Evidence Portfolio – Exposure Subcommittee, Question 4[1]

What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?

Sources of Evidence: Original Research

Conclusion Statements and Grade:

Insufficient evidence is available to determine whether a relationship exists between step counts per day and all-cause and cardiovascular disease mortality. **PAGAC Grade: Not assignable.**

Limited evidence suggests that step count per day is associated with reduced incidence of cardiovascular disease events and risk of type 2 diabetes. **PAGAC Grade: Limited.**

Limited evidence suggests a dose-response relationship between the measure of steps per day and cardiovascular disease events and type 2 diabetes risk. **PAGAC Grade: Limited.**

Insufficient evidence is available to determine whether the relationship between the measure of steps per day and cardiovascular disease events and type 2 diabetes risk is influenced by age, sex, race/ethnicity, socioeconomic status, or weight status. **PAGAC Grade: Not assignable.**

Description of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports did not identify sufficient literature to answer the research question as determined by the Exposure Subcommittee. A complete de novo search of original research was conducted.

Original Research

Overview

A total of 9 original research studies that examined the relationship between step counts and different health outcomes were included as sources of evidence. Of these, 4 were prospective cohort studies,[1-4] 4 were cross-sectional studies,[5-8] and 1 was a randomized control trial.[9] The studies were published between 2011 and 2017.

The analytical sample size ranged from 68[9] to 7,118.[1] Of the studies that reported location, 1 was conducted in Brazil,[5] 1 in Canada,[6] 1 in the United Kingdom,[8] 1 in Finland,[9] and 1 in Australia.[2]

[1] Question 1 in Chapter 1. Physical Activity Behaviors: Steps, Bouts, And High Intensity Training

Exposure

All the included studies examined step counts per day. All studies used pedometers to measure steps, except for Herzig et al,[9] in which the authors used an accelerometer.

Outcomes

The majority of the studies examined cardiometabolic risk factors, including blood glucose levels, using measures such as fasting and 2-hour plasma glucose. One study examined metabolic syndrome[1] and 1 examined risk of having a cardiovascular event.[4] No study was found that examined the relationship between step counts per day and mortality (all-cause or disease-specific).

Populations Analyzed

The table below lists the populations analyzed in each article.

Table 1. Populations Analyzed by All Sources of Evidence

	Sex	Race/ Ethnicity	Age	Weight Status	Chronic Conditions	Other
Colpani, 2013	Female		Adults 45–72			Postmenopausal; Perimenopausal/ Premenopausal
Herzig, 2014		White	Mean age 58.8	Overweight and Obese		Impaired fasting glucose or glucose tolerance
Huffman, 2014			Adults ≥50		Existing cardiovascular disease (if ≥50) or with at least 1 additional cardiovascular risk factor (if ≥55)	Impaired glucose tolerance
Johnson, 2017			Adults ≥55			
Newton, 2013		Black or African American	Adults 37–81			
Ponsonby, 2011			Adults ≥25			
Yates, 2015			Adults ≥50		Existing cardiovascular disease (if ≥50) or with at least 1 additional cardiovascular risk factor (if ≥55)	Impaired glucose tolerance
Yates, 2014			Adults ≥50		Existing cardiovascular disease (if ≥50) or with at least 1 additional cardiovascular risk factor (if ≥55)	Impaired glucose tolerance
Yates, 2013		White European, South Asian	Mean age 64			High risk of impaired glucose regulation

Supporting Evidence

Original Research

Table 2. Original Research Individual Evidence Summary Tables

<table>
<tr><td colspan="2">Original Research
Citation: Colpani V, Oppermann K, Spritzer PM. Association between habitual physical activity and lower cardiovascular risk in premenopausal, perimenopausal, and postmenopausal women: a population-based study. Menopause. 2013;20(5):525-531. doi:10.1097/GME.0b013e318271b388.</td></tr>
<tr><td colspan="2">Purpose: To measure pedometer-determined habitual PA in a Brazilian cohort of premenopausal, perimenopausal, and postmenopausal women and to assess its effect on anthropometric measures and cardiovascular disease risk factors.</td></tr>
<tr><td>Study Design: Cross-sectional study</td><td rowspan="6">Abstract:
OBJECTIVE: Menopause is associated with an increased risk of cardiovascular disease. Habitual physical activity, defined as any form of body movement with energy expenditure above resting levels, may improve health parameters. We assessed the level of habitual physical activity and its effect on anthropometric measures and cardiovascular risk factors in a cohort of premenopausal, perimenopausal, and postmenopausal women. METHODS: This cross-sectional study is nested on a longitudinal population-based study that was begun in 1995 in the city of Passo Fundo, Brazil. For the present analysis, 292 women were included. Anthropometric and metabolic profile was evaluated. Habitual physical activity was assessed by a digital pedometer for 7 days, and participants were stratified into active and inactive (>/=6,000 and <6,000 steps/day, respectively). RESULTS: The mean (SD) age was 57.1 (5.4) years. The average number of steps per day for the total sample was 5,250.7 (3,372.9): 3,472.4 (1,570.2) in the inactive group (61.8%) and 9,055.9 (3,033.4) in the active group (31.9%). A negative and statistically significant correlation was found between physical activity and smoking (P = -0.019), body mass index (P = -0.006), waist circumference (P = -0.013), and waist-to-hip ratio of 0.85 or higher (P = -0.043). Inactive women presented a higher risk of overweight/obesity (odds ratio [OR], 2.1; 95% CI, 1.233-3.622; P = 0.006) and waist circumference larger than 88 cm (OR, 1.7; 95% CI, 1.054-2.942; P = 0.03), even after adjustment for age, menopause status, smoking, and hormone therapy. Inactive women also had a higher risk of diabetes mellitus (OR, 2.7; 95% CI, 1.233-6.295; P = 0.014) and metabolic syndrome (OR, 2.5, 95% CI, 1.443-4.294; P = 0.001). CONCLUSIONS: Habitual physical activity, specifically walking 6,000 or more steps daily, was associated with a decreased risk of cardiovascular disease and diabetes in middle-aged women, independently of menopause status.</td></tr>
<tr><td>Location: Brazil</td></tr>
<tr><td>Sample: 292
Attrition Rate: 18.43%
Sample Power: Not Reported</td></tr>
<tr><td>Intervention: No</td></tr>
<tr><td>Exposure Measurement
Self-Reported:
Device-Measured: Pedometer: habitual physical activity (steps/day) measured for 7 days and averaged. Participants were classified as physically inactive (maximum of 5,999 steps/day) or active (≥6,000 steps/day).
Measures Steps: Yes
Measures Bouts: No
Examines HIIT: No</td></tr>
</table>

Refers to Other Materials: Yes **Examine Cardiorespiratory Fitness as Outcome:** No	**Outcomes Examined:** Cardiovascular disease risk factors: Body weight and height (BMI), waist circumference, hip circumference, waist-to-hip ratio, total cholesterol, high density lipoprotein cholesterol, triglycerides, glucose, low-density lipoprotein cholesterol, dichotomous hypertension. Diabetes: self-report, use of anti-diabetic drugs, or a fasting blood glucose level of 126 mg/dL or higher.
Populations Analyzed: Female; Adults 45–72; Postmenopausal, Perimenopausal/Premenopausal.	**Author-Stated Funding Source:** Conselho Nacional de Desenvolvimento Científico e Tecnologico.

Original Research	
Citation: Herzig KH, Ahola R, Leppäluoto J, Jokelainen J, Jämsä T, Keinänen-Kiukaanniemi S. Light physical activity determined by a motion sensor decreases insulin resistance, improves lipid homeostasis and reduces visceral fat in high-risk subjects: PreDiabEx study RCT. *Int J Obes (Lond).* 2014;38(8):1089-1096. doi:10.1038/ijo.2013.224.	
Purpose: To investigate the effects of a 3-month structured aerobic walking exercise on fasting and 2-hour glucose and insulin concentrations and lipid homeostasis in sedentary overweight subjects with impaired fasting glucose and/or impaired glucose tolerance.	
Study Design: Randomized trial **Location:** Finland **Sample:** 68 **Attrition Rate:** 12.82% **Sample Power:** Yes **Intervention:** Yes **Intervention Type:** Provision of information/education, behavioral **Intervention Length:** 12 weeks **Exposure Measurement** **Self-Reported:** Leisure-time PA assessed by questionnaire and converted in metabolic equivalent hours per week using reported intensity and duration. **Device-Measured:** Accelerometer: mean total number of steps per day and number of steps at different acceleration; classes were used to describe PA during the 12-week trial. Daily steps were further classified into quartiles (I: 1,780–2,810, II: 2,940–4,010, III: 4,010–6,020, IV: 6,520–21,000). **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No **Exposure/Intervention** **Frequency:** 3 times per week **Intensity:** Low intensity (walking speed of 3–4 kilometers/hour) **Time:** 60 minutes (2 intervals of 20 minute walking with a 5-minute stretching/balance break in between; after 1.5 months, 45 minutes of continuous walking. **Type:** Cardiorespiratory: walking; balance and flexibility: break and cool down	**Abstract:** OBJECTIVE: To examine physical activity (PA) thresholds affecting glucose, insulin and lipid concentrations and body fat composition in high-risk patients for type 2 diabetes (T2D). INTERVENTION: A total of 113 subjects of both genders having abnormal glucose levels in the oral glucose tolerance test were contacted. A total of 78 subjects with age 58.8±10.4 years and body mass index 31.7±5.3 kgm_2 were randomly assigned to intervention and control groups. Intervention consisted of a supervised walking (60 min three times weekly) for 3 months. All the subjects received standard care for PA and weight reduction and wore an accelerometer during the whole wakeful time. RESULTS: Over 80% of the daily steps clustered at an acceleration level of 0.3–0.7 g (2–3 km h_1 of walking) and were 5870 in the intervention and 4434 in the control group (Po0.029). Between 0 and 3 months no significant changes were observed in fasting and 2-h glucose, body weight or maximal oxygen uptake. In contrast, changes in fasting and 2-h insulin (_3.4mUl_1, P¼0.035 and _26.6, P¼0.003, respectively), homeostasis model assessment-estimated insulin resistance (_1.0, P¼0.036), total cholesterol (_0.55 mmol l_1, P¼0.041), low-density lipoprotein (LDL) cholesterol (_0.36 mmol l_1, P¼0.008) and visceral fat area (_5.5 cm2, P¼0.030) were significantly greater in the intervention than in control subjects. The overall effects of PA were analyzed by quartiles of daily steps of all subjects. There were significant reductions in total and LDL cholesterol and visceral fat area between the highest (daily steps over 6520) and the lowest quartile (1780–2810 daily steps). The changes associated with PA remained significant after adjustments of baseline, sex, age and body weight change. CONCLUSION: Habitual and structured PAs with the acceleration levels of 0.3–0.7 g and daily steps over 6520, equivalent to walking at 2–3 km h_1 for 90 min daily, standing for the relative PA intensity of 30–35% of the maximal oxygen uptake, are clinically beneficial for overweight/obese and physically inactive individuals with a high risk for T2D.

