cross-over trialThree conditions lasted 4 days with a wash-out period of at least 10 days | 4 days of 8h/day sleeping,4h/day walking at leisure pace,2h/day of standing | 4 days of 8h/day sleeping, 14h/day sitting,1h/day walking,1h/day standing | ActivPALActivity pattern (sitting, standing, stepping, sleeping) | TriglyceridesTotal cholesterolHDL-cholesterolNon-HDL-cholesterolLDL-cholesterolApo A-IApo BInsulin sensitivity indexFasting glucoseFasting insulinAUC glucoseAUC InsulinAUC c-peptide | Repeated Measures ANOVA comparing the three conditions with Least Significant Difference test for post hoc analyses (p<0.017 considered as significant)Not reported | Compared to the sitting condition, the LIPA condition resulted in significantly lower triglycerides, non-HDL cholesterol, APO-B and AUC insulin | 68 |
| Duvivier et al 2017 [7] The Netherlands | Adults with T2D (68.4% men, 63 ± 9 years)N=19 | Randomised cross-over designThree regimens under free-living conditions each lasting 4 days | Sit Less: 4.7 h/day of sitting replaced by standing (2.5h) and LIPA walking (2.2h) | Sitting (14h/day)Exercise (1.1h/day of sitting replaced by MVPA cycling) | activPAL monitor | 24 h glucose, insulin resistance and lipids | Linear mixed model | Breaking sitting with standing and light-intensity walking effectively improved 24h glucose levels and improved insulin sensitivity in individuals with type 2 diabetes to a greater extent than structured exercise. Thus, our results suggest that breaking sitting with standing and light-intensity walking may be an alternative to structured exercise to promote glycaemic control in patients type 2 diabetes. | 73 |
| Duvivier et al 2017 b[8]The Netherlands  | Sedentary overweight/obese adults (54.2% men, 64±7years old, BMI 29 ±2 kg/m2)N= 24  | Randomized cross-over design Two regimens under free-living conditions each lasting 4 days | “Sit Less”: sitting 7.6 h/day, standing 4.0 h/day, self-perceived light-intensity walking 4.3 h/day | “Sit” (sitting 13.5 h/day, standing 1.4 h/day, self-perceived light-intensity walking 0.7 h/day) | activPAL monitor | Insulin sensitivity lips, blood pressure | Linear mixed modelSex  | Reducing sitting time in free-living conditions markedly improved insulin sensitivity, circulating lipids, and diastolic blood pressure. Substituting sitting with standing and self-perceived light walking is an effective strategy to improve cardiometabolic risk factors in overweight/obese subjects. | 73 |
| Grace et al. 2017[9]Australia | Inactive overweight/0bese adults with T2DN=21 | Randomized crossover experimental trialthree 7-hour conditions: | light-intensity walking interruptions (LW)  | uninterrupted sitting (SIT); simple resistance activity interruptions (SRA) | treadmill (3.2 km/h,zero gradient | percentage change in 338 lipid species using mass spectrometry (baseline to7 hours) | mixed model analysisbaseline outcome variable,gender, body mass index, and condition order | Compared with SIT, LW and SRA were associated with reductions in lipids associated with inflammation; increased concentrations of lipids associated with antioxidant capacity; and differential changes in species associated with platelet activation. Acutely interrupting prolonged sitting time may impart beneficial effects on the postprandial plasma lipidome of adults with T2D.Evidence on longer-term intervention is needed | 85 |
| Henson et al.2016[10]UK | Overweight/obese, disglycemic, postmenopausal women (aged 66.6 ± 4.7)N=22 | Balanced, incomplete block design | Prolonged, unbroken sitting (7.5hrs)Prolonged sitting broken up with either standing or walking at a self-perceived light intensity (for 5 mins every 30 mins) | No comparison condition | Accelerometer (GT3X), ActivPAL3Freedson cut-points to categorize activity intensity | GlucoseInsulinNonesterified fatty acidsTriglycerides | Multilevel mixed-effects linear regressionNot reported | Interrupting periods of prolonged sitting with 5 minutes of standing every 30 minutes changes postprandial glucose metabolism similar to breaking up sitting with identical periods of self-perceived light-intensity walking in overweight, postmenopausal women with dysglycemia.  | 72 |
| Larsen et al. 2012[11] Australia | Overweight/obese adults (aged 45-65 years)N=19 | Randomized crossover trialThree conditions: 7 hours per condition | Sitting with 2 min bouts of light-intensity walking at 3.2km/h every 20 min | Uninterrupted sitting or sitting with 2 min bouts of moderate-intensity walking between 5.8 – 6.4 km/h every 20 mins | Borg Relative Exertion rating | Systolic and diastolic blood pressure | Generalized estimating equations (GEE) used to compare overall means of BP for each condition.Age, sex, BMI, fasting BP, period effects (treatment order) | Interrupting sitting with LIPA significantly reduced SBP (p=0.002) and DBP (p=0.006) compared to uninterrupted sitting. Removal of patients on antihypertensive therapy resulted in DBP difference no longer being statistically significant (p=0.16) | 79 |
| McCarthy et al 2017 [12]UK | Adults (age 40±9 years, BMI 24.5 ± 3 kg/m2)N=34  | Randomized crossover trialTwo 7.5-h experimental conditions | Sitting interspersed with 5 min light walking (3km/h on treadmill) bouts every 30 min (totalling 1h of activity and 6.5h of sitting) | Prolonged sitting | activPAL monitor | Blood glucoseInsulin  | Repeated measures ANOVAVO2peak, sex | Breaking sedentary time with light walking breaksreduced blood glucose and insulin after adjustment for VO2peak and sex.Participants with lower fitness had worse postprandial glucose and insulin responses during prolonged sitting, and were able to gain greater metabolic benefit throughbreaking their sitting time with light activities compared with individuals with higher fitness. Future interventions aimed atalleviating the deleterious metabolic impacts of sedentary behavior may therefore be optimized by tailoring to CRF levelsof the general population | 77 |
| Mendham et al. 2011[13]Australia | Sedentary menN=12 | Randomised cross-over trialFour conditions: 24 hours per condition (PA session: 40 minutes)  | LIPA resistance protocol performed at 60% of 1 repetition maximum for 40 mins including leg, shoulder and chest press. LIPA aerobic protocol performed via stationary cycling at 30% of maximal aerobic workload for 40mins | MIPA resistance protocol performed at 80% of RMP for 40 mins (same exercises). MIPA aerobic protocol performed via stationary cycling at 50% of maximal aerobic workload for 40 mins.  | Graded exercise testVO2maxMaximal aerobic power output | IL-6, C reactive protein, total leukocyte count,  | Two-way repeated measures ANOVATukey’s pairwise comparisonsNot reported | Light intensity resistance resulted in significant increase in Il-6 in pre to immediately post-exercise values but LI aerobic did not. LIPA (resistance or aerobic) did not significantly impact CRP.  | 68 |
