Evidence Portfolio – Exposure Subcommittee, Question 6[1]

What is the relationship between high intensity interval training and reduction in cardiometabolic risk?

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: Existing Systematic Review and Meta-Analyses

Conclusion Statements and Grades

Moderate evidence indicates that high intensity interval training can effectively improve insulin sensitivity, blood pressure, and body composition in adults. These high intensity interval training-induced improvements in cardiometabolic disease risk factors are comparable to those resulting from continuous, moderate-intensity aerobic exercise and are more likely to occur in adults at higher risk of cardiovascular disease and diabetes, compared to healthy adults. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between the quantity of high intensity interval training and several risk factors for cardiovascular disease and diabetes. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the effects of high intensity interval training on cardiometabolic risk factors are influenced by age, sex, race/ethnicity, or socioeconomic status. **PAGAC Grade: Not assignable.**

Moderate evidence indicates that weight status influences the effectiveness of high intensity interval training to reduce cardiometabolic disease risk. Adults with overweight or obesity are more responsive than adults with normal weight to high intensity interval training's effects on improving insulin sensitivity, blood pressure, and body composition. **PAGAC Grade: Moderate.**

Description of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer the research question as determined by the Exposure Subcommittee. Additional searches for original research were not needed.

Existing Systematic Review and Meta-Analyses

Overview

A total of 3 existing reviews were included: 1 systematic review[1] and 2 meta-analyses.[2, 3] The reviews were published from 2012 to 2017.

[1] Question 3 in Chapter 1. Physical Activity Behaviors: Steps, Bouts, And High Intensity Training

The systematic review[1] included 24 studies and covered a timeframe from inception to 2011.

The meta-analyses included a large number of studies. Batacan et al[2] included 65 studies and Jelleyman et al[3] included 50 studies. They also covered extensive timeframes: from 1970 to 2015 and from 1946 to 2015, respectively.

Exposures

The three existing reviews examined physical activity performed as high-intensity interval training. Batacan et al[2] and Jelleyman et al[3] defined high-intensity interval training as bouts of vigorous activity or maximal effort interspersed with periods of lower intensity exercise or complete rest. Kessler et al[1] examined two distinct types of high-intensity interval training: sprint interval training and aerobic interval training.

Outcomes

All existing reviews examined cardiometabolic risk factors including maximal oxygen uptake (VO2max) and body composition[1-3]; insulin sensitivity[1, 3]; and blood pressure.[1, 2]

Populations Analyzed

The table below lists the populations analyzed in each article.

Table 1. Populations Analyzed by All Sources of Evidence

	Age	Weight Status	Chronic Conditions	Other
Batacan, 2017	Adults ≥18	Normal weight, overweight and obese		
Jelleyman, 2015	Adults 21–68	Overweight and obese	Metabolic syndrome/type 2 diabetes, other chronic disease	Healthy
Kessler, 2012	All ages			

Supporting Evidence

Existing Systematic Review and Meta-Analyses

Table 2. Existing Systematic Review and Meta-Analyses Individual Evidence Summary Tables

Meta-Analysis **Citation:** 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.	
Purpose: To synthesize the effects of high intensity interval training (HIIT) on cardiometabolic health markers. **Timeframe:** 1970–2015 **Total # of Studies:** 65 **Exposure Definition:** HIIT: Short-term (<12 weeks) or long-term (≥12 weeks). HIIT defined as intermittent bouts of activity performed at maximal effort (lasting ≤4 min/set (combined with an interval of recovery. Modalities included treadmill, swimming, and cycling. Intervention duration ranged from 12 weeks to 52 weeks. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** Yes **Outcomes Addressed:** Waist circumference, BMI, Body fat (%), VO2 max (ml/kg/min), blood pressure(mmHg), fasting glucose (mmol/L), lipid profile (mmol/L), triglycerides, VO2 max **Examine Cardiorespiratory Fitness as Outcome:** Yes	**Abstract:** The current review clarifies the cardiometabolic health effects of high-intensity interval training (HIIT) in adults. A systematic search (PubMed) examining HIIT and cardiometabolic health markers was completed on 15 October 2015. Sixty-five intervention studies were included for review and the methodological quality of included studies was assessed using the Downs and Black score. Studies were classified by intervention duration and body mass index classification. Outcomes with at least 5 effect sizes were synthesized using a random-effects meta-analysis of the standardized mean difference (SMD) in cardiometabolic health markers (baseline to postintervention) using Review Manager 5.3. Short-term (ST) HIIT (<12 weeks) significantly improved maximal oxygen uptake (VO2 max; SMD 0.74, 95% CI 0.36 to 1.12; p<0.001), diastolic blood pressure (DBP; SMD -0.52, 95% CI -0.89 to -0.16; p<0.01) and fasting glucose (SMD -0.35, 95% CI -0.62 to -0.09; p<0.01) in overweight/obese populations. Long-term (LT) HIIT (>/=12 weeks) significantly improved waist circumference (SMD -0.20, 95% CI -0.38 to -0.01; p<0.05), % body fat (SMD -0.40, 95% CI -0.74 to -0.06; p<0.05), VO2 max (SMD 1.20, 95% CI 0.57 to 1.83; p<0.001), resting heart rate (SMD -0.33, 95% CI -0.56 to -0.09; p<0.01), systolic blood pressure (SMD -0.35, 95% CI -0.60 to -0.09; p<0.01) and DBP (SMD -0.38, 95% CI -0.65 to -0.10; p<0.01) in overweight/obese populations. HIIT demonstrated no effect on insulin, lipid profile, C reactive protein or interleukin 6 in overweight/obese populations. In normal weight populations, ST-HIIT and LT-HIIT significantly improved VO2 max, but no other significant effects were observed. Current evidence suggests that ST-HIIT and LT-HIIT can increase VO2 max and improve some cardiometabolic risk factors in overweight/obese populations.
Populations Analyzed: Adults ≥18; Normal/Healthy Weight, Overweight and Obese	**Author-Stated Funding Source:** Central Queensland University; National Heart Foundation of Australia