Refers to Other Materials: Yes **Adverse Events Addressed:** No **Examine Cardiorespiratory Fitness as Outcome:** Yes	**Outcomes Examined:** Fasting and 2-hour glucose and insulin: compare baseline and after 3-month intervention.
Populations Analyzed: White; Mean age 58.8; Overweight and obese; Impaired fasting glucose or glucose tolerance.	**Author-Stated Funding Source:** Finnish Diabetes Foundation, Pohjois-Pohjanmaa Hospital District, and Oulu University Hospital.

Original Research **Citation:** Huffman KM, Sun JL, Thomas L, et al. Impact of baseline physical activity and diet behavior on metabolic syndrome in a pharmaceutical trial: results from NAVIGATOR. *Metabolism*. 2014;63(4):554-561. doi:10.1016/j.metabol.2014.01.002.	
Purpose: To assess the association between PA (pedometer steps) at baseline and metabolic syndrome.	
Study Design: Prospective cohort study **Location:** Not Reported **Sample:** 7,118 **Attrition Rate:** 23.51% **Sample Power:** Not Reported **Intervention:** No **Exposure Measurement** **Self-Reported:** Pedometer, daily steps. **Device-Measured:** Pedometer, daily steps; subsequently median daily steps categorized into quartiles. **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No **Refers to Other Materials:** Yes **Examine Cardiorespiratory Fitness as Outcome:** No **Populations Analyzed:** Adults ≥50; Impaired glucose tolerance and existing cardiovascular disease (if ≥50) or with at least 1 additional cardiovascular risk factor (if ≥55).	**Abstract:** OBJECTIVE: The cardiometabolic risk cluster metabolic syndrome (MS) includes >/=3 of elevated fasting glucose, hypertension, elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-c), and increased waist circumference. Each can be affected by physical activity and diet. Our objective was to determine whether determine whether baseline physical activity and/or diet behavior impact MS in the course of a large pharmaceutical trial. MATERIALS/METHODS: This was an observational study from NAVIGATOR, a double-blind, randomized (nateglinide, valsartan, both, or placebo), controlled trial between 2002 and 2004. We studied data from persons (n=9306) with impaired glucose tolerance and cardiovascular disease (CVD) or CVD risk factors; 7118 with pedometer data were included in this analysis. Physical activity was assessed with 7-day pedometer records; diet behavior was self-reported on a 6-item survey. An MS score (MSSc) was calculated using the sum of each MS component, centered around the Adult Treatment Panel III threshold, and standardized according to sample standard deviation. Excepting HDL-c, assessed at baseline and year 3, MS components were assessed yearly. Follow-up averaged 6 years. RESULTS: For every 2000-step increase in average daily steps, there was an associated reduction in average MSSc of 0.29 (95% CI (-)0.33 to (-)0.25). For each diet behavior endorsed, there was an associated reduction in average MSSc of 0.05 (95% CI (-)0.08 to (-)0.01). Accounting for the effects of pedometer steps and diet behavior together had minimal impact on parameter estimates with no significant interaction. Relations were independent of age, sex, race, region, smoking, family history of diabetes, and use of nateglinide, valsartan, aspirin, antihypertensive, and lipid-lowering agent. CONCLUSIONS: Baseline physical activity and diet behavior were associated independently with reductions in MSSc such that increased attention to these lifestyle elements provides cardiometabolic benefits. Thus, given the potential to impact outcomes, assessment of physical activity and diet should be performed in pharmacologic trials targeting cardiometabolic risk.

	Outcomes Examined: Metabolic syndrome score: calculated as the sum of each continuous component (fasting glucose, triglycerides, high-density lipoprotein cholesterol, mean arterial pressure [(systolic blood pressure +2 x diastolic blood pressure)/3], and waist circumference), which was centered around the sex-specific sample standard deviation.
	Author-Stated Funding Source: Novartis Pharmaceuticals.

Original Research **Citation:** Johnson ST, Eurich DT, Lytvyak E, et al. Walking and type 2 diabetes risk using CANRISK scores among older adults. *Appl Physiol Nutr Metab.* 2017;42(1):33-38. doi:10.1139/apnm-2016-0267.	
Purpose: To determine whether objective estimates of ambulatory activity (i.e., pedometer steps) were associated with diabetes risk, while accounting for demographic, health, and neighborhood walkability variables.	
Study Design: Cross-sectional study	**Abstract:** The objective of this study was to determine the association between pedometer-assessed steps and type 2 diabetes risk using the Public Health Agency of Canada-developed 16-item Canadian Diabetes Risk Questionnaire (CANRISK) among a large population-based sample of older adults across Alberta, Canada. To achieve our study objective, adults without type 2 diabetes (N = 689) aged 55 years and older provided demographic data and CANRISK scores through computer-assisted telephone interviews between September and November 2012. Respondents also wore a step pedometer over 3 consecutive days to estimate average daily steps. Logistic regression was used to assess the association between achieving 7500 steps/day and risk of diabetes (low vs. moderate and high). Overall, 41% were male, average age was 63.4 (SD 5.5) years, body mass index was 26.7 (SD 5.0) kg/m2, and participants averaged 5671 (SD 3529) steps/day. All respondents indicated they were capable of walking for at least 10 min unassisted. CANRISK scores ranged from 13-60, with 18% in the low-risk category (<21). After adjustment, those not achieving 7500 steps/day (n = 507) were more than twice as likely to belong to the higher risk categories for type 2 diabetes compared with those walking >/=7500 steps/day (n = 182) (73.6% vs. 26.4%; odds ratio: 2.37; 95% confidence interval: 1.58 - 3.57). Among older adults without diabetes, daily steps were strongly and inversely associated with diabetes risk using the CANRISK score. Walking remains an important modifiable risk factor target for type 2 diabetes and achieving at least 7500 steps/day may be a reasonable target for older adults.
Location: Canada	
Sample: 689 **Attrition Rate:** 46.04% **Sample Power:** Not Reported	
Intervention: No	
Exposure Measurement **Self-Reported:** **Device-Measured:** Pedometer: number of steps for each of 3 consecutive days, recorded by participant, to be averaged into daily step counts (7,500 steps/day was considered “sufficiently active” while less than 7,500 steps/day was “insufficiently active”). Dose-response also assessed using tertiles of step counts (≤3,719; 3,720–6,811; and ≥6,812). **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No	
Refers to Other Materials: Yes **Examine Cardiorespiratory Fitness as Outcome:** No	**Outcomes Examined:** Type II diabetes risk: Canadian Diabetes Risk Questionnaire.
Populations Analyzed: Adults ≥55	**Author-Stated Funding Source:** Alberta Innovates – Health Solutions.

Original Research

Citation: Newton RL Jr, Han H, Johnson WD, et al. Steps/day and metabolic syndrome in African American adults: the Jackson Heart Study. *Prev Med.* 2013;57(6):855-859. doi:10.1016/j.ypmed.2013.09.018.

Purpose: To assess the relationship between pedometer-measured step count data and metabolic syndrome in a large sample of African American adults.

Study Design: Cross-sectional study

Location: Not Reported

Sample: 379
Attrition Rate: 21.20%
Sample Power: Not Reported

Intervention: No

Exposure Measurement
Self-Reported: Step log, participants recorded daily steps at the end of each day.
Device-Measured: Pedometer: daily steps for 3 consecutive days. Steps/day was categorized into tertiles (tertile 1 was <3,717 steps/day, tertile 2 was 3,717–6,238 steps/day, and tertile 3 was >6,238 steps/day) and categories ("basal activity" was <2,500 steps/day, "limited activity" was 2,500–4,999 steps/day, "low active" was 5,000–7,499 steps/day, and "somewhat active" to "highly active" was ≥7,500 steps/day).
Measures Steps: Yes
Measures Bouts: No
Examines HIIT: No

Abstract:
OBJECTIVE: To examine the relationship between pedometer-measured step count data and the Metabolic Syndrome (MetS) in African American adults. METHOD: 379 African American adults (mean age 60.1 years; 60% female) enrolled in the Jackson Heart Study (Jackson, MS) from 2000 to 2004 provided sufficient pedometer data for inclusion in this analysis. MetS was classified according to the International Diabetes Federation Task Force on Epidemiology and Prevention. RESULTS: Using steps/day categorized as tertiles (<3717 (referent), 3717-6238, >6238), participants taking 3717-6238 (Odds Ratio (OR)(95% Confidence Interval (CI))=0.34 (0.19, 0.61)) and >6238 steps/day (OR(95% CI)=0.43 (0.23, 0.78)) had lower odds of having MetS compared to participants in the lowest tertile. Using previously suggested steps/day cut-points (<2500 (referent), 2500-4999, 5000-7499, >/=7500), the odds of having MetS were lower for participants taking 2500-4999 (OR(95% CI)=0.32 (0.14, 0.72)), 5000-7499 (OR(95% CI)=0.22 (0.09, 0.53)), and >7500 (OR(95% CI)=0.26 (0.11, 0.65)) steps/day compared to those taking <2500 steps/day. CONCLUSION: Compared to lower levels, higher levels of steps/day are associated with a lower prevalence of MetS in this older African American population.

Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No

Outcomes Examined: Metabolic syndrome (MetS): any 3 of the following 5 criteria were required to meet MetS definition: (1) large waist circumference (≥102 cm for men and ≥88 cm for women); (2) high triglyceride levels (≥150 mg/dL or on drug treatment); (3) low high-density lipoprotein cholesterol levels (≤40 mg/dL for men and ≤50 mg/dL in women or on drug treatment); (4) elevated blood pressure (≥130 mm Hg systolic or ≥ 85 mm Hg diastolic or on drug treatment); or, (5) elevated fasting glucose (≥100 mg/dL or on drug treatment).

Populations Analyzed: Black or African American; Adults 37–81

Author-Stated Funding Source: National Heart, Lung, and Blood Institute; National Institute on Minority Health and Health Disparities; National Institute on Biomedical Imaging and Bioengineering.