| Mestek et al. 2008[14]USA | Men with metabolic syndrome N=14 | Randomized crossover trial Four conditions: Approximately 14 hours per condition & 6 hours for control  | Walked on a treadmill at 35-45% of VO2max until 500kcal expended | Resting quietly and walking on a treadmill at 60-70% of VO2max until 500kcal expended in continuous session and in two accumulated sessions | Graded exercise testVO2peakVO2maxRating perceived exertion (Borg scale) | Triglycerides (TG) AUC and temporal postprandial, insulin AUC and temporal,  | Two-way ANOVA (comparison postprandial TG and insulin responses)One-way repeated measures ANOVA (differences in AUC and TG and insulin concentrations)Duncan’s New Multiple Range TestNot reported | LIPA significantly reduces TG AUC (p=0.02). Temporal postprandial TG significantly reduced at 4hr (p<0.05) but not 2 or 6hr after test meal. Insulin AUC and temporal response did not significantly differ with LIPA compared to control (p=0.55).  | 64 |
| Newsom et al. 2013[15]USA | Sedentary obese adults (BMI 37±1kg/m2) N=11 | Randomized cross-over designThree conditions: 27 hours per condition | Exercise at 50% of VO2peak until 350kcal were expended. Included treadmill walking/jogging and cycling | Sedentary or exercise at 65% of VO2peak until 350kcal were expended. Included treadmill walking/jogging and cycling | Incremental test on a stationary cycle ergonometerVO2peak | Glucose and insulin AUC, insulin sensitivity, basal hepatic glucose production, muscle glycogen and lipid concentrations | Repeated measures two-way ANOVARepeated measures one-way ANOVATukey pairwise comparisonsNot reported | No significant difference in glucose and insulin responses to meals after LIPA. Insulin sensitivity the morning after exercise was significantly elevate (p=0.01) with LIPA compared to control and MIPA, as a result of enhanced peripheral glucose metabolism (as hepatic glucose output was the same for control, LIPA and MIPA). LIPA did not significantly decrease muscle glycogen. LIPA significantly associated (p=0.02) with reduction in fatty acid the morning after exercise compared to control.  | 64 |
| Pulsford et al. 2016[16]UK | Men (aged 40.2 ± 12.2 years)N=25 | Randomized cross-over trialThree conditions: 1 day (7 hours) | 2min walking at 2mph every 20 minutes | Sitting continuously/ Standing for 2 mins every twenty minutes | Indirect calorimetrySteady state energy expenditure values for sitting, standing & walking | Blood glucose and insulin | Generalized estimating equation (GEE)MVPA, baseline values | Interrupting sustained sitting with brief repeated bouts of light-intensity walking but not standing reduced insulin demand and improved glucose uptake during a simulated sedentary working day. The benefits of such minor behavioural changes could inform future workplace health interventions. | 78 |
| Schwarz et al. 1996[17]USA | Healthy, adult men (mean age 27.5 ± 1.7 years)N=10 | Not explicitly describedThree conditions: 1 day each | 10 mins of constant-work-rate exercise on the cycle ergometer at high intensity10 mins of constant-work-rate exercise on the cycle ergometer at low intensity | Resting | Breath-to-breath measurements of gas exchangeO2max, Lactate threshold | Insulin-like growth factor | Repeated Measures ANOVANot reported | Acute exercise-induced proteolysis of IGFBP-3 may contribute to anabolic effects of physical activity by increasing the bioavailability of IGF-I. | 52 |
| Thorpe et al. 2014[18]Australia | Men and women(48.2 ±7.9 years)N=23 | Randomized cross-over trialTwo conditions: 5 days each condition for 8 hours each day (minimum of 7 days washout period) | 4 hours standing, systematically changing between a seated andstanding posture every 30-min for 8 hours at work.  | 4 hour standing, for a total of 8 hours seated at work  | ActiGraph GT3X+ accelerometerLIPA & MVPA (daily PA) | After a mixed test drink werecollected hourly for 4 h on days 1 and 5 of each condition serum insulin, plasma glucose, and triglycerides. | Linear mixed models with a single random effectWithin-subject(condition, time, and order) and between-subject (baseline predrink values for the outcome of interest, sex, age,waist circumference, and dietary intake during the condition(kJIdj1)). | Alternating standing and sitting in 30-min bouts results in modestbeneficial effects on postprandial glucose responses in overweight/obese office workers. | 75 |
| Zeigler et al. 2015[19]USA | Men and women (between 25 & 65 years old)N=10 | Randomized crossover trialTwo conditions: each 1 day (workday of 8 hours) | Walking at a walking (workstation 1.0 mph) during progressively longer intervals (2x10 min, 2x15min, 2x20min, 2x30min = in total 2.5h) | Normal daily office activities | ActiGraph GT3X+ accelerometerFreedson cut-points: time spent in sedentary, light and MVPA | Ambulatory blood pressure | Linear mixed modelsNot reported | Accumulation of 2,5h of walking at 1.0 mph over the course of an 8-h workday significantly reduced ambulatory SBP & DBP, and DBP load.  | 57 |
| Zeigler et al. 2016[8]USA | Overweight or obese adults (28.7 ± 2.7 kg/m2; 30±15 years)N=9  | Randomized crossover full-factorial studyFour conditions (workday) randomly performed 1 wk apart | Standing for a predetermined time each hour on a treadmill: 10 min at 0850 and 0950 h, 15 min at 1045 and 1145 h, 20 min at 1240 and 1320 h, and 30 min at 1400 and 1530 h, for a total of 2.5 h of standing over the 8-h day Walking (walked at 1.0 mph, 0% grade on treadmill, matched to standing time)Cycling (cycle on ergometer at similar time intervals and at a work rate (approximately 20 W) and cadence that matched the intensity and step rate of the WALK day) | Sitting (remain seated at a desk for the whole day. Participants were free to use the restroom when needed, but no other PA was permitted) | ActivPALGENEActiv | Ambulatory blood pressure | Linear mixed models | Accumulation of 2.5 h of standing or performing light-intensity (approximately 2 METs) walking or cycling over the course of an 8-h workday significantly reduced systolic ABP and BP load compared with a control day spent primarily sitting. | 57 |