Meta-Analysis **Citation:** 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.	
Purpose: To quantify the impact of high-intensity interval training (HIIT) on glucose insulin regulation, body weight, and cardiorespiratory fitness. **Timeframe:** 1946–March 2015 **Total # of Studies:** 50 **Exposure Definition:** HIIT defined as at least two bouts of vigorous or higher intensity exercise interspersed with periods of lower intensity exercise or complete rest. Included studies had HIIT for ≥3 times per week for 2 weeks. Duration of HIIT between 4 sec and 5 min and intensity between 65% VO2max and Wingate effort. Recovery intervals varied with a duration range of 12 sec–5 min and intensity range of complete rest to 70% HR max. Session duration: 10–60 min and total length of intervention (range 2–16 weeks). **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** Yes **Outcomes Addressed:** Glucose regulation (HbA1c or fasting glucose levels); Insulin resistance; BMI; VO2max **Examine Cardiorespiratory Fitness as Outcome:** Yes	**Abstract:** The aim of this meta-analysis was to quantify the effects of high-intensity interval training (HIIT) on markers of glucose regulation and insulin resistance compared with control conditions (CON) or continuous training (CT). Databases were searched for HIIT interventions based upon the inclusion criteria: training >/=2 weeks, adult participants and outcome measurements that included insulin resistance, fasting glucose, HbA1c or fasting insulin. Dual interventions and participants with type 1 diabetes were excluded. Fifty studies were included. There was a reduction in insulin resistance following HIIT compared with both CON and CT (HIIT vs. CON: standardized mean difference [SMD] = -0.49, confidence intervals [CIs] -0.87 to -0.12, P = 0.009; CT: SMD = -0.35, -0.68 to -0.02, P = 0.036). Compared with CON, HbA1c decreased by 0.19% (-0.36 to -0.03, P = 0.021) and body weight decreased by 1.3 kg (-1.9 to -0.7, P < 0.001). There were no statistically significant differences between groups in other outcomes overall. However, participants at risk of or with type 2 diabetes experienced reductions in fasting glucose (-0.92 mmol L(-1), -1.22 to -0.62, P < 0.001) compared with CON. HIIT appears effective at improving metabolic health, particularly in those at risk of or with type 2 diabetes. Larger randomized controlled trials of longer duration than those included in this meta-analysis are required to confirm these results.
Populations Analyzed: 21–68 years; Healthy, Overweight and obese, Metabolic Syndrome/Type 2 Diabetes, other Chronic Disease.	**Author-Stated Funding Source:** National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care