<table>
<tr><td colspan="2">Original Research
Citation: Ponsonby AL, Sun C, Ukoumunne OC, et al. Objectively measured physical activity and the subsequent risk of incident dysglycemia: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). Diabetes Care. 2011;34(7):1497-1502. doi:10.2337/dc10-2386.</td></tr>
<tr><td colspan="2">Purpose: To investigate pedometer-measured PA in 2000 and change in PA over 5 years with subsequent risk of dysglycemia by 2005.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="6">Abstract:
OBJECTIVE: To investigate pedometer-measured physical activity (PA) in 2000 and change in PA over 5 years with subsequent risk of dysglycemia by 2005. RESEARCH DESIGN AND METHODS: This prospective cohort study in Tasmania, Australia, analyzed 458 adults with normal glucose tolerance and a mean (SD) age of 49.7 (12.1) years in 2000. Variables assessed in 2000 and 2005 included PA, by pedometer and questionnaire, nutrient intake, and other lifestyle factors. Incident dysglycemia was defined as the development of impaired fasting glucose or impaired glucose tolerance revealed by oral glucose tolerance testing in 2005, without type 2 diabetes. RESULTS: Incident dysglycemia developed in 26 participants during the 5-year period. Higher daily steps in 2000 were independently associated with a lower 5-year risk of incident dysglycemia (adjusted odds ratio [AOR] 0.87 [95% CI 0.77-0.97] per 1,000-step increment). Higher daily steps in 2005, after controlling for baseline steps in 2000 (thus reflecting change in steps over 5 years), were not associated with incident dysglycemia (AOR 1.02 [0.92-1.14]). Higher daily steps in 2000 were also associated with lower fasting blood glucose, but not 2-h plasma glucose by 2005. Further adjustment for BMI or waist circumference did not remove these associations. CONCLUSIONS: Among community-dwelling adults, a higher rate of daily steps is associated with a reduced risk of incident dysglycemia. This effect appears to be not fully mediated through reduced adiposity.</td></tr>
<tr><td>Location: Australia</td></tr>
<tr><td>Sample: 458
Attrition Rate: 0
Sample Power: Not Reported</td></tr>
<tr><td>Intervention: No</td></tr>
<tr><td>Exposure Measurement
Self-Reported: Active Australia Questionnaire, frequency and duration of PA in the previous week. A weighted sum of the responses (with vigorous-intensity activity given double-weighting) was calculated to quantify total hours of PA.
Device-Measured: Pedometer: steps/day were measured for 2 consecutive days at baseline and 5 years later and averaged. Daily steps were classified into 5 categories: persistent low steps (the lowest third tertile of daily steps in both 2000 and 2005), decreasing steps (dropped by 1 or 2 categories between 2000 and 2005), persistent moderate steps (middle third at both waves), increasing steps (increase of 1 or 2 categories), and persistent high steps (highest third at both waves).
Measures Steps: Yes
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Incident dysglycemia: fasting plasma glucose and 2-hour plasma glucose levels were measured after a 5-year follow-up.</td></tr>
<tr><td>Populations Analyzed: Adults ≥25</td><td>Author-Stated Funding Source: Pharmaceutical companies, laboratories, Australian Kidney Foundation, Diabetes Australia, Queensland Health, South Australian, Tasmanian and Victorian Department of Human Services, and Health Department of Western Australia.</td></tr>
</table>

<table>
<tr><td colspan="2">Original Research
Citation: Yates T, Davies MJ, Haffner SM, et al. Physical activity as a determinant of fasting and 2-h post-challenge glucose: a prospective cohort analysis of the NAVIGATOR trial. Diabet Med. 2015;32(8):1090-1096. doi:10.1111/dme.12762.</td></tr>
<tr><td colspan="2">Purpose: To investigate whether previous PA levels are associated with blood glucose levels in individuals with impaired glucose tolerance in the context of an international pharmaceutical trial.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="5">Abstract:
AIM: To investigate whether previous physical activity levels are associated with blood glucose levels in individuals with impaired glucose tolerance in the context of an international pharmaceutical trial. METHODS: Data were analyzed from the NAVIGATOR trial, which involved 9306 individuals with impaired glucose tolerance and high cardiovascular risk from 40 different countries, recruited in the period 2002-2004. Fasting glucose, 2-h post-challenge glucose and physical activity (pedometer) were assessed annually. A longitudinal regression analysis was used to determine whether physical activity levels 2 years (t-2) and 1 year (t-1) previously were associated with levels of glucose, after adjusting for previous glucose levels and other patient characteristics. Those participants with four consecutive annual measures of glucose and two consecutive measures of physical activity were included in the analysis. RESULTS: The analysis included 3964 individuals. Change in physical activity from t-2 to t-1 and activity levels at t-2 were both associated with 2-h glucose levels after adjustment for previous glucose levels and baseline characteristics; however, the associations were weak: a 100% increase in physical activity was associated with a 0.9% reduction in 2-h glucose levels. In addition, previous physical activity only explained an additional 0.05% of the variance in 2-h glucose over the variance explained by the history of 2-h glucose alone (R^2 = 0.3473 vs. 0.3468). There was no association with fasting glucose. CONCLUSIONS: In the context of a large international clinical trial, previous physical activity levels did not meaningfully influence glucose levels in those with a high risk of chronic disease, after taking into account participants' previous trajectory of glucose control.</td></tr>
<tr><td>Location: Not Reported</td></tr>
<tr><td>Sample: 3964
Attrition Rate: 57.40%
Sample Power: Not Reported</td></tr>
<tr><td>Intervention: Yes
Intervention Type: Provision of information/education, behavioral
Intervention Length: 12 months</td></tr>
<tr><td>Exposure Measurement
Self-Reported:
Device-Measured: Pedometer, daily step count was recorded by participants in a log book. Pedometers were worn for 7 consecutive days. Habitual PA levels were measured as the average number of steps taken per day (total summed pedometer counts divided by the number of days that data were captured).
Measures Steps: Yes
Measures Bouts: No
Examines HIIT: No
Exposure/Intervention
Frequency: Personnel within each site administered the program at each clinic visit (at 0.5, 1, 3, 6, and 12 months).
Intensity: Not Specified
Time: Lifestyle intervention designed to help increase PA to 150 minutes/week.
Type: Cardiorespiratory. The NAVIGATOR study intervention included educational material and reinforcement calls. No additional description in the present manuscript.</td></tr>
<tr><td>Refers to Other Materials: Yes
Adverse Events Addressed: No</td><td>Outcomes Examined: Fasting glucose levels; 2-hour glucose levels.</td></tr>
</table>

Examine Cardiorespiratory Fitness as Outcome: No	
Populations Analyzed: Adults ≥50, Individuals with impaired glucose tolerance and either existing cardiovascular disease (if ≥50) or with at least 1 additional cardiovascular risk factor (if ≥55).	**Author-Stated Funding Source:** Novartis Pharmaceuticals.

Original Research **Citation:** Yates T, Haffner SM, Schulte PJ, et al. Association between change in daily ambulatory activity and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis. *Lancet*. 2014;383(9922):1059-1066. doi:10.1016/S0140-6736(13)62061-9.	
Purpose: To investigate whether baseline and change in objectively assessed ambulatory activity is associated with the risk of a cardiovascular event in individuals at high cardiovascular risk with impaired glucose tolerance.	
Study Design: Prospective cohort study	**Abstract:** Background The extent to which change in physical activity can modify the risk of cardiovascular disease in individuals at high cardiovascular risk is uncertain. We investigated whether baseline and change in objectively-assessed ambulatory activity is associated with the risk of a cardiovascular event in individuals at high cardiovascular risk with impaired glucose tolerance. Methods We assessed prospective data from the NAVIGATOR trial involving 9306 individuals with impaired glucose tolerance who were recruited in 40 countries between January, 2002, and January, 2004. Participants also either had existing cardiovascular disease (if age >50 years) or at least one additional cardiovascular risk factor (if age =55 years). Participants were followed-up for cardiovascular events (defi ned as cardiovascular mortality, non-fatal stroke, or myocardial infarction) for 6 years on average and had ambulatory activity assessed by pedometer at baseline and 12 months. Adjusted Cox proportional hazard models quantifi ed the association of baseline and change in ambulatory activity (from baseline to 12 months) with the risk of a subsequent cardiovascular event, after adjustment for each other and potential confounding variables. This study is registered with ClinicalTrials.gov NCT00097786. Findings During 45 211 person-years follow-up, 531 cardiovascular events occurred. Baseline ambulatory activity (hazard ratio [HR] per 2000 steps per day 0.90, 95% CI 0.84-0.96) and change in ambulatory activity (0.92, 0.86-0.99) were inversely associated with the risk of a cardiovascular event. Results for change in ambulatory activity were unaff ected when also adjusted for changes in body-mass index and other potential confounding variables at 12 months. Interpretation In individuals at high cardiovascular risk with impaired glucose tolerance, both baseline levels of daily ambulatory activity and change in ambulatory activity display a graded inverse association with the subsequent risk of a cardiovascular event. Funding Novartis Pharmaceuticals.
Location: Not Reported	
Sample: 4,345 **Attrition Rate:** 46% **Sample Power:** Not Reported	
Intervention: Yes **Intervention Type:** Provision of information/education, behavioral **Intervention Length:** 12 months	
Exposure Measurement **Device-Measured:** Pedometer, habitual ambulatory activity (steps/day) was assessed. Change in ambulatory activity (calculated by subtracting pedometer counts at 12 months from those at baseline). Results reported by category of change (more than 1,500 step per day decrease, 0–1,500 step per day decrease, 1–1,500 step per day increase, or more than 1,500 step per day increase) from baseline to 12 months. **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No **Exposure/Intervention Frequency:** Program administered at each clinic visit (at 0.5, 1, 3, 6, and 12 months). **Intensity:** Not Specified **Time:** Lifestyle intervention designed to help increase PA to 150 minutes/week. **Type:** The NAVIGATOR study intervention included educational material and reinforcement calls. No additional description in the present manuscript.	
Refers to Other Materials: Yes **Adverse Events Addressed:** No **Examine Cardiorespiratory Fitness as Outcome:** No description in the present manuscript.	

Populations Analyzed: Adults ≥ 50, Individuals with impaired glucose tolerance and either existing cardiovascular disease (if ≥50) or with at least 1 additional cardiovascular risk factor (if ≥55).	**Outcomes Examined:** Risk of a cardiovascular event: a single cardiovascular composite of time to death from cardiovascular causes or non-fatal myocardial infarction or non-fatal stroke.
	Author-Stated Funding Source: Novartis Pharmaceuticals.

Original Research **Citation:** Yates T, Henson J, Khunti K, et al. Effect of physical activity measurement type on the association between walking activity and glucose regulation in a high-risk population recruited from primary care. *Int J Epidemiol*. 2013;42(2):533-540. doi:10.1093/ije/dyt015.	
Purpose: To establish, through a multi-ethnic cohort recruited from primary care, whether the strength of the association of walking activity with glucose regulation varies across 2 of the most widely used self-reported and objective measures: the International Physical Activity Questionnaire and the pedometer.	
Study Design: Cross-sectional study	**Abstract:** BACKGROUND: We investigate associations of self-reported and objectively assessed walking activity with measures of glucose regulation in a multi-ethnic population at high risk of type 2 diabetes. METHODS: This study reports data from a 2009-2011 screening programme for impaired glucose regulation (IGR) within a high-risk primary care population in Leicestershire, UK; 2532 participants (38% women, 8% South Asian) with a mean age of 64 +/- 8 years and an average BMI of 32.1 +/- 5.6 kg/m(2) were included. Walking activity was measured by self-report (International Physical Activity Questionnaire) and objectively (pedometer). Glucose regulation assessments included 2h post-challenge glucose, fasting glucose and HbA1c. RESULTS: Higher levels of self-reported walking activity and pedometer steps were associated with lower 2h post-challenge glucose after controlling for several known confounding variables, including BMI. Similarly, when categorized in tertiles, both measures were associated with a lower odds of having any form of IGR; odds ratio for lowest vs highest tertile was 0.64 (0.51-0.80) for self-report and 0.69 (0.55-0.87) for pedometer steps. There was no significant difference between self-reported and objective measures in the strength of associations with glucose regulation; associations with self-report were maintained when further adjusted for pedometer steps. Stronger associations between self-reported walking activity and glucose regulation were observed in South Asians compared with White Europeans. CONCLUSIONS: Self-reported and objectively measured walking activity were equally associated with indices of glucose regulation. Associations with self-reported walking activity were maintained when further adjusted for pedometer steps, suggesting that self-reported walking activity may measure facets of physical activity that are beyond total volume.
Location: United Kingdom	
Sample: 2,532 **Attrition Rate:** 26.60% **Sample Power:** Not Reported	
Intervention: No	
Exposure Measurement **Self-Reported:** IPAQ, total moderate-to-vigorous intensity physical activity (MVPA) and walking activity (metabolic equivalent hours/week). Low, moderate, and high tertiles of walking and steps/day created for analysis. **Device-Measured:** Pedometer: ambulatory activity measured over 7 consecutive days, averaged, and reported as steps/day. Further placed into low, moderate, and high tertiles. **Measures Steps:** Yes **Measures Bouts:** No **Examines HIIT:** No	

Refers to Other Materials: Yes **Examine Cardiorespiratory Fitness as Outcome:** No	**Outcomes Examined:** Oral glucose tolerance test: diagnosis of diabetes; impaired fasting glucose; impaired glucose tolerance; impaired glucose regulation; HbA1c.
Populations Analyzed: White European, South Asian; Mean age 64; High risk of impaired glucose regulation.	**Author-Stated Funding Source:** National Institute for Health Research.