**Table S2: Characteristics of the physical activity programme intervention studies included in the review**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author****Year****Reference****Country** | **Population + characteristics****Sample size** | **Design****Trial duration** | **LIPA programme intervention** | **Comparison condition** | **Measurement method of LIPA****LIPA outcome** | **Health outcomes** | **Statistical analyses****Covariates** | **Conclusion** | **Quality****Score (%)** |
| de Lannoy et al. 2017 [20]USA | Sedentary, middle-aged abdominally obese adults ()N=171 | single-center, randomized controlled trial with a parallel group design (4 arms)24 weeks | Low amount, low-intensity exercise (walking 50% oxygen consumption on treadmill)High amount, low-intensity exercise (walking 50% oxygen consumption on treadmill) | No exercise controlHigh amount, high-intensity exercise (walking 75% oxygen consumption on treadmill) | Heart rate and oxygen consumption data obtained from the baseline fitness (VO2peak) test | 2-hour glucose, insulin AUC, and fasting insulin | Linear regression | The improvement in glucose and insulin measures did not exceed the day-to-day variability of measurement for approximately 80% of the participants independent of exercise amount or intensity. | 73 |
| Krause et al. 2014[21]Ireland | Sedentary, obese males (aged 52.8 ± 7.2 yrs) with/without type 2 diabetes mellitusN=25 (n=6 LIPA no T2DM, n=7 LIPA, T2DM) | Randomized controlled trialTwo conditions: 16 weeks | 30 mins walking, three times per week at 30-45% VO2max  | 30 mins walking, three times per week at 55-65% VO2max | Submaximal incremental walking testVO2max | Nitric oxide availability, oxidative stress, inflammatory markers | Logarithmic transformations, ANOVA GLM, post hoc TukeyAge, body fat percentage, estimate VO2max  | LIPA did not alter glycaemic or lipid profiles or nitric oxide production in obese, sedentary males with or without T2DM from baseline to post-intervention | 79 |
| Nishida et al.2001[22]Japan | Healthy men (18-25 years of age)N=8 | Quasi Experimental6 weeks | Ergometer training at lactate threshold intensity for 60min/day for 5 days/week for 6 weeks | No comparison condition | Graded exercise testVO2 | GlucoseInsulin | Wilcoxon’s signed-rank testNot reported | Mild exercise training at lactate threshold is considered to be an effective method for preventing glucose intolerance. | 65 |
| Nishida et al. 2010[23] [RN11746]Japan | Healthy men (22.6 ± 0.5 years)N=14 | Quasi Experimental6 weeks | Cycle ergometer aerobic training at the lactate threshold level for 60 minutes per day, five times a week for six weeks | No comparison condition | Graded exercise testVO2 | Plasma glucose levels, serum insulin, leptin concentrations, IGF | Wilcoxon’s signed-rank testNot reported | Short-term aerobic exercise training at the lactate threshold level decreases circulating IGF-I and increases IGFBP-1 levels. | 55 |
| Okano et al. 1990[24]Japan | Female caddies (aged 40-57 years)N=15 | Quasi Experimental12 weeks | 12 consecutive weeks of 7 to 8 km walks per day for 5 to 6 days a week | No comparison condition | Heart ratePedometer | Total cholesterol, HDL cholesterol, triglycerides, LDL cholesterol, haematocrit, blood pressure | Students’ t-test for paired dataNot reported | 12 weeks of walk habit decreased resting SBP, DBP and mean blood pressure. Reduction in serum HDL-C was observed after 12 week of walk habit. No significant changes in ratios of TC to HDL or HDL to LDL in the serum. | 59 |
| Paoli et al. 2013[25]Italy | Healthy, untrained men (aged 61±3.3 years; BMI 29.8±0.9)N=58 | Randomized controlled trial3 conditions:12 weeks | 3 experimental conditions: Endurance Group, Circuit Low intensity Group, Circuit High intensity Group. Each group trained three times per week, 50 minutes per session, for 12 weeks | No comparison condition | 1-yr PA recall questionnaire for older adultsMaximal graded exercise test + heartrateVO2max Heartrate (Karvonen) | Total cholesterol, triacyglicerol, HDL-C, LDL-C, apolipoprotein B (ApoB), apolipoprotein A1(ApoA1) | Multivariate analysis of variance (MANOVA)Not reported | Larger effect of high intensity circuit on blood lipids compared to lighter circuit or endurance training. Light intensity circuit improved systolic blood pressure more compared to the other conditions | 46 |
| Skoro-Kondza et al. 2009[26]UK | Patients with type 2 diabetes, not taking insulinN=59 | Randomized controlled trial12 weeks | 2xweekly 90 min yoga class | Waiting list for the yoga class | Not reportedNot reported | HbA1c, BMI, waist-hip ratio, SBP, DBP, lipid levels (total cholesterol, LDL, HDL) blood glucose levels | Paired sample t-testsANCOVANot reported | No significant differences between LIPA and control groups in any outcome measures | 64 |

**Table S3: Characteristics of cross-sectional studies included in the review**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author****Year****Reference****Country** | **Population + characteristics****Sample size****Study name** | **Measurement method of LIPA** **LIPA outcome** | **Health outcomes** | **Statistical analyses****Covariates included** | **Association coefficient/****Effect size**  | **Conclusion** | **Quality****Score (%)** |
| Amadid et al 2017 [27]Denmark | Adults at high risk of T2D (65.6 ± 6.8 years)N=1501ADDITION-PRO study | Accelerometer and heart rate monitor  | Impaired glucose metabolism | Decision tree modelling | Decision tree | Amongst people aged >53 and of normal weight higher LIPA time is associated with a lower prevalence of glucose impairment | 77 |
| Bakrani et al. 2016 [10][RN457][28] UK | Men and women (49.3% men; mean age 50.8±0.47 years) N=21312008 Health Survey for England | Actigraph accelerometer (Freedson cutpoints)4 behavioural categories based on PA and SB: ‘light movers’ vs ‘busy bees’, ‘sedentary exercisers’ and ‘couch potatoes’ | BMI, waist circumference, HDL-cholesterol, total cholesterol, glycated haemoglobin | Weighted multiple linear regression modelsAge, BMI, CVD index, ethnicity, fruit and vegetable consumption sex, smoking status, socioeconomic status, accelerometer wear time, medication | SB-to-light-intensity PA ratio (beta 99% CI; p)BMI: -0.1109 (-0.3918 , 0.1700); 0.305WC: 0.1380 (-0.2502, 0.5261); 0.355HDL: -0.0253 (-0.0476 ,- 0.0030); 0.004Total cholesterol: -0.0480 (-0.1335 , 0.0376); 0.146Glycated haemoglobin: -0.0079 (-0.0564 , 0.0407); 0.673 | Lower ratio of sedentary time to light activity (‘Light Movers’) had positive associations with HDL-cholesterol. | 77 |
| Balkau et al.2008[28]Europe | Men and women (43.2% men; aged 30-60 years) N=801European Relationship between Insulin Sensitivity and Cardiovascular risk (RISC) study | Actigraph accelerometer (Freedson cutpoints)% of time spent in LIPA | Insulin sensitivity | Mixed linear models Age, recruitment center, sex, BMI, waist, fasting glucose, alcohol intake, smoking, diabetes in family, menopause | % time in LIPA -> insulin sensitivity (adj for age, center, activity intensity): β=0.0064  | LIPA associated with insulin sensitivity but was not significant when adjusted for total PA | 54 |
| Buman et al.2014[29] USA | Noninstitutionalized civilians N=2 185 (fasting subsample: n=923)NHANES | Actigraph accelerometer (Freedson cutpoints)30 minutes/day units | SBP, DBP, HDL cholesterol, C-reactive protein, LDL cholesterol (fasting subsample), triglycerides (fasting subsample), plasma glucose (fasting subsample), insulin (fasting subsample) | Single & partition models, isotemporal substitution models, interaction analysesAge, sex, , race/ethnicity | Results from isotemporal substitution regression modelHDL cholesterol (SB to LIPA): RR=1.003Triglycerides (SB to LIPA): RR=0.981Insulin (SB to LIPA):RR=0.976 | Reallocating SB to LIPA is associated with a reduced CVD risk profile | 63 |
| Chastin et al.2015[30]USA | Adults N=1 937NHANES (National and Health and Nutrition Examination Survey) 2005-2006 cycle | ActiGraph accelerometer: 1min epoch, 7 days wear (include if 5 days of at least 10h). LIPA 100-1951 counts/min. | Cardio-metabolic markers:BMI; waist circumference; systllic blood pressure; diastolic blood pressure; HDL cholesterol; LDL cholesterol; triglycerides; C-reactive prtein; plasma glucose; plasma insulin; HOMA | Linear regression modelsAge, gender, ethnicity/race, self-reported health, diagnosis of health conditions, education, SES, smoking, alcohol, average daily dietary intake, fat intake, caffeine intake, blood pressure medication, diabetes medications | Composiitonal Association coefficitent (γ) of LIPA with all-cause mortality:BMI: -2.21waist circ: -11.39syst BP: 5.39diast BP: 4.26HDL: 0.08LDL: -0.53Triglycerides: -1.26CRP: -0.73Glucose: -0.01Insulin: -0.72HOMA: -0.87 | More LIPA is beneficially associate with waist circumference, trigycerides, plasma insulin and HOMA, if it replaces sedentary time. | 90 |
| Dahl-Petersen et al. 2017[31]Greenland | N = 1536 | Accelerometer and HR monitor measured total physical activity energy expenditure (PAEE) and intensities of PA | BMI, WC, Visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) | Isotemporal substitution modeling | Exchanging 1 h of sedentary time with light-intensity PA was associated with lower WC (-0.6 cm, P = 0.01), SAT (-0.08 cm, P < 0.001), and VAT (-0.04 cm, P = 0.359). | Physical activity energy expenditure is associated with lower BMI, WC, and abdominal fat among Greenland Inuit. The importance of promoting an upward shift of the whole PA intensity distribution and to spur even short bouts of MVPA to limit excessive accumulation of SAT and VAT is highlighted. | 84 |
| Dickie et al.2016[32]South Africa | Urban; black; women Mean age = 34N=76 | Accelerometer100–1951 counts/min | Cardiometabolic disease | Pearson product-moment correlation coefficientsSocioeconomic status, body composition, body fat distribution, resting BP, lipid profile, insulin sensitivity | Light-intensity PA(min/day) correlation coefficientsWeight: -0.21 BMI: -0.17 FM: -0.20 %BF: -0.17 WC: -0.24 TFM: -0.25 %TFM: -0.25AFM: 0.12 %AFM: 0.23 VAT: -0.19 SAT: 0.00 VAT/SAT: 0.04 | Both light intensity physical activity and cardiorespiratory fitness were associated with reduced total and centralfat mass, VAT, and reduced cardiometabolic risk for CVD and T2D | 64 |
| Ekelund et al.2007[33]UK | Both sexes (aged 30-50 years) N=258ProActive Study | Actigraph accelerometer LIPA (min/day): 309 ± 80 (men); 320 ± 68 (women) | Clustered metabolic risk, waist circumference, blood pressure, fasting triglycerides, HDL cholesterol, glucose, insulin | Stepwise multiplelinear regression analysisSex, age, and measurementtime | Standarized β coefficients (95% CI) with LIPA: waist= 0.03 (\_0.08 to 0.13); BP=\_0.02 (\_0.12 to 0.09); Insulin=\_0.06 (\_0.18 to 0.07); Glucose= 0.03 (\_0.08 to 0.14); Triglycerides= \_0.12 (\_0.23 to \_0.001); HDL=\_0.06 (\_0.17 to 0.05); Clustered risk score=\_0.03 (\_0.12 to 0.05) | Time spent at light intensity was inversely associate with triglycerides. No association with five other metabolic risk factors or a clustered metabolic risk index | 63 |
| Green et al.2014[34]USA | Women; age 29-30 yearsN=50  | Accelerometer150–2,689 counts min−1 | Insulin resistance, inflammation, and cardiovascular disease | Two-tailed Pearson product-moment correlationAge, weight, height, BMI, body fat | Correlation coefficientsWaist: −0.09Glucose 0.08SBP: 0.07DBP 0.13Triglycerides: −0.44Total cholesterol: −0.29\*HDL: −0.11LDL: −0.16LAP: −0.35HOMA-IR: −0.29Insulin: −0.23Hs-CRP: −0.15IL-6 : 0.12TNF-α: 0.18Adiponectin −0.20 | Light physical activitycorrelated with markers of cardiometabolichealth in young, adult women.  | 54 |
| Hamer et al.2014 [35]UK | Healthy men and women (mean age, 66 ± 6 yrs) N=445Whitehall II epidemiological cohort | GT3X-Accelerometer1.5-3METs  | Cardiometabolic risk markers - glycated hemoglobin, BMI, HDL-C and triglycerides | Linear regressionpartition models, isotemporal substitution modelsSmoking, statin use, civil service work grade | Β linear model coefficient for LIPA glycated hemoglobin: 0.001 (-0.007 to 0.009)BMI: -0.02 (-0.075 to 0.043)HDL-C: 0.006 (0.00 to 0.013)Triglycerside: -0.005 (-0.015 to 0.005) | LIPA favourably associate with HDL cholesterol | 54 |
| Hawkins et al.2013[36]USA | Participants aged 40 and older N=561NHANES | Actigraph accelerometer (Freedson cutpoints)LIPA: min/day | Framingham risk score  | Multiple logistic regression  | Single activity model:LIPA (normal ABI):-0.001 | LIPA not associate with FRS  | 50 |
| Hawkins et al.2012[37]USA | 3771 participants, 51% women N=3 771NHANES | Actigraph accelerometer (uniaxial)Total LIPA / day based on cut-points of Freedson | Chronic inflammation (CRP) | Multivariate linear regressionAge, smoking status, HDL, triglycerides, CVD, use of lipid-lowering medication and BMI | β=-0.0574 | Non-diabetic women: LIPA inversely associated with CRP. LIPA likely contributes to reducing inflammation in non-diabetic persons | 50 |
| Healy et al.2008[38]Australia | mean age= 53.4 (range= 30-87 yrs) N=169 AusDiab | Accelerometry, LIPA defined as between 100 and 1951 counts/minLIPA in % of monitoring time | Waist circumference (cm); triglycerides (log, mmol/l); HDL cholesterol (mmol/l); resting systolic blood pressure (mmHg); resting distolic blood pressure (mmHg); fasting plasma glucose (mmol/l); clustered metabolic risk score (based on a rincipal component analysis) | Multiple linear regression analysisAge, gender, employment status, alcohol intake, income, education, smoking, diet quality, family history of diabetes | Linear regression coefficients β for LIPAwaist circumference: -0.20triglycerides: -0.14HDL cholesterol: 0.11resting systolic blood pressure: -0.07resting diastolic blood pressure: -0.05fasting plasma glucose: -0.12clustered metabolic risk score: -0.20 | LIPA was sign related to waist circumference and clustered metabolic risk scoreLight activity time is significantly associate with reduced waist circumference and reduced clustered metabolic risk | 81 |