Table 3. Original Research Bias Assessment Chart

Nutrition Evidence Library (NEL) Bias Assessment Tool (BAT): Original Research					
	Colpani, 2013	Herzig, 2014	Huffman, 2014	Johnson, 2017	Newton, 2013
(???) = Can't Determine					
Inclusion/exclusion criteria similar across study groups.	Yes	N/A	Yes	Yes	Yes
Strategy for recruiting or allocating participants similar across study groups.	Yes	N/A	Yes	Yes	Yes
Allocation sequence randomly generated.	N/A	Yes	N/A	N/A	N/A
Group allocation concealed (i.e., assignments could not be predicted).	N/A	Yes	N/A	N/A	N/A
Distribution of critical confounding factors similar across study groups at baseline, or analysis controlled for differences between groups.	Yes	Yes	Yes	Yes	Yes
Accounted for variations in execution of study from proposed protocol or research plan.	N/A	N/A	N/A	N/A	N/A
Adherence to study protocols similar across study groups.	Yes	Yes	Yes	Yes	Yes
Investigators accounted for unintended concurrent exposures that were differentially experienced by study groups and might bias results.	Yes	Yes	Yes	Yes	No
Participants blinded to their intervention or exposure status.	N/A	No	N/A	N/A	N/A
Investigators blinded to participants intervention or exposure status.	N/A	No	N/A	N/A	N/A
Outcome assessors blinded to participants intervention or exposure status.	Yes	Yes	Yes	Yes	Yes
Valid and reliable measures used consistently across study groups to assess inclusion/exclusion criteria, exposures, outcomes, and confounders.	Yes	Yes	Yes	Yes	Yes
Length of follow-up similar across study groups.	N/A	Yes	Yes	N/A	Yes
In cases of high or differential loss to follow-up, impact assessed through sensitivity analysis or other adjustment.	N/A	N/A	Yes	No	Yes
Other sources of bias taken into account in design and/or analysis of study through matching or other statistical adjustment.	Yes	Yes	Yes	Yes	Yes
Adequate statistical methods used to assess primary outcomes.	Yes	Yes	Yes	Yes	Yes

Nutrition Evidence Library (NEL) Bias Assessment Tool (BAT): Original Research				
	Ponsonby, 2011	Yates, 2015	Yates, 2014	Yates, 2013
(???) = Can't Determine				
Inclusion/exclusion criteria similar across study groups.	N/A	N/A	Yes	Yes
Strategy for recruiting or allocating participants similar across study groups.	N/A	N/A	Yes	Yes
Allocation sequence randomly generated.	N/A	N/A	N/A	N/A
Group allocation concealed (i.e., assignments could not be predicted).	N/A	N/A	N/A	N/A
Distribution of critical confounding factors similar across study groups at baseline, or analysis controlled for differences between groups.	N/A	N/A	Yes	Yes
Accounted for variations in execution of study from proposed protocol or research plan.	Yes	Yes	Yes	N/A
Adherence to study protocols similar across study groups.	N/A	N/A	Yes	Yes
Investigators accounted for unintended concurrent exposures that were differentially experienced by study groups and might bias results.	Yes	Yes	Yes	Yes
Participants blinded to their intervention or exposure status.	N/A	N/A	N/A	N/A
Investigators blinded to participants' intervention or exposure status.	N/A	N/A	N/A	N/A
Outcome assessors blinded to participants' intervention or exposure status.	Yes	Yes	Yes	Yes
Valid and reliable measures used consistently across study groups to assess inclusion/exclusion criteria, exposures, outcomes, and confounders.	No	Yes	Yes	Yes
Length of follow-up similar across study groups.	Yes	N/A	Yes	N/A
In cases of high or differential loss to follow-up, impact assessed through sensitivity analysis or other adjustment.	N/A	Yes	N/A	No
Other sources of bias taken into account in design and/or analysis of study through matching or other statistical adjustment.	Yes	Yes	Yes	Yes
Adequate statistical methods used to assess primary outcomes.	Yes	Yes	Yes	Yes

Appendices

Appendix A: Analytical Framework

Topic Area
Exposure

Systematic Review Question

What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, weight status, or socio-economic status?

Population
Adults, 18 years and older

Exposure
- PA performed in **step counts** per day assessed with a device.

Comparison
- Different step counts per day

Endpoint Health Outcomes
- All-cause and cardiovascular disease (CVD) mortality
- CVD incidence
- Type 2 diabetes incidence

Key Definitions

Scope of CVD incidence:
- Coronary heart disease/ischemic heart disease
- Coronary artery disease
- Stroke
- Heart failure

Exclusion:
- Congenital heart disease

Appendix B: Final Search Strategy

Search Strategy: PubMed (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: PubMed; Date of Search: 5/4/2017; 233 results

Set	Search Strategy
Physical activity	(("Activity bouts"[tiab] OR "Daily steps"[tiab] OR "High intensity activity"[tiab] OR "Interval training"[tiab] OR "Pedometer"[tiab] OR "Step count"[tiab] OR "Steps/day"[tiab] OR 'high intensity interval training'[tiab]) OR ((("High intensity"[tiab] AND "training")[tiab] OR 'Interval training'[tiab] OR 'Pedometer'[tiab]) NOT medline[sb])
Limit: Publication Type Include (Systematic Reviews/Meta-Analyses)	AND (systematic[sb] OR meta-analysis[pt] OR review [tiab] OR “systematic review”[tiab] OR “systematic literature review”[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "pooled analysis"[tiab] OR “pooled analyses”[tiab] OR "pooled data"[tiab])
Limit: Publication Type Exclude (Systematic Reviews/Meta-Analyses)	NOT (“comment”[Publication Type] OR “editorial”[Publication Type])
Limit: language	AND (English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Exclude child only	NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) AND "adult"[Mesh]))

Search Strategy: CINAHL (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: CINAHL; Date of Search: 5/4/2017; 16 results
Terms searched in title or abstract

Set	Search Strategy
Physical activity	("Activity bouts" OR "Daily steps" OR "High intensity activity" OR "Interval training" OR Pedometer OR "Step count" OR "Steps/day" OR 'high intensity interval training" OR ("High intensity" AND "training"))
Systematic Reviews and Meta-Analyses	AND (“systematic review” OR “systematic literature review” OR review OR metaanalysis OR "meta analysis" OR metanalyses OR "meta analyses"" OR "pooled analysis" OR “pooled analyses” OR "pooled data")
Limits	English language Peer reviewed Exclude Medline records Human All years searched

Search Strategy: Cochrane (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: Cochrane; Date of Search: 5/4/17; 25 results
Terms searched in title, abstract, or keywords

Set	Search Terms
Physical activity	("Activity bouts" OR "Daily steps" OR "High intensity activity" OR "Interval training" OR Pedometer OR "Step count" OR "Steps/day" OR "high intensity interval training" OR ("High intensity" AND training))
Limits	Word variations not searched Cochrane Reviews and Other Reviews All years searched

Search Strategy: PubMed (Original Research)

Database: PubMed; Date of Search: 6/28/2017; 454 results

Set	Search Strategy
Steps	(("Walking"[mh] OR "Pedometer"[tiab] OR "Step count"[tiab] OR "Steps/day"[tiab] OR "Daily steps"[tiab]) OR (("Walking"[tiab]) NOT medline[sb]))
(Cardiovascular disease OR Type 2 diabetes)	AND (("Arteriosclerosis"[mh] OR "Heart failure"[mh] OR "Myocardial ischemia"[mh] OR "myocardial infarction"[mh] OR "Stroke"[mh] OR "Subarachnoid hemorrhage"[mh] OR "Intracranial hemorrhages"[mh] OR "insulin resistance"[mh] OR "Blood glucose"[mh] OR "insulin resistance"[tiab] OR Hyperglycemia[mh] OR "Diabetes Mellitus, Type 2"[mh]) OR ((Arterioscliero*[tiab] OR Atheroscleró*[tiab] OR "Cerebral infarction"[tiab] OR "Cerebrovascular diseases"[tiab] OR "Cerebrovascular disease"[tiab] OR "Coronary heart disease"[tiab] OR "Heart failure"[tiab] OR "Intracerebral Hemorrhage"[tiab] OR "Intracerebral Hemorrhages"[tiab] OR "Intracranial hemorrhage"[tiab] OR "Intracranial hemorrhages"[tiab] OR "myocardial infarction"[tiab] OR "Stroke"[tiab] OR "Subarachnoid hemorrhages"[tiab] OR "Subarachnoid hemorrhage"[tiab] OR "Ischemic heart diseases"[tiab] OR "Ischemic heart disease"[tiab]) NOT medline[sb]))
Incidence OR Mortality	AND ("risk"[tiab] OR "risks"[tiab] OR "Incidence"[tiab] OR "incident"[tiab] OR "Death"[mh] OR "Death"[tiab] OR "Dying"[tiab] OR Fatal*[tiab] OR Mortalit*[tiab] OR "Mortality"[mh] OR "Postmortem"[tiab])
Limit: Publication Type Exclude (Original)	NOT (“comment”[Publication Type] OR “editorial”[Publication Type] OR “review”[Publication Type] OR systematic[sb] OR "meta-analysis"[publication type] OR “systematic review”[tiab] OR “systematic literature review”[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "pooled analysis"[tiab] OR “pooled analyses”[tiab] OR "pooled data"[tiab])
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Date	(“2011/01/01”[PDAT] : “3000/12/31”[PDAT])
Limit: Exclude child only	NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) NOT (("infant"[Mesh] OR "child"[mesh] OR "adolescent"[mh]) AND "adult"[Mesh]))

Search Strategy: CINAHL (Original Research)

Database: CINAHL; Date of Search: 6/28/2017; 26 results
Terms searched in title or abstract

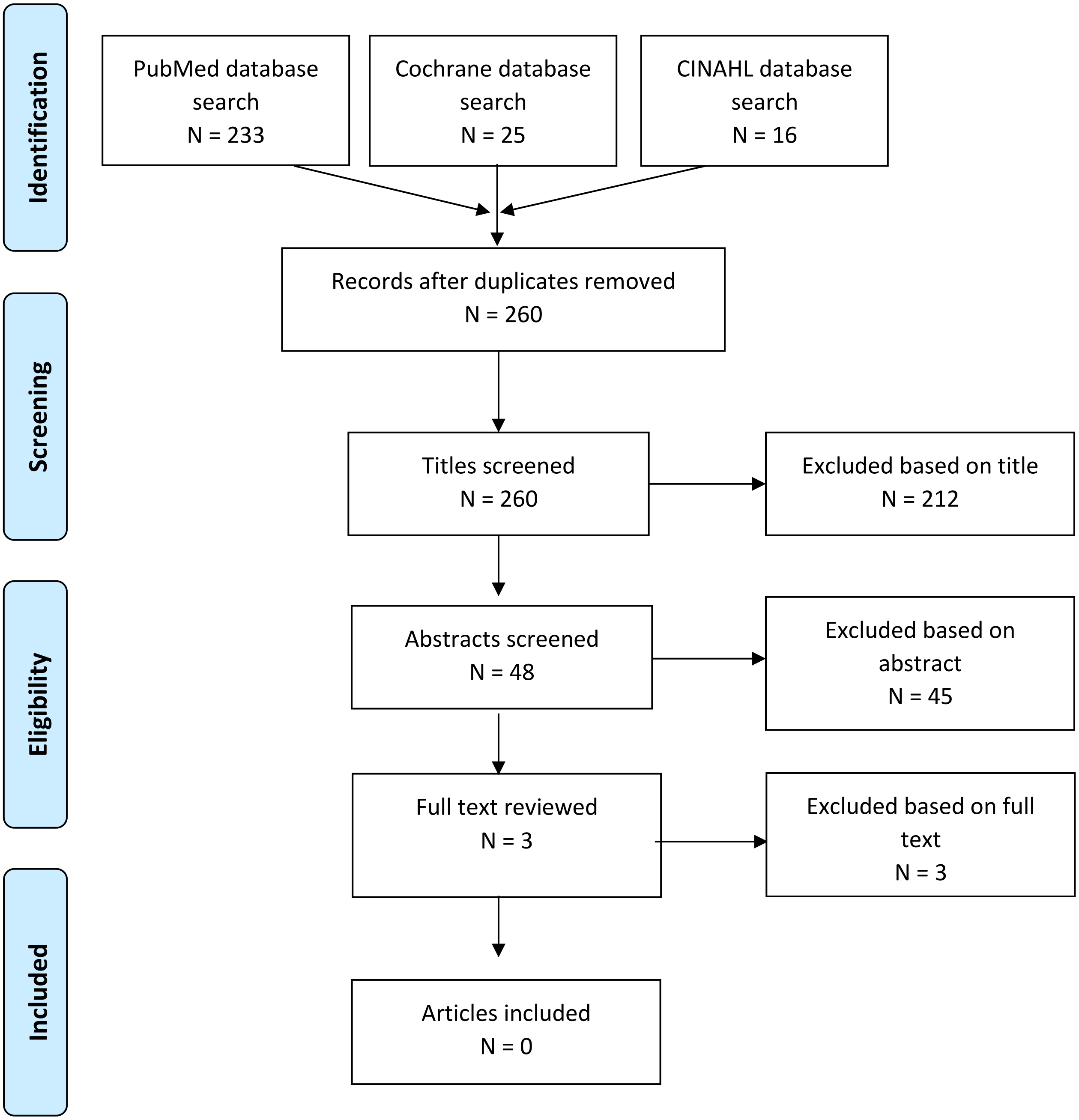
Set	Search Strategy
Steps	("Pedometer" OR "Step count" OR "Steps/day" OR "Daily steps" OR "Walking")
(Cardiovascular disease OR Type 2 Diabetes)	AND (Arterioscleró* OR "Arteriosclerosis" OR Atherosclero* OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "Myocardial ischemia" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhage" OR "Subarachnoid hemorrhages" OR "Ischemic heart diseases" OR "Ischemic heart disease" OR "insulin resistance" OR "Blood glucose" OR Hyperglycemia OR "Diabetes Mellitus, Type 2")
Incidence OR Mortality	AND ("risk" OR "risks" OR "Incidence" OR "incident" OR "Death" OR "Dying" OR Fatal* OR Mortalit* OR "Mortality" OR "Postmortem")
Original Research	NOT (“systematic review” OR “systematic literature review” OR metaanalysis OR "meta analysis" OR metanalyses OR "meta analyses"" OR "pooled analysis" OR “pooled analyses” OR "pooled data")
Limits	English language Peer reviewed Exclude Medline records Human 2011-present

Search Strategy: Cochrane (Original Research)
Database: Cochrane; Date of Search: 6/28/17; 286 results
Terms searched in title, abstract, or keywords

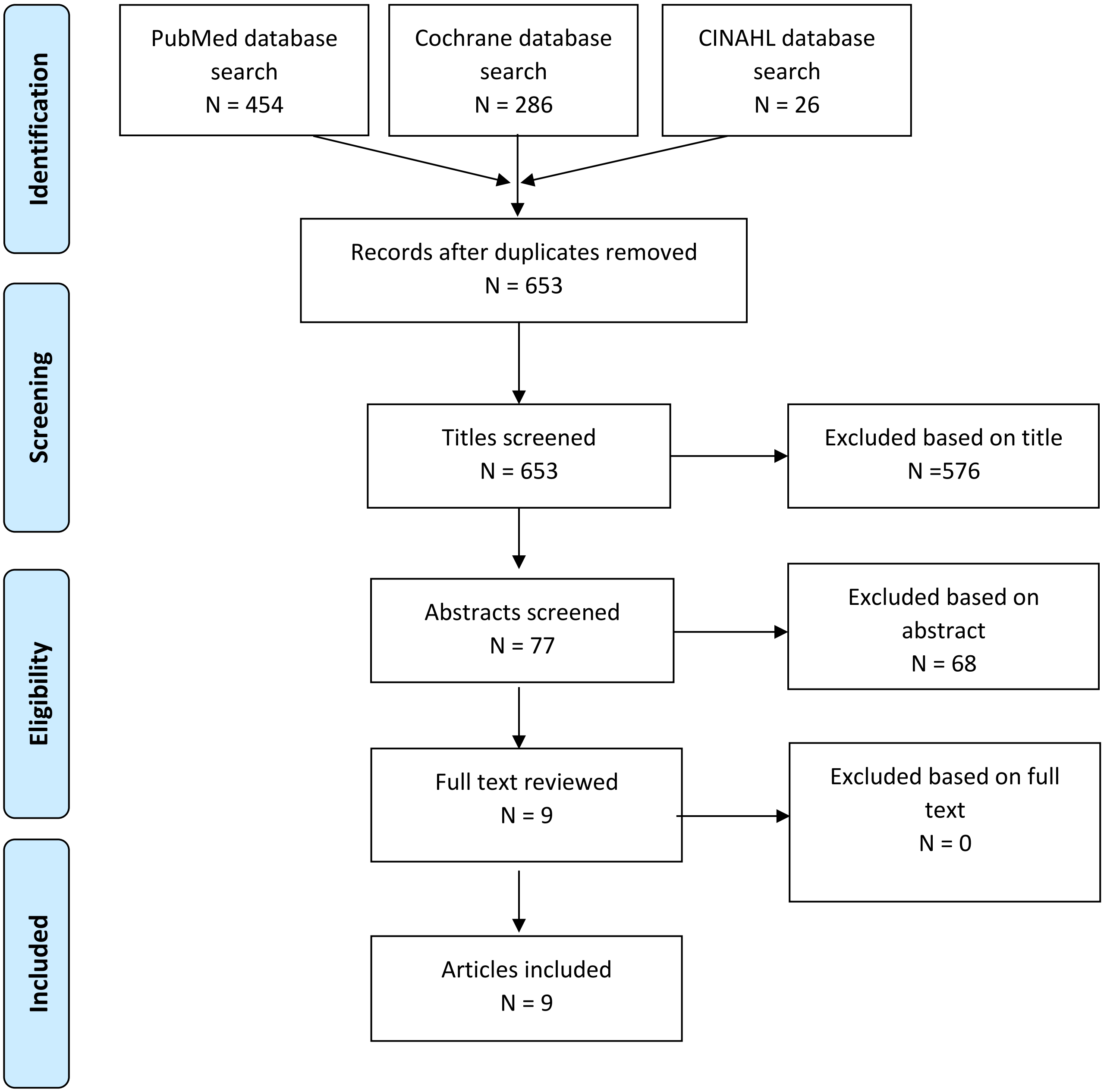
Set	Search Terms
Steps	("Pedometer" OR "Step count" OR "Steps/day" OR "Daily steps" OR "Walking")
(Cardiovascular disease OR Type 2 diabetes)	AND (Arterioscler* OR "Arteriosclerosis" OR Atheroscler* OR "Cerebral infarction" OR "Cerebrovascular diseases" OR "Cerebrovascular disease" OR "Coronary heart disease" OR "Heart failure" OR "Intracerebral Hemorrhage" OR "Intracerebral Hemorrhages" OR "Intracranial hemorrhage" OR "Intracranial hemorrhages" OR "Myocardial ischemia" OR "myocardial infarction" OR "Stroke" OR "Subarachnoid hemorrhage" OR "Subarachnoid hemorrhages" OR "Ischemic heart diseases" OR "Ischemic heart disease" OR "insulin resistance" OR "Blood glucose" OR Hyperglycemia OR "Diabetes Mellitus, Type 2")
Risk OR Mortality	AND ("risk" OR "risks" OR "Incidence" OR "incident" OR "Death" OR "Dying" OR Fatal* OR Mortalit* OR "Mortality" OR "Postmortem")
Limits	Trials Word variations will not be searched 2011-present

Appendix C: Literature Tree

Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports Literature Tree



Original Research Literature Tree



Appendix D: Inclusion/Exclusion Criteria

Exposure Subcommittee

What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?

b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?

Category	Inclusion/Exclusion Criteria	Notes/Rationale
Publication Language	**Include:** • Studies published with full text in English	
Publication Status	**Include:** • Studies published in peer-reviewed journals • Reports determined to have appropriate suitability and quality by PAGAC **Exclude:** • Grey literature, including unpublished data, manuscripts, abstracts, conference proceedings	
Research Type	**Include:** • Original research • Meta-analyses • Systematic reviews • Reports determined to have appropriate suitability and quality by PAGAC	
Study Subjects	**Include:** • Human subjects	
Age of Study Subjects	**Include:** • 18 years of age and above	
Health Status of Study Subjects	**Include:** • Only studies conducted in general population. **Exclude:** • Studies on patients with existing cardiovascular disease. • Studies on high performance athletes.	
Comparison	**Include studies in which the comparison is:** • Adults exposed to different doses of step counts.	
Date of Publication	**Include:** • 2011–present	
Study Design/Type of research	**Include:** • Original research articles ○ Cross-sectional studies ○ Longitudinal/cohort ○ Intervention studies	

	Exclude: • Systematic reviews • Meta-analyses • Report • Pooled analysis • literature reviews • Commentaries	
Size of Study Groups	**Include:** • All	
Intervention/ Exposure	**Include:** • Studies that qualify steps per day as an exposure (no other measure of walking should be included). **Exclude:** • Exposure measured by a single measure of physical fitness (cardiovascular fitness, strength, flexibility, walking speed in older adults) • Studies of a specific therapeutic exercise (range of motion exercise, inspiratory muscle training)	
Outcome	**Include studies in which the outcome is:** • All-cause and cardiovascular disease (CVD) mortality • CVD incidence • Type 2 diabetes incidence **Exclude:** • Congenital heart disease • Studies on progression of CVD.	
Multiple Publications of Same Data	**Include:** More than 1 article per dataset. **Exclude:** No restriction.	