| Healy et al.2007[39]Australia | mean age= 53.4 (range= 30-87 yrs) N=173 AusDiab | Accelerometry, LIPA defined as between 100 and 1951 counts/minLIPA in % of monitoring time | 2h plasma glucose | Multiple linear regression analysisAge, gender, employment status, alcohol intake, income, education, smoking, diet quality, family history of diabetes | Linear association between LIPA and 2h plasma glucose(β = -0.22, -0.42 to -0.03, P = 0.023) | LIPA beneficially associated with reduced 2h plasma glucose independently of time spent in MVPA | 63 |
| Howard et al.2015[40]USA | Adults (47 ± 17yrs; 48% male) N=7 092 NHANES | Actigraph accelerometer (Freedson cutpoints)LIPA/day: low light PA & high light PA | Blood pressure, HDL cholesterol, CRP, triglycerides, plasma glucose, insulin | Linear regression modelsRace/ethnicity, education, marital status, family poverty income ratio, smoking status, total energy, saturated fat, alcohol intake, medical history, current medication use | Low LIPA:SBP: 1.01DBP: 0.56CRP: 0.95HDL: 1.01Triglycerides: 0.97LDL: 0.01Plasma glucose: 1.01Insulin: 0.95High LIPA:SBP: 1.00DBP: 0.40CRP: 0.90HDL: 1.01Triglycerides: 0.97LDL: 0.03Plasma glucose: 1.00Insulin: 0.91 | Increases in LIPA may have beneficial impacts on biomarkers of cardio metabolic health | 90 |
| Kim et al.2013[41]Japan  | Japanese adults; mean age = 47.9; 37.1% men; health middle-aged without diabetes, cardiovascular disease or musculoskeletal diseases living in Tsukuba City who underwent medical examinations.N=521 | Accelerometer1.6–2.9 metabolic equivalents (METs) | Metabolic syndrome | Logistic regression Age, BMI, sex, calorie intake, smoking status | Outcomes <11.1 METs-h/day (n = 161) 11.2–14.5 METs-h/day (n = 161) ≥14.6 METs-h/day (n = 161) P-value for trendMetS 1 (Reference) 0.51 (0.29 to 0.89)\* 0.44 (0.24 to 0.81)\* 0.012Abdominal obesity 1 (Reference) 0.46 (0.28 to 0.76)\* 0.50 (0.30 to 0.84)\* 0.005Hypertension 1 (Reference) 0.98 (0.61 to 1.58) 0.97 (0.59 to 1.60) 0.993Hyperglycemia 1 (Reference) 0.68 (0.38 to 1.23) 0.94 (0.51 to 1.72) 0.394Dyslipidemia 1 (Reference) 0.68 (0.39 to 1.17) 0.39 (0.20 to 0.74)\* 0.016 | Light-intensity lifestyle activity was significantly associated withthe risk of MetS, independently of MVPA | 54 |
| Lakka et al.2003 [42]Finland | Middle-aged men, mean age= 51.4 ± 5.8 (among those without metabolic syndrome) and 51.2 ± 5.9 (among those with metabolic syndrome) N=1 069 The Kuopio Ischemic Heart Disease Risk Factor Study (KIHD) | Self-reportvalidated KIHD 12-month LTPA-questionnaireLow-intensity leisure-time PA was defined as <4.5 METsLIPA in min/wk (categorized into tertiles, highest tertile= reference) | Metabolic syndrome (based on modified WHO-definition) | Logistic regression analysescorrelations between LIPA and all components of the metabolic syndrome were also reported age, smoking, alcohol intake, SES | 1st (lowest) tertile: 1.232nd tertile: 1.12 | No significant relationship between LIPA and metabolic syndrome | 54 |
| Loprinzi et al.2015 [43]USA | Both sexes aged 65 years or moreN=1496NHANES 2003-2006 | Actigraph accelerometer Unknown time in LIPA (total sample) | BMI, BP, WC, triceps and subscapular skinfolds, C-reactive protein, White blood cells, neutrophils, total cholesterol, LDL cholesterol, TG, glucose, insulin, insulin resistance, HbA1c | Mean differences. Poisson regression analysisLIPA and MVPA | Weighted mean statistical differences: associations with BMI, BP, WC, triceps skinfold, C-reactive protein, white blood cells, neutrophils, glucose, insulin, insulin resistance, HbA1c. Association with a multivariable poisson regression between less LIPA time (300 min/week) and one comorbidity index 1.18 (1.09-1.27) | LIPA was associate with more favourable BMI, systolic blood pressure, waist circumference,triceps skinfold, C-reactive protein, white blood cells, neutrophils, glucose,insulin, insulin resistance, and HbAlc, and had fewer chronic diseases | 77 |
| McGuire et al.2012[44]Canada | Inactive and overweight adultsN=126 | ActiGraph accelerometer (GT3X), 7 days, 1min epochs. LPS 100-1951 counts/min (Freedson). Non wear >=60min zero counts. Included if >=4 days (1 weekend), of >=10 hours wear time per day.Group mean time in LIPA 290.5 ± 94.5 min/day (30.4 ± 7.6%) | Body composition: visceral adipose tissue (VAT); subcutaneous adipose tssue (ASAT), total adipose tissue (TAAT), all measured by MRI, waist circumference | Logistic regression of association of LIPA duration and measures of adiposityAccelerometer wear time, age, sex, BMI, caloric intake | Unstandardised β (beta) values:VAT: -0.00ASAT: 0.00TAAT: 0.00Waist circumference: 0.04 | LIPA was not associated with any measures of adiposity | 82 |
| Qader et al..2008[45]Sweden | Middle-aged women, mean age= 56.9 ± 3.1 yrs N=6 913Women's Health in the Lund Area study (WHILA) | Self-reported PA during leisure was divided into low PA (defined as 2-4h/wk of light exercise such as walking and dancing) or more intensive activity (defined as regular physical exercise 1-2 h/week including vigorous training such as running and swimming).self-reported PA during work categorized into sedentary, light (mostly walking but not lifting heavily) and heavy | Metabolic syndrome (as defined by NCEP ATP 3) | Logistic regression analyses Age, hormonal status, education, alcohol intake, smoking, working status, number of children, food intake  | Leisure LIPA (low versus high): 1.83Work LIPA (light versus high): 0.71 |  | 55 |
| Robson et al.2015[46]USA | Adults aged over 20 yrs N=1 974NHANES 2003-2006 | AccelerometryLIPA defined as between 100 and 2019 counts/minuteBouted LIPA (bouts of at least 10 minutes)sporadic LIPABoth expressed in 30 min/day | Metaboli syndrome (based on the 2009 Joint Interim Societies definition) | Logistic regression analysesAge, sex, ethnicity, poverty–income ratio, alcohol, smoking, and the other physical activity variables with the exception of bouted MVPA for sporadic LIPA and with the exception of embedded MVPA for bouted LIPA | Sporadic LIPAMetabolic syndrome: 0.91high waist circumference: 0.88high triglycerides: 0.94Low LDL cholesterol: 0.99High blood pressure: 0.96High glucose: 0.99Bouted LIPAMetabolic syndrome: 0.96 high waist circumference: 0.96high triglycerides: 0.93Low LDL cholesterol: 0.98High blood pressure: 0.98High glucose: 0.97 | Bouted LIPA was sign negatively related to metabolic syndrome, high waist circumference and high triglycerides. No other significant relationships were observed | 54 |
| Rossen et al. 2017[47]USA | Participants diagnosed with prediabetes and type 2 diabetes (50% men, mean age = 63.8 ± 7.5 years)N=124Sophia Step Study | Actigraph accelerometer(LIPA defined as 100–1,951 cpm) | fasting blood samples of HbA1c, fasting plasma glucose, triglycerides, HDL cholesterol, LDL cholesterol and resting systolic and diastolic blood pressure, BMI, WC | Isotemporal substitution framework with linear regression modelsage, gender and education, health status, use of medication, having other diseases, dietary habits and sleep quality | SB replacing with LIPAWC: -0.21 (-1.47,1.05) regr coeffBMI: -0.12 (-0.060,0.37) regr coeffHDL:0.01 (-0.03 0.05) regr coeffHbA1c: 1.01 (0.99,1.03) rel rateFasting plasma glucose:1.02 (0.97,1.07) rel rate | Reallocating sedentary time in bouts to LPA was associated only with lower waist circumference | 82 |
| Ross et al.2011[48] Canada | Inactive and overweight adultsN=135 | ActiGraph accelerometer (GT3X), 7 days, 1min epochs. LPS 100-1951 counts/min (Freedson). Non wear >=60min zero counts. Included if >=4 days (1 weekend), of >=10 hours wear time per day.Group mean time spent in LIPA: 289.0 ± 91.7 min/day | Cardio-respiratory fitness (VO2 max, measures during a maximal treadmill test) | Logistic regression Gender, BMI, MVPA | Unstandardised β (beta) values0.06 | LIPA was not associated with cardiorespiratory fitness (after adjusted for time in MVPA) | 82 |
| Sakuta et al.2006[49]Japan | Middle-aged personnel of self-defense forcesN=974 | Subjectively (self-completion questionnaire & interview)LIPA= walking, cycling in flat place and golf (<3.0 METs) | Cholesterol, triglycerides, fasting plasma glucose, systolic blood pressure, hypercholesterolemia, hypertriglyceridemia,Type 2 diabetes, hypertension | Univariate and multivariate logistic regression analysisEthanol consumption, vegetable intake, daily number of cigarettes smoked and rank (officer/non-officer) | Β Regression coefficients:Total cholesterol: -0.038Triglyceride: 0.014Fasting plasma glucose: -0.069SBP: 0.048OR per increment in PA duration (1h/week):Hypercholesterolemia: 0.97Hypertriglyceridemia: 1.02Type 2 diabetes: 1.06Hypertension: 1.04 | LIPA not associate with CVD risk factors | 36 |
| Scheers et al.2013[50]Belgium | Adults, meang age= 41.7 ± 9.8 yrsN=442 | SenseWear Pro ArmbandLIPA defined as activities with a MET-level between 1.51 and 2.99. LIPA in h/day | Metabolic syndrome (based on the NCEP-ATP 3 guidelines)Abdominal obesity (based on waist circumference)hypertriglyceridemialow HDL-cholHypertensionHyperglycemia | Logistic regression analyses Gender, age, education, smoking, alcohol intake and MVPA | Metabolic syndrome: 0.88Abdominal obesity: 0.89hypertriglyceridemia: 0.85low HDL-chol: 1.12Hypertension: 0.93Hyperglycemia: 1.15 | LIPA was not significantly related to the health outcomes | 91 |
| Stamatakis et al.2012 [51]UK | Older adults, mean age= about 70 yearsN=649 2008 Health Survey for England | AccelerometryLIPA defined as between 100 and 2019 counts/minLIPA in 30 min/day | BMIWaist circumferenceCholesterol ratioHb1Ac | Linear regression analyses Age, gender, employment status, smoking, education, depression score (GHQ12), alcohol consumption, fruit and vegetable consumption, accelerometer wear time, cardiovascular medication (diabetes medication for Hb1Ac), and frequency of unhealthy foods consumption  | Β linear regression coefficients for LIPABMI: -0.277Waist circumference: -0.853Cholesterol ratio: -0.068Hb1Ac: -0.014 | LIPA significantly negatively related to BMI, waist circumference and cholesterol ratio | 82 |
| Talbot et al.2000[52]USA | Community dwelling volunteersN=11 116Baltimore Longitudinal Study of Aging | Subjectively, self-reported; leisure-time physical activitiesLeisure time physical activities, low LTPA = <4MET | Cardiorespiratory fitness | Univariate regression analysis | Men:β=0.002Women: β=0.039 | Low LIPAminimally correlate with peak VO2 | 95 |
| Yates et al.2015[53]UK | Participants with increased risk of impaired glucose regulation (IGR), mean age=65 years, 34% female N=508Walking Away from Type 2 Diabetes study | ActiGraph accelerometer (GT3X) LIPA/day, based on the cut-points of Freedson (≥25 to <488 counts/15s) | Insulin sensitivity | Isotemporal substitution regression modelsAge, sex, ethnicity, social deprivation, smoking status, beta-blocker & statin medication status, BMI | Isotemporal model reallocation of sedentary time to LIPA Fasting glucose: 1.00Fasting insulin: 0.992-h glucose: 0.972-h insulin: 0.96HOMA-IS: 1.01Matsuda-ISI: 1.04 | Reallocation of sedentary time into either LIPA or MVPA was associate with enhance insulin sensitivity in those with an increased risk of type 2 diabetes | 81 |

**Table S4: Characteristics of the prospective studies included in the review**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author****Year****Reference****Country** | **Population** **Sample size****Study name or data set name (if available)** | **Design** | **Measurement method of LIPA** **LIPA outcome** | **Health outcomes** | **Statistical analyses****Covariates included** | **Effect size**  | **Conclusion** | **Quality****Score (%)** |
| Beddhu et al.2015[54]USA | Individuals (20yrs or older), of which 383 with CKD N=3 626NHANES | Prospective mean follow-up of 2.86 years | Actigraph accelerometer (Freedson cutpoints) | Mortality | Cox regression analysesAge, gender, race, education, smoking, alcohol use, lung disease and mobility limitations | Sedentary -> low-intensity: HR = 1.01Sedentary -> light intensity: HR=0.67Low -> light intensity: HR=0.66 | Replacing sedentary activity with light-intensity activity might confer a survival benefit  | 86 |
| Dohrn et al.2017[55]Sweden | Individuals (35yrs or older, 44% men)N=851Sweden Attitute Behaviour and Change Study (ABC) | Longitudinal prospective cohort design with 15 years of follow-up | Actigraph accelerometer LIPA defined asbetween 100-2019 counts/min | mortality | Cox regression analysesAge, education, smoking status, history of chronic disease, MVPA | Adjusted for education smoking, health conditions and achieving MVPA guidelines HR (95% CI); p:All-cause mortality: Tertile 2: 0.46 (0.27,0.78); 0.004Tertile 3: 0.34 (0.17,0.67); 0.002CVD mortality:Tertile 2:0.48 (0.19,1.19); 0.116Tertile 3: n/aCancer mortality:Tertile 2: 0.33 (0.13,0.87); 0.024Tertile 3: 0.32 (0.11,0.92); 0.034 | Strong inverse relationship between MVPA and mortality and LIPA can give substantial survival benefits  | 77 |