Appendix E: Rationale for Exclusion at Abstract or Full-Text Triage for Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Albright C, Thompson DL. The effectiveness of walking in preventing cardiovascular disease in women: a review of the current literature. *J Womens Health (Larchmt).* 2006;15(3):271-280. doi:10.1089/jwh.2006.15.271.				X		
Azuma K, Matsumoto H. Potential universal application of high-intensity interval training from athletes and sports lovers to patients. *Keio J Med*. 2017;66(2):19-24. doi:10.2302/kjm.2016-0006-IR.			X	X		
Bacon AP, Carter RE, Ogle EA, Joyner MJ. VO_2max trainability and high intensity interval training in humans: a meta-analysis. *PLoS One*. 2013;8(9):e73182. doi:10.1371/journal.pone.0073182.	X					
Baker G, Gray SR, Wright A, et al. The effect of a pedometer-based community walking intervention "Walking for Wellbeing in the West" on physical activity levels and health outcomes: a 12-week randomized controlled trial. *Int J Behav Nutr Phys Act*. Sept 2008:44. doi:10.1186/1479-5868-5-44.			X			
Barr-Anderson DJ, AuYoung M, Whitt-Glover MC, Glenn BA, Yancey AK. Integration of short bouts of physical activity into organizational routine: a systematic review of the literature. *Am J Prev Med*. 2011;40(1):76-93. doi:10.1016/j.amepre.2010.09.033.				X		
Batacan RB Jr, Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. *Br J Sports Med*. 2017;51(6):494-503. doi:10.1136/bjsports-2015-095841.				X		
Bohannon RW. Number of pedometer-assessed steps taken per day by adults: a descriptive meta-analysis. *Phys Ther*. 2007;87(12):1642-1650. doi:10.2522/ptj.20060037.	X			X		
Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA.* 2007;298(19):2296-2304. doi:10.1001/jama.298.19.2296.				X		
Buchheit M, Laursen PB. High-intensity interval training, solutions to the programming puzzle. Part II: anaerobic energy, neuromuscular load and practical applications.			X			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Sports Med. 2013;43(10):927-954. doi:10.1007/s40279-013-0066-5.						
Buchheit M, Laursen PB. High-intensity interval training, solutions to the programming puzzle: Part I: cardiopulmonary emphasis. *Sports Med*. 2013;43(5):313-338. doi:10.1007/s40279-013-0029-x.			X			
Cassidy S, Thoma C, Houghton D, Trenell MI. High-intensity interval training: a review of its impact on glucose control and cardiometabolic health. *Diabetologia.* 2017;60(1):7-23. doi:10.1007/s00125-016-4106-1.			X			
Choi BC, Pak AW, Choi JC, Choi EC. Daily step goal of 10,000 steps: a literature review. *Clin Invest Med*. 2007;30(3):E146-E151.			X			
Eliakim A, Nemet D. Interval training and the GH-IGF-I axis—a new look into an old training regimen. *J Pediatr Endocrinol Metab*. 2012;25(9-10):815-821. doi:10.1515/jpem-2012-0209.			X			
Fleg JL. Salutary effects of high-intensity interval training in persons with elevated cardiovascular risk. *F1000 Research*. Sept 2016:F1000 Faculty Rev-2254. doi:10.12688/f1000research.8778.1.			X			
Freese EC, Gist NH, Cureton KJ. Effect of prior exercise on postprandial lipemia: an updated quantitative review. *J Appl Physiol (1985).* 2014;116(1):67-75. doi:10.1152/japplphysiol.00623.2013.				X		
Garcia-Hermoso A, Cerrillo-Urbina AJ, Herrera-Valenzuela T, Cristi-Montero C, Saavedra JM, Martínez-Vizcaíno V. Is high-intensity interval training more effective on improving cardiometabolic risk and aerobic capacity than other forms of exercise in overweight and obese youth? A meta-analysis. *Obes Rev.* 2016;17(6):531-540. doi:10.1111/obr.12395.		X				
Gibala MJ, Little JP, Macdonald MJ, Hawley JA. Physiological adaptations to low-volume, high-intensity interval training in health and disease. *J Physiol*. 2012;590(5):1077-1084. doi:10.1113/jphysiol.2011.224725.			X			
Gist NH, Fedewa MV, Dishman RK, Cureton KJ. Sprint interval training effects on aerobic capacity: a systematic review and meta-analysis. *Sports Med*. 2014;44(2):269-279. doi:10.1007/s40279-013-0115-0.	X					
Hoffmann JJ Jr, Reed JP, Leiting K, Chiang CY, Stone MH. Repeated sprints, high-intensity interval training, small-sided games: theory and application to field sports. *Int J Sports Physiol Perform*. 2014;9(2):352-357. doi:10.1123/ijspp.2013-0189.		X	X			

Exposure Subcommittee: Q4. What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Hussain SR, Macaluso A, Pearson SJ. High-intensity interval training versus moderate-intensity continuous training in the prevention/management of cardiovascular disease. *Cardiol Rev*. 2016;24(6):273-281. doi:10.1097/CRD.0000000000000124.			X			
Hwang CL, Wu YT, Chou CH. Effect of aerobic interval training on exercise capacity and metabolic risk factors in people with cardiometabolic disorders: a meta-analysis. *J Cardiopulm Rehabil Prev*. 2011;31(6):378-385. doi:10.1097/HCR.0b013e31822f16cb.		X				
Jelleyman C, Yates T, O'Donovan G, et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. *Obes Rev*. 2015;16(11):942-961. doi:10.1111/obr.12317.				X		
Kang M, Marshall SJ, Barreira TV, Lee JO. Effect of pedometer-based physical activity interventions: a meta-analysis. *Res Q Exerc Sport*. 2009;80(3):648-655. doi:10.1080/02701367.2009.10599604.				X		
Karlsen T, Aamot IL, Haykowsky M, Rognmo Ø. High intensity interval training for maximizing health outcomes. *Prog Cardiovasc Dis*. 2017;60(1):67-77. doi:10.1016/j.pcad.2017.03.006.			X			
Kessler HS, Sisson SB, Short KR. The potential for high-intensity interval training to reduce cardiometabolic disease risk. *Sports Med*. 2012;42(6):489-509. doi:10.2165/11630910-000000000-00000.				X		
Kolmos M, Krawcyk RS, Kruuse C. Effect of high-intensity training on endothelial function in patients with cardiovascular and cerebrovascular disease: a systematic review. *SAGE Open Med*. Dec 2016:2050312116682253. doi:10.1177/2050312116682253.		X				
MacInnis MJ, Gibala MJ. Physiological adaptations to interval training and the role of exercise intensity. *J Physiol.* 2017;595(9):2915-2930. doi:10.1113/JP273196.			X			
Meyer J, Morrison J, Zuniga J. The benefits and risks of CrossFit: a systematic review. *Workplace Health Saf*. March 2017:2165079916685568. doi:2165079916685568.	X					
Milanovic Z, Sporis G, Weston M. Effectiveness of high-intensity interval training (HIT) and continuous endurance training for VO2max improvements: a systematic review and meta-analysis of controlled trials*. Sports Med*. 2015;45(10):1469-1481. doi:10.1007/s40279-015-0365-0.	X					

Exposure Subcommittee: Q4. What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Murtagh EM, Murphy MH, Boone-Heinonen J. Walking: the first steps in cardiovascular disease prevention. *Curr Opin Cardiol*. 2010;25(5):490-496. doi:10.1097/HCO.0b013e32833ce972.			X	X		
Oliveros MJ, Gaete-Mahn MC, Lanas F, Martinez-Zapata MJ, Seron P. Interval training exercise for hypertension. *Cochrane Database Syst Rev*. Jan 2017:CD012511. doi:10.1002/14651858.CD012511.			X			
Ramos JS, Dalleck LC, Tjonna AE, Beetham KS, Coombes JS. The impact of high-intensity interval training versus moderate-intensity continuous training on vascular function: a systematic review and meta-analysis. *Sports Med*. 2015;45(5):679-692. doi:10.1007/s40279-015-0321-z.		X				
Regnaux JP, Lefevre-Colau MM, Trinquart L, et al. High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. *Cochrane Database Syst Rev*. 2015;(10):CD010203. doi:10.1002/14651858.CD010203.		X				
Shiraev T, Barclay G. Evidence based exercise— clinical benefits of high intensity interval training. *Aust Fam Physician*. 2012;41(12):960-962.		X	X			
Sloth M, Sloth D, Overgaard K, Dalgas U. Effects of sprint interval training on VO2max and aerobic exercise performance: a systematic review and meta-analysis. *Scand J Med Sci Sports*. 2013;23(6):e341-e352. doi:10.1111/sms.12092.					X	
Soares FH, de Sousa MB. Different types of physical activity on inflammatory biomarkers in women with or without metabolic disorders: a systematic review. *Women Health*. 2013;53(3):298-316. doi:10.1080/03630242.2013.782940.	X					
Tudor-Locke C, Bassett DR Jr. How many steps/day are enough? Preliminary pedometer indices for public health. *Sports Med*. 2004;34(1):1-8.			X			
Tudor-Locke C, Craig CL, Aoyagi Y, et al. How many steps/day are enough? For older adults and special populations. *Int J Behav Nutr Phys Act*. July 2011:80. doi:10.1186/1479-5868-8-80.				X		
Tudor-Locke C, Craig CL, Beets MW, et al. How many steps/day are enough? For children and adolescents. *Int J Behav Nutr Phys Act.* July 2011:78. doi:10.1186/1479-5868-8-78.		X		X		
Tudor-Locke C, Craig CL, Brown WJ, et al. How many steps/day are enough? For adults. *Int J*				X	X	

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Behav Nutr Phys Act. July 2011:79. doi:10.1186/1479-5868-8-79.						
Tudor-Locke C, Craig CL, Thyfault JP, Spence JC. A step-defined sedentary lifestyle index: <5000 steps/day. *Appl Physiol Nutr Metab*. 2013;38(2):100-114. doi:10.1139/apnm-2012-0235.				X	X	
Tudor-Locke C, Hart TL, Washington TL. Expected values for pedometer-determined physical activity in older populations. *Int J Behav Nutr Phys Act*. Aug 2009:59. doi:10.1186/1479-5868-6-59.	X					
Vollaard NB, Metcalfe RS, Williams S. Effect of number of sprints in a SIT session on change in VO2max: a meta-analysis. *Med Sci Sports Exerc*. 2017;49(6):1147-1156. doi:10.1249/MSS.0000000000001204.	X					
Weston KS, Wisloff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. *Br J Sports Med*. 2014;48(16):1227-1234. doi:10.1136/bjsports-2013-092576.		X				
Weston M, Taylor KL, Batterham AM, Hopkins WG. Effects of low-volume high-intensity interval training (HIT) on fitness in adults: a meta-analysis of controlled and non-controlled trials. *Sports Med*. 2014;44(7):1005-1017. doi:10.1007/s40279-014-0180-z.	X			X		
Wewege M, van den Berg R, Ward RE, Keech A. The effects of high-intensity interval training vs. moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis. *Obes Rev*. 2017;18(6):635-646. doi:10.1111/obr.12532.		X		X		
Wisloff U, Ellingsen O, Kemi OJ. High-intensity interval training to maximize cardiac benefits of exercise training? *Exerc Sport Sci Rev*. 2009;37(3):139-146. doi:10.1097/JES.0b013e3181aa65fc.			X	X		

Rationale for Exclusion at Abstract or Full-Text Triage for Original Research

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

Citation	Outcome	Population	Study Design	Exposure	Other
Anjana RM, Sudha V, Lakshmipriya N, et al. Physical activity patterns and gestational diabetes outcomes—the wings project. *Diabetes Res Clin Pract.* June 2016;116:253-262.doi:10.1016/j.diabres.2016.04.041		X			
Arjunan SP, Deighton K, Bishop NC, et al. The effect of prior walking on coronary heart disease risk markers in South Asian and European men. *Eur J Appl Physiol.* 2015;115(12):2641-2651. doi:10.1007/s00421-015-3269-7.				X	
Braun LM, Rodriguez DA, Song Y, et al. Changes in walking, body mass index, and cardiometabolic risk factors following residential relocation: longitudinal results from the CARDIA study. *J Transp Health*. 2016;3(4):426-439. doi:10.1016/j.jth.2016.08.006.				X	
Butner KL, Creamer KW, Nickols-Richardson SM, Clark SF, Ramp WK, Herbert WG. Fat and muscle indices assessed by pQCT: relationships with physical activity and type 2 diabetes risk. *J Clin Densitom.* 2012;15(3):355-361. doi:10.1016/j.jocd.2012.01.012.	X				
Camhi SM, Sisson SB, Johnson WD, Katzmarzyk PT, Tudor-Locke C. Accelerometer-determined moderate intensity lifestyle activity and cardiometabolic health. *Prev Med.* 2011;52(5):358-360. doi:10.1016/j.ypmed.2011.01.030.			X		
Cocate PG, de Oliveira A, Hermsdorff HH, et al. Benefits and relationship of steps walked per day to cardiometabolic risk factor in Brazilian middle-aged men. *J Sci Med Sport*. 2014;17(3):283-287. doi:10.1016/j.jsams.2013.04.017.				X	
Davenport MH, Giroux I, Sopper MM, Mottola MF. Postpartum exercise regardless of intensity improves chronic disease risk factors. *Med Sci Sports Exerc*. 2011;43(6):951-958. doi:10.1249/MSS.0b013e3182051155.	X				
DiPietro L, Gribok A, Stevens MS, Hamm LF, Rumpler W. Three 15-min bouts of moderate postmeal walking significantly improves 24-h glycemic control in older people at risk for impaired glucose tolerance. *Diabetes Care*. 2013;36(10):3262-3268. doi:10.2337/dc13-0084.	X			X	
Faria CD, Paula de Carvalho-Pinto B, Nadeau S, Fuscaldi Teixeira-Salmela L. 180 degrees turn while walking: characterization and comparisons between subjects with and without stroke. *J Phys Ther Sci*. 2016;28(10):2694-2699. doi:10.1589/jpts.28.2694.				X	
Freak-Poli R, Wolfe R, Brand M, de Courten M, Peeters A. Eight-month postprogram completion: change in risk factors for chronic disease amongst participants in a 4-month pedometer-based workplace health program. *Obesity (Silver Spring).* 2013;21(9):E360-E368. doi:10.1002/oby.20342.	X				

Citation	Outcome	Population	Study Design	Exposure	Other
Fritz T, Caidahl K, Krook A, et al. Effects of Nordic walking on cardiovascular risk factors in overweight individuals with type 2 diabetes, impaired or normal glucose tolerance. *Diabetes Metab Res Rev.* 2013;29(1):25-32. doi:10.1002/dmrr.2321.		X			
Fukuoka Y, Gay CL, Joiner KL, Vittinghoff E. A novel diabetes prevention intervention using a mobile app: a randomized controlled trial with overweight adults at risk. *Am J Prev Med.* 2015;49(2):223-237. doi:10.1016/j.amepre.2015.01.003.	X				
Georgiopoulou VV, Kalogeropoulos AP, Chowdhury R, et al. Exercise capacity, heart failure risk, and mortality in older adults: the Health ABC Study. *Am J Prev Med.* 2017;52(2):144-153. doi:10.1016/j.amepre.2016.08.041.				X	
Girotra S, Kitzman DW, Kop WJ, Stein PK, Gottdiener JS, Mukamal KJ. Heart rate response to a timed walk and cardiovascular outcomes in older adults: the cardiovascular health study. *Cardiology*. 2012;122(2):69-75. doi:10.1159/000338736.				X	
Henson J, Yates T, Biddle SJ, et al. Associations of objectively measured sedentary behaviour and physical activity with markers of cardiometabolic health. *Diabetologia*. 2013;56(5):1012-1020. doi:10.1007/s00125-013-2845-9.				X	X
Jefferis BJ, Whincup PH, Papacosta O, Wannamethee SG. Protective effect of time spent walking on risk of stroke in older men. *Stroke*. 2014;45(1):194-199. doi:10.1161/STROKEAHA.113.002246.				X	
Johnsen AM, Alfredsson L, Knutsson A, Westerholm PJ, Fransson EI. Association between occupational physical activity and myocardial infarction: a prospective cohort study. *BMJ Open*. 2016;6(10):e012692. doi:10.1136/bmjopen-2016-012692.				X	
Joseph JJ, Echouffo-Tcheugui JB, Golden SH, et al. Physical activity, sedentary behaviors and the incidence of type 2 diabetes mellitus: the Multi-Ethnic Study of Atherosclerosis (MESA). *BMJ Open Diabetes Res Care*. 2016;4(1):e000185. doi:10.1136/bmjdrc-2015-000185.				X	
Julius BR, Ward BA, Stein JH, McBride PE, Fiore MC, Colbert LH. Ambulatory activity associations with cardiovascular and metabolic risk factors in smokers. *J Phys Act Health*. 2011;8(7):994-1003.		X			
Kato M, Goto A, Tanaka T, Sasaki S, Igata A, Noda M. Effects of walking on medical cost: a quantitative evaluation by simulation focusing on diabetes. *J Diabetes Investig*. 2013;4(6):667-672. doi:10.1111/jdi.12114.			X		
Kim C, Draska M, Hess ML, Wilson EJ, Richardson CR. A web-based pedometer programme in women with a recent history of gestational diabetes. *Diabet Med*. 2012;29(2):278-283. doi:10.1111/j.1464-5491.2011.03415.x.	X	X			

Citation	Outcome	Population	Study Design	Exposure	Other
Kim J, Tanabe K, Yoshizawa Y, Yokoyama N, Suga Y, Kuno S. Lifestyle-based physical activity intervention for one year improves metabolic syndrome in overweight male employees. *Tohoku J Exp Med*. 2013;229(1):11-17.	X				
Knight E, Stuckey MI, Petrella RJ. Physical activity prescription and remote self-monitoring technologies: can we reduce cardiovascular disease risk? *Can J Diabetes*. 2013;37(4):S48. doi:10.1016/j.jcjd.2013.08.142.	X				
Koniak-Griffin D, Brecht ML, Takayanagi S, Villegas J, Melendrez M. Physical activity and cardiometabolic characteristics in overweight Latina women. *J Immigr Minor Health.* 2014;16(5):856-864. doi:10.1007/s10903-013-9782-z.	X		X		
Koolhaas CM, Dhana K, Golubic R, et al. Physical activity types and coronary heart disease risk in middle-aged and elderly persons: the Rotterdam Study. *Am J Epidemiol.* 2016;183(8):729-738. doi:10.1093/aje/kwv244.				X	
Kraus WE, Califf RM, Tuomilehto J, et al. Relations between baseline physical activity by pedometer counts and future cardiovascular events in the navigator study [Abstract A12297]. *Circulation*. 2012;126(suppl 21).					X
Lejczak A, Josiak K, Węgrzynowska-Teodorczyk K, et al. Nordic walking may safely increase the intensity of exercise training in healthy subjects and in patients with chronic heart failure. *Adv Clin Exp Med.* 2016;25(1):145-149. doi:10.17219/acem/35094.				X	
Lu S, Su J, Xiang Q, Zhang F, Wu M. Active transport and health outcomes: findings from a population study in Jiangsu, China. *J Environ Public Health*. 2013;2013:624194. doi:10.1155/2013/624194.			X		
Mayor S. Walking an extra 2000 steps a day reduces cardiovascular events in people at high risk of type 2 diabetes. *BMJ*. 2013;347:f7678.doi:10.1136/bmj.f7678.			X		
McNeilly AM, McClean C, Murphy M, et al. Exercise training and impaired glucose tolerance in obese humans. *J Sports Sci*. 2012;30(8):725-732. doi:10.1080/02640414.2012.671952.	X			X	
Moe B, Mork PJ, Holtermann A, Nilsen TI. Occupational physical activity, metabolic syndrome and risk of death from all causes and cardiovascular disease in the HUNT 2 cohort study. *Occup Environ Med.* 2013;70(2):86-90. doi:10.1136/oemed-2012-100734.				X	
Morrell JS, Cook SB, Carey GB. Cardiovascular fitness, activity, and metabolic syndrome among college men and women. *Metab Syndr Relat Disord*. 2013;11(5):370-376. doi:10.1089/met.2013.0011.			X		
Müller-Riemenschneider F, Pereira G, Villanueva K, et al. Neighborhood walkability and cardiometabolic risk factors in Australian adults: an observational			X	X	