| Ekelund et al.2009[56]UK | Participants with a family history of type 2 diabetes N=192ProActive UK trial | Longitudinal | Accelerometry, LIPA defined asbetween 101-1951 counts/min | HOMA-scoreFasting insuline(based on the hexokinase method) | Multiple linear regression analyses (with log transformed fasting insuline and HOMA-scores). 3 different analyses were performed:-longitudinal (baseline LIPA and follow-up insulin resistance)-changes in PA and changes in insulin resistance)Gender, age, smoking status and waist circumference. Longitudinal analyses were also adjusted for baseline phenotypes and follow-up time | LongitudinalHOMA-score: -0.001Fasting insuline: -0.001ChangesHOMA-score: not reportedFasting insuline: not reported | LIPA was not significantly related to the 2 measures of insulin resistance in the different analyses | 73 |
| Ensrud et al.2014[57]USA | Men aged >=65 (in 2000 - 2002) N=2 918Osteoporotic Fractures in men (mrOS) | Prospective cohort study.recruited 200-2002, LIPA measured 2007-2009, mean follow up 4.5 years (1.0)  | SenseWear Pro armband; 7-day measurement; 1min epochs; 24-h; classified using proprietary algorithm (Innerview Professional 5.1); ppt chars used in classification (age, height, weight, handedness, smoking status). LIPA (MET >1.51 – 2.99)Time min/24hours (4 categories <42.4, 42.4-63.9, 64.0-88.3, >=88.4Overall time spent in LIPS mean (SD) 67.7 (34.4) min/24 hours | Mortality(categorised as cardiovascular, cancer, other causes) | Cox’s proportional Hazard models. Highest LIPA duration as referenceAge, race, site, season, education, martial status, health status, smoking, comorbidity, depressive symptoms, cognitive function, number of instrumented activities of daily living, percent body fatMV+ model additionally adjusted for: PA (self-report, PASE questionnaire), gait speed, time spent asleep | All cause mortality , Multivariate model:respective to categorical HR1.701.421.061.00All mortality, MV+ model: respective to categorical HR1.571.401.061.00CVD cause mortality, multivariate model:respective to categorical HR1.731.921.291.00Cancer cause mortality, multivariate model:respective to categorical HR1.711.400.921.00 | Less time spent in LIPA was associate with an increased risk of mortality in older men  | 95 |
| Evenson et al.2016 [58]USA | Mean age (all >= 40 years) was 55.3 years; 54.6% werefemaleN=3 809National Health and Nutrition Examination Survey(NHANES) | Prospective  | Accelerometer and self-reported100–2,019CPM100–759CPM | All-cause mortality, CVD mortality | Multivariable Cox proportional hazards modelsAge, BMI, hypertension, Type 2 diabetes, cancer | LIPA (100-2,019CPM)= 332.9 (2.0)LIPA (100–759CPM)= 258.6 (1.3) | Accelerometer-assessed light-intensity activity was not associated with all-cause or CVD mortality in fully adjusted models | 73 |
| Fishman et al. 2016[59]USA | Adults aged 50-79N=3029NHANES | Data are from the 2003-2004 and 2005-2006 waves werelinked to death records from the National Death Index through December 31, 2011 | Actigraph accelerometer (LIPA defined as 100-2019 counts/min) | Mortality | Cox proportional hazards modelsIsotemporal substitution modelAge, sex, race/ethnicity, education, body mass index, and the presence of comorbid conditions | Tertile 2: 0.37 (0.20-0.69)Tertile 3: 0.47 (0.250.86); p=0.508 Replacing thirty minutes of sedentary time with light activity was associated with significant reduction in mortality risk (After 5 years of follow-up: HR = 0.80, 95% CI: 0.75, 0.85). | Greater total activity is associated with lower all-cause mortality risk. Replacing sedentary time with light activity or MVPA may reduce mortality risk for older adults | 86 |
| Hamer et al.2014[60]UK | Men and women aged ≥50 yearsN=10 426The English Longitudinal Study of Ageing | Longitudinal (7.8 yrs follow-up) | Self-reported frequency of participation in vigorous, moderate and mild activities | Mortality (all-cause, CVD, cancer, other) | Cox proportional hazards modelsAge, gender and marital status, SEP and time-varying chronic diseases, time-varying smoking, elevated depressivesymptoms, BMI, and waist circumference | Reference is physical inactivityAll-cause mortality:Mild PA: 0.76 (0.69, 0.83) CVD mortality:Mild PA: 0.74 (0.64, 0.85)Cancer mortality:Mild PA: 1.02 (0.85, 1.24)Other mortality:Mild PA: 0.67 (0.58, 0.78) | Older adults may also gain survival benefit from participation in lower-intensity activity that is below the threshold set by the present PA guidelines | 95 |
| Hu et al.2003 [61]Finland | Adults aged 35-64 yrsN=14 920  | Prospective(12 yrs follow-up)  | Self-reportquestion assessing occupational PA with 3 categories:light (very easy, sitting office work, reference category)moderate (work including standing and walking)active (work including walking and lifting, or heavy manual labour)"moderate" versus "light" occupational PA | Incident type 2 diabetes | Cox proportional hazards modelAge, study year, systolic blood pressure, smoking status,education, other two physical activity and BMI | Men: 0.67Women: 0.72Men and women combined: 0.70  | Occupational LIPA was significantly related to a lower risk for developing diabetes in the total sample, but not in men and women separately | 86 |
| Jefferis et al. 2018[62]UK | Men aged 71-92 yearsN=1655British Regional Heart Study | Prospective population-based cohort study (recruitment in 1978-1980, follow-up in 2010-2012) | Actigraph accelerometerLIPA defined as between 100-1040 counts/min (1.5-3 MET) | All-cause mortality | Cox proportional hazards modelsAccelerometer wear time, season of wear, social class, living alone, duration of sleep, smoking status, alcohol consumption, BMI, mobility disability, MVPA, LIPA and SB | Total LIPA: 0.86 (0.78-0.94) | In older men, all activities (of light intensity upwards) were beneficial and accumulation of activity in bouts ≥10 min did not appear important beyond total volume of activity. | 86 |
| Laaksonen et al.2002 [63]Finland | Middle-aged men, mean age= 50.9 ± 6.6 (among those not developing metababolic syndrome) and 52.7 ± 6.1 (among those developing metabolic syndrome) N=612 The Kuopio Ischemic Heart Disease Risk Factor Study (KIHD) | Prospective(4 yrs follow-up) | Self-reportvalidated KIHD 12-month LTPA-questionnaireLow-intensity leisure-time PA was defined as <4.5 METsLIPA in min/wk (categorized into tertiles, lowest tertile= reference) | Metabolic syndrome (based on modified WHO-definition and NCEP definition (as sensitivity analyses)) | Logistic regression analysesAge category, BMI, waist-to-hip ratio, use of antihypertensive medications, systolic and diastolic blood pressure, and concentrations of HDL, triglycerides insulin, glucose levels, and family history of diabetesNOT CLEAR whether all PA variabels were included simultaneously in the model | 2nd tertile: 0.97 3rd tertile: 0.66 | LIPA was not related to the development of metabolic syndrome | 54 |
| Lee et al, 2017[64]USA | Women (age 72.0 ± 5.7 years)N=16741Women’s Health Study | Follow-up of 2.3 years | Actigraph accelerometer (LIPA defined as 200-2689 counts per minute) | All-cause mortality | Proportional hazard regressionAge, accelerometer wear time, MVPA, smoking, alcohol, intakes of saturated fat, fiber, fruits and vegetables, hormone therapy, parental history of myocardial infarction, family history of cancer, general health, history of CVD, history of cancer, cancer screening | Q2: 0.97 (0.67-1.39)Q3: 0.79 (0.52-1.21)Q4: 1.06 (0.69-1.64; p=0.82) | This study provides support for the 2008 federal guideline recommendation of MVPA, but it does not support either increasing LPA or decreasing sedentary behavior for mortality risk reduction.  | 64 |
| Loprinzi et al.2016[65]USA | Adults and older adults N=5 575 NHANES (National Health and nutrition Examination) 2003-2006 | Prospective(6.6 yrs follow-up) | Actigraph accelerometer: 7164. 1min epochs; LIPA cut-points 100-2019 (Troiano). Included if >=4 days >=10h/dwear. Automatic non-wear exclusion (60min consecutive zero, allowance 1 to 2 min with counts)weighted mean 349.8 min/day | Mortality | Cox proportional hazardMVPA (continuous m/day, >=2020 counts), age, gender, race-ethnicity, cotinine, weight status, poverty-income ratio, C-reactive protein, comorbid illness (total number of arthritis, coronanry artery disease, congestive heart failure, heart attack, stroke, emphysema, chronic bronchitis, hypertension)) | For every 60-min increase in LIPA, HR.0.84 | Independent of MVPA and age (and other confounders), greater LIPA was associate with reduced all-cause mortality risk | 73 |
| Matthews et al.2016 [66]USA | Mean age = 56.8; mean BMI = 29.0 N=4 840National Health and Nutrition Examination Survey(NHANES) | Prospective | Accelerometer<3 METs | Mortality | Cox proportional hazard modelsAge, BMI, diabetes, coronary heart disease, stroke, cancer, mobility limitation, ethnicity, education, alcohol consumption | Single factor models: 0.50 (0.38, 0.65)2-factor model: 0.53 (0.40, 0.71); 2-factor model: 0.83 (0.74, 0.93); partition model: 0.84 (0.75, 0.95) | Health promotion efforts for physical activity havemostly focused on moderate-to-vigorous activity. However,findings derived from accelerometer-based measurements suggestthat increasing light-intensity activity and reducing sedentary timeare also important, particularly for inactive adults | 91 |
| Mekary et al.2009 [67]USA | Healthy, pre-menopausal women (nurses), mean age= about 35 years N=4 558The Nurses Health Study 2 | Prospective(6 yrs follow-up) | Self-reported easy walking (<2 miles/hour, in 30 min/day)Changes in easy walking | Weight change | Single activity modelspartition modelsisotemporal substitution modelsALL are linear regression modelsAge, baseline weight and height, alcohol intake, sugar-sweetened beverage intake, transfat intake, fiber intake, contraceptive use, smoking, parity, antidepressant use | *Single activity models*: β= -0.11*Partition models*: β= -0.54isotemporal substitution models: β= -1.02 (when 30min/day increase in TV watching is replaced by a 30min/day increase in slow walking) | LIPA does not significantly related to weight change in the single activity model, but significantly negatively related to weight change in the partition and isotemporal substitution model | 91 |
| Sabia et al.2012[68]UK | Men and women (55.9 ± 6.0 years) N=7 456Whitehall II study | Prospective(5 yrs follow-up)  | Questionnaire“mild PA” = less than 3 MET: hours per week | Mortality | Cox regressionAge, gender, marital status, socioeconomic status, employment grade, smoking status, alcohol consumption, frequency of fruit and vegetable consumption, coronary heart disease prevalence, stroke, diabetes, self-rated health | Model 4 (adjusted for all covariates):Mild PA:5.5-8.9hr.week: 0.85≥9hr/week: 0.93Walking:3.5-5.9h/week: 0.83≥6hr/week: 0.81 | LIPA not associate with mortality | 70 |
| Talbot et al.2007 [69]USA | Men and women aged 19-90+ years, generally high SES N=2 092Baltimore Longitudinal Study of Aging (BLSA) | Longitudinal(men 21.2 yrs follow-up; women: 10.2 yrs follow-up)  | Self-reportedpp reported amount of time spent in 97 leisure activities (incl housework) over the past 2 yrs.Intensity of leisure activities was derived based on compendium of Ainsworth et al and Jetté et al.LIPA was defined as activities of 4 METs or less.MET-min/day in LIPA were calculated.LIPA in MET-min/day (standardized)Rate of change in LIPA (standardized) | Deathcoronary heart disease mortality (only in men) | Cox proportional hazard modelsCholesterol, BMI, smoking and hypertension | All-cause mortalityMen < 70yrsLIPA: 0.96change in LIPA: 0.90Men > 70yrsLIPA: 0.95change in LIPA: 1.07Women < 70yrsLIPA: 0.75change in LIPA: 1.02Women > 70yrsLIPA: 0.85change in LIPA: 1.10CHD mortalityMen < 70yrsLIPA: 0.90change in LIPA: 0.83Men > 70yrsLIPA: 1.01change in LIPA: 1.17 | No significant relationships between LIPA and mortality were observed | 95 |
| Tanasescu et al.2002[70]USA | Men N=44 452Health Professionals’ Follow-up study | Prospective | Subjectively, questionnaireTime spent at each activity in hours per week was multiplied by its typical energy expenditure, expressed in METs / no difference between lower or higher than 3MET, walking was a separate categoryMET-h/wk | Coronary heart disease | Cox proportional hazard modelsAlcohol consumption, smoking, family history of myocardial infarction, nutrient intake, baseline diabetes, high cholesterol levels, hypertension | RR for coronary heart disease, model 1:Quintile 2: 1.00Quintile 3: 0.90Quintile 4: 1.02Quintile 5: 0.82 | Inverse relationship between walking and risk of CHD, only for the highest quintile of multivariate analysis | 77 |

**FUNNEL PLOTS**



Figure S1: Funnel plot for meta-analysis of acute mechanistic studies investigating postprandial glucose.



Figure S2: Funnel plot for acute mechanistic studies investigating postprandial insulin



Figure S3: Funnel plot for acute mechanistic studies investigating triglycerides



Figure S4: Funnel plot for prospective studies investigating risk of all-cause mortality

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