Citation	Outcome	Population	Study Design	Exposure	Other
study. *BMC Public Health*. 2013;13:755. doi:10.1186/1471-2458-13-755.					
Newman AB, Dodson JA, Church T, et al. Cardiovascular events in a physical activity intervention compared with a successful aging intervention: the LIFE Study randomized trial. *JAMA Cardiol.* 2016;1(5):568-574. doi:10.1001/jamacardio.2016.1324.				X	
Pagels P, Raustorp A, Archer T, Lidman U, Alricsson M. Influence of moderate, daily physical activity on body composition and blood lipid profile in Swedish adults. *J Phys Act Health*. 2012;9(6):867-874.	X				
Philippe M, Gatterer H, Eder EM, et al. The effects of 3 weeks of uphill and downhill walking on blood lipids and glucose metabolism in pre-diabetic men: a pilot study. *J Sports Sci Med*. 2017;16(1):35-43.	X			X	
Pospieszna B, Karolkiewicz J, Tarnas J, Lewandowski J, Laurentowska M, Pilaczyńska-Szcześniak Ł. Influence of 12-week Nordic Walking training on biomarkers of endothelial function in healthy postmenopausal women. *J Sports Med Phys Fitness.* 2017;57(9):1178-1185. doi:10.23736/S0022-4707.16.06528-2.	X				
Preiss D, Thomas LE, Wojdyla DM, et al, on behalf of the NAVIGATOR investigators. Prospective relationships between body weight and physical activity: an observational analysis from the NAVIGATOR study. *BMJ Open*. 2015;5(8):e007901. doi:10.1136/bmjopen-2015-007901.	X				
Riesco E, Tessier S, Lacaille M, et al. Impact of a moderate-intensity walking program on cardiometabolic risk markers in overweight to obese women: is there any influence of menopause? *Menopause*. 2013;20(2):185-193. doi:10.1097/gme.0b013e31826f7ebf.				X	
Rossen J, Yngve A, Hagströmer M, et al. Physical activity promotion in the primary care setting in pre- and type 2 diabetes—the Sophia step study, an RCT. *BMC Public Health*. 2015;15:647. doi:10.1186/s12889-015-1941-9.			X		X
Rowe-Roberts D, Cercos R, Mueller F. Preliminary results from a study of the impact of digital activity trackers on health risk status. *Stud Health Technol Inform*. 2014;204:143-148.	X				
Rye PL, Reeson ME, Pekrul CM, et al. Comparing health behaviours of internal medicine residents and medical students: an observational study. *Clin Invest Med*. 2012;35(1):E40-E44.	X				X
Saevereid HA, Schnohr P, Prescott E. Speed and duration of walking and other leisure time physical activity and the risk of heart failure: a prospective cohort study from the Copenhagen City Heart Study. *PLoS One.* 2014;9(3):e89909. doi:10.1371/journal.pone.0089909.				X	

Exposure Subcommittee: Q4. What is the relationship between step count per day and (1) all-cause and cardiovascular disease mortality and (2) incidence for cardiovascular disease events and risk of type 2 diabetes?

Citation	Outcome	Population	Study Design	Exposure	Other
Samawi HM. Daily walking and life expectancy of elderly people in the Iowa 65+ Rural Health Study. *Front Public Health.* 2013;1:11. doi:10.3389/fpubh.2013.00011.				X	
Sang H, Yao S, Zhang L, et al. Walk-run training improves the anti-inflammation properties of high-density lipoprotein in patients with metabolic syndrome. *J Clin Endocrinol Metab*. 2015;100(3):870-879. doi:10.1210/jc.2014-2979.	X				
Schulz AJ, Israel BA, Mentz GB, et al. Effectiveness of a walking group intervention to promote physical activity and cardiovascular health in predominantly non-Hispanic black and Hispanic urban neighborhoods: findings from the walk your heart to health intervention. *Health Educ Behav.* 2015;42(3):380-392. doi:10.1177/1090198114560015.	X				
Shapiro S, Stuckey M, Sabourin K, Munoz C, Petrella RJ. Smartphone technology versus paper-based logs for type II diabetes prevention: psychological and behavioral outcomes. *Can J Cardiol.* 2011;27(5)(suppl 1):S180-S181. doi:10.1016/j.cjca.2011.07.231.	X				
Silva-Smith AL, Fleury J, Belyea M. Effects of a physical activity and healthy eating intervention to reduce stroke risk factors in older adults. *Prev Med.* 2013;57(5):708-711. doi:10.1016/j.ypmed.2013.07.004.	X				
Slentz CA, Bateman LA, Willis LH, et al. Effects of exercise training alone vs a combined exercise and nutritional lifestyle intervention on glucose homeostasis in prediabetic individuals: a randomised controlled trial. *Diabetologia*. 2016;59(10):2088-2098. doi:10.1007/s00125-016-4051-z.	X				
Soares-Miranda L, Siscovick DS, Psaty BM, Longstreth WT Jr, Mozaffarian D. Physical activity and risk of coronary heart disease and stroke in older adults: the Cardiovascular Health Study. *Circulation*. 2016;133(2):147-155. doi:10.1161/CIRCULATIONAHA.115.018323.				X	
Soon HK, Saad HA, Taib MN, Rahman HA, Mun CY. Effects of combined physical activity and dietary intervention on obesity and metabolic parameters in adults with abdominal obesity. *Southeast Asian J Trop Med Public Health*. 2013;44(2):295-308.	X				
Stop sitting, get moving, to lower diabetes risk. *Harv Health Lett.* 2012;37(10):8.			X		
Stuckey MI, Gill DP, Shapiro S, Sabourin K, Petrella RJ. Does a prescriptive exercise program with mobile health tracking improve cardio-metabolic risk factors to a greater extent than exercise prescription alone? *Circulation*. 2013;128(22)(suppl 1):A14062.	X				
Suboc TB, Knabel D, Strath SJ, et al. Associations of reducing sedentary time with vascular function and insulin sensitivity in older sedentary adults. *Am J*	X				

Citation	Outcome	Population	Study Design	Exposure	Other
Hypertens. 2016;29(1):46-53. doi:10.1093/ajh/hpv063.					
Take a walk, reduce your risk of suffering a stroke: women who walk every week are less likely to have a stroke than women who don't. *Harv Health Lett*. 2013;38(9):6.			X		
Talbot LA, Metter EJ, Morrell CH, Frick KD, Weinstein AA, Fleg JL. A pedometer-based intervention to improve physical activity, fitness, and coronary heart disease risk in National Guard personnel. *Mil Med.* 2011;176(5):592-600.	X				
Tiessen AH, Smit AJ, Broer J, Groenier KH, van der Meer K. Randomized controlled trial on cardiovascular risk management by practice nurses supported by self-monitoring in primary care. *BMC Family Practice*. 2012;13:90. doi:10.1186/1471-2296-13-90.	X				
Tudor-Locke C, Swift DL, Schuna JM, et al. WalkMore: a randomized controlled trial of pedometer-based interventions differing on intensity messages. *BMC Public Health*. 2014;14:168. doi:10.1186/1471-2458-14-168.			X		
Venojärvi M, Korkmaz A, Wasenius N, et al. 12 weeks' aerobic and resistance training without dietary intervention did not influence oxidative stress but aerobic training decreased atherogenic index in middle-aged men with impaired glucose regulation. *Food Chem Toxicol.* 2013;61:127-135. doi:10.1016/j.fct.2013.04.015	X				
Venojärvi M, Wasenius N, Manderoos S, et al. Nordic walking decreased circulating chemerin and leptin concentrations in middle-aged men with impaired glucose regulation. *Ann Med.* 2013;45(2):162-170. doi:10.3109/07853890.2012.727020.	X				
Walking lowers stroke risks in women. *Harv Womens Health Watch.* 2013;20(8):1, 8.			X		
Wang X, Hsu FC, Isom S, et al. Effects of a 12-month physical activity intervention on prevalence of metabolic syndrome in elderly men and women. *J Gerontol A Biol Sci Med Sci*. 2012;67(4):417-424. doi:10.1093/gerona/glr187.	X				
Wijndaele K, Sharp SJ, Wareham NJ, Brage S. Mortality risk reductions from substituting screen time by discretionary activities. *Med Sci Sports Exerc.* 2017;49(6):1111-1119. doi:10.1249/MSS.0000000000001206.				X	
Wiklund P, Alen M, Munukka E, et al. Metabolic response to 6-week aerobic exercise training and dieting in previously sedentary overweight and obese pre-menopausal women: a randomized trial. *J Sport Health Sci.* 2014;3(3):217-224. doi:10.1016/j.jshs.2014.03.013.	X				
Williams PT, Thompson PD. Walking versus running for hypertension, cholesterol, and diabetes mellitus risk reduction. *Arterioscler Thromb Vasc Biol.*				X	

Citation	Outcome	Population	Study Design	Exposure	Other
2013;33(5):1085-1091. doi:10.1161/ATVBAHA.112.300878.					
Yates T, Davies MJ, Sehmi S, Gorely T, Khunti K. The Pre-diabetes Risk Education and Physical Activity Recommendation and Encouragement (PREPARE) programme study: are improvements in glucose regulation sustained at 2 years? *Diabet Med.* 2011;28(10):1268-1271. doi:10.1111/j.1464-5491.2011.03357.x.	X				
Zeki Al Hazzouri A, Mayeda ER, Elfassy T, et al. Perceived walking speed, measured tandem walk, incident stroke, and mortality in older Latino adults: a prospective cohort study. *J Gerontol A Biol Sci Med Sci.* 2017;72(5):676-682. doi:10.1093/gerona/glw169.				X	

References

1. Huffman KM, Sun JL, Thomas L, et al. Impact of baseline physical activity and diet behavior on metabolic syndrome in a pharmaceutical trial: results from NAVIGATOR. *Metabolism*. 2014;63(4):554-561. doi:10.1016/j.metabol.2014.01.002.

2. Ponsonby AL, Sun C, Ukoumunne OC, et al. Objectively measured physical activity and the subsequent risk of incident dysglycemia: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Diabetes Care*. 2011;34(7):1497-1502. doi:10.2337/dc10-2386.

3. Yates T, Davies MJ, Haffner SM, et al. Physical activity as a determinant of fasting and 2-h post-challenge glucose: a prospective cohort analysis of the NAVIGATOR trial. *Diabet Med*. 2015;32(8):1090-1096. doi:10.1111/dme.12762.

4. Yates T, Haffner SM, Schulte PJ, et al. Association between change in daily ambulatory activity and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis. *Lancet*. 2014;383(9922):1059-1066. doi:10.1016/S0140-6736(13)62061-9.

5. Colpani V, Oppermann K, Spritzer PM. Association between habitual physical activity and lower cardiovascular risk in premenopausal, perimenopausal, and postmenopausal women: a population-based study. *Menopause*. 2013;20(5):525-531. doi:10.1097/GME.0b013e318271b388.

6. Johnson ST, Eurich DT, Lytvyak E, et al. Walking and type 2 diabetes risk using CANRISK scores among older adults. *Appl Physiol Nutr Metab*. 2017;42(1):33-38. doi:10.1139/apnm-2016-0267.

7. Newton RL Jr, Han H, Johnson WD, et al. Steps/day and metabolic syndrome in African American adults: the Jackson Heart Study. *Prev Med*. 2013;57(6):855-859. doi:10.1016/j.ypmed.2013.09.018.

8. Yates T, Henson J, Khunti K, et al. Effect of physical activity measurement type on the association between walking activity and glucose regulation in a high-risk population recruited from primary care. *Int J Epidemiol*. 2013;42(2):533-540. doi:10.1093/ije/dyt015.

9. Herzig KH, Ahola R, Leppäluoto J, Jokelainen J, Jämsä T, Keinänen-Kiukaanniemi S. Light physical activity determined by a motion sensor decreases insulin resistance, improves lipid homeostasis and reduces visceral fat in high-risk subjects: PreDiabEx study RCT. *Int J Obes (Lond)*. 2014;38(8):1089-1096. doi:10.1038/ijo.2013.224.