Systematic Review **Citation:** 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.	
Purpose: To examine the impact of high-intensity interval training (HIT) on clinical cardiometabolic risk factors including glucose metabolism, serum lipids, blood pressure, and anthropometric outcomes. **Timeframe:** Inception–2011 **Total # of Studies:** 24 **Exposure Definition:** Two distinct types of HIT were included: Sprint interval training (SIT): 4–6 cycles of 30 second 'all out sprints' followed by 4–4.5 minutes of recovery. Aerobic interval training (AIT): 4 minutes of high-intensity work at 80–95%. VO2max followed by 3–4 minutes of recovery time, for 4–6 cycles performed on a treadmill or bicycle ergometer. Duration of exposure ranged from 2 weeks to 6 months. **Measures Steps:** No **Measures Bouts:** No **Examines HIT:** Yes **Outcomes Addressed:** Insulin resistance; asting glucose; lipid profile; Hypertension; Body composition – body weight, BMI, body-fat percentage (BF%), lean body mass percentage, waist-to-hip ratio, waist circumference; VO2 max **Examine Cardiorespiratory Fitness as Outcome:** Yes	**Abstract:** In the US, 34% of adults currently meet the criteria for the metabolic syndrome defined by elevated waist circumference, plasma triglycerides (TG), fasting glucose and/or blood pressure, and decreased high-density lipoprotein cholesterol (HDL-C). While these cardiometabolic risk factors can be treated with medication, lifestyle modification is strongly recommended as a first-line approach. The purpose of this review is to focus on the effect of physical activity interventions and, specifically, on the potential benefits of incorporating higher intensity exercise. Several recent studies have suggested that compared with continuous moderate exercise (CME), high-intensity interval training (HIT) may result in a superior or equal improvement in fitness and cardiovascular health. HIT is comprised of brief periods of high-intensity exercise interposed with recovery periods at a lower intensity. The premise of using HIT in both healthy and clinical populations is that the vigorous activity segments promote greater adaptations via increased cellular stress, yet their short length, and the ensuing recovery intervals, allow even untrained individuals to work harder than would otherwise be possible at steady-state intensity. In this review, we examine the impact of HIT on cardiometabolic risk factors, anthropometric measures of obesity and cardiovascular fitness in both healthy and clinical populations with cardiovascular and metabolic disease. The effects of HIT versus CME on health outcomes were compared in 14 of the 24 studies featuring HIT. Exercise programmes ranged from 2 weeks to 6 months. All 17 studies that measured aerobic fitness and all seven studies that measured insulin sensitivity showed significant improvement in response to HIT, although these changes did not always exceed responses to CME comparison groups. A minimum duration of 12 weeks was necessary to demonstrate improvement in fasting glucose in four of seven studies (57%). A minimum duration of 8 weeks of HIT was necessary to demonstrate improvement in HDL-C in three of ten studies (30%). No studies reported that HIT resulted in improvement of total cholesterol, low-density lipoprotein cholesterol (LDL-C), or TG. At least 12 weeks of HIT was required for reduction in blood pressure to emerge in five studies of participants not already being treated for hypertension. A minimum duration of 12 weeks was necessary to see consistent improvement in the six studies that examined anthropometric measures of obesity in overweight/obese individuals. In the 13 studies with a matched-exercise-volume CME group, improvement in aerobic fitness in response to HIT was equal to (5 studies), or greater than (8 studies) in response to CME. Additionally, HIT has been shown to be safe and effective in patients with a range of cardiac and metabolic

	dysfunction. In conclusion, HIT appears to promote superior improvements in aerobic fitness and similar improvements in some cardiometabolic risk factors in comparison to CME, when performed by healthy subjects or clinical patients for at least 8-12 weeks. Future studies need to address compliance and efficacy of HIT in the real world with a variety of populations.
Populations Analyzed: All Ages	**Author-Stated Funding Source:** National Institutes of Health

Table 3. Existing Systematic Review and Meta-Analyses Quality Assessment Chart

AMSTARExBP: SR/MA			
	Batacan, 2017	Jelleyman, 2015	Kessler, 2012
Review questions and inclusion/exclusion criteria delineated prior to executing search strategy.	Yes	Yes	Yes
Population variables defined and considered in methods.	No	Yes	No
Comprehensive literature search performed.	Partially Yes	Yes	Yes
Duplicate study selection and data extraction performed.	No	No	No
Search strategy clearly described.	Yes	Yes	Yes
Relevant grey literature included in review.	No	No	No
List of studies (included and excluded) provided.	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	Yes	Yes	N/A
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes	No
Results depended on study quality, either overall, or in interaction with moderators.	No	No	N/A
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	N/A
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	N/A
Effect size index chosen justified, statistically.	Yes	Yes	N/A
Individual-level meta-analysis used.	No	No	N/A
Practical recommendations clearly addressed.	Yes	Yes	Yes
Likelihood of publication bias assessed.	No	Yes	No
Conflict of interest disclosed.	Yes	Yes	Yes

Appendices

Appendix A: Analytical Framework

Exposure

Systematic Review Questions

What is the relationship between high intensity interval training and reduction in cardiometabolic risk?

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, or socio-economic status?

Population

Adults, 18 years and older

Exposure

- PA performed as high-intensity interval training
- PA exposure of at least 12 weeks

Comparison

- Different PA intensities

Endpoint Health Outcomes

- All-cause and CVD mortality
- CVD incidence
- Type 2 Diabetes
- Cardiorespiratory fitness
- Cardiometabolic risk factors:
  - Blood Pressure
  - Blood lipids (total cholesterol, HDL-cholesterol, LDL- cholesterol, triglycerides)
  - Body mass, BMI
  - Waist circumference

Key Definitions

- High-intensity interval training (HIIT), also called high-intensity intermittent exercise (HIIE), sprint interval training (SIT), supramaximal interval training (SIT): a form of interval training (IT), an exercise strategy alternating short periods of intense anaerobic exercise with less-intense recovery periods.

Appendix B: Final Search Strategy

Search Strategy: PubMed Q4-Q6 (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 Commentaries/ Editorials	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 Q4-Q6 (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: CINAHL; Date of Search: 5/4/2017; 16 unique 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 Q4-Q6 (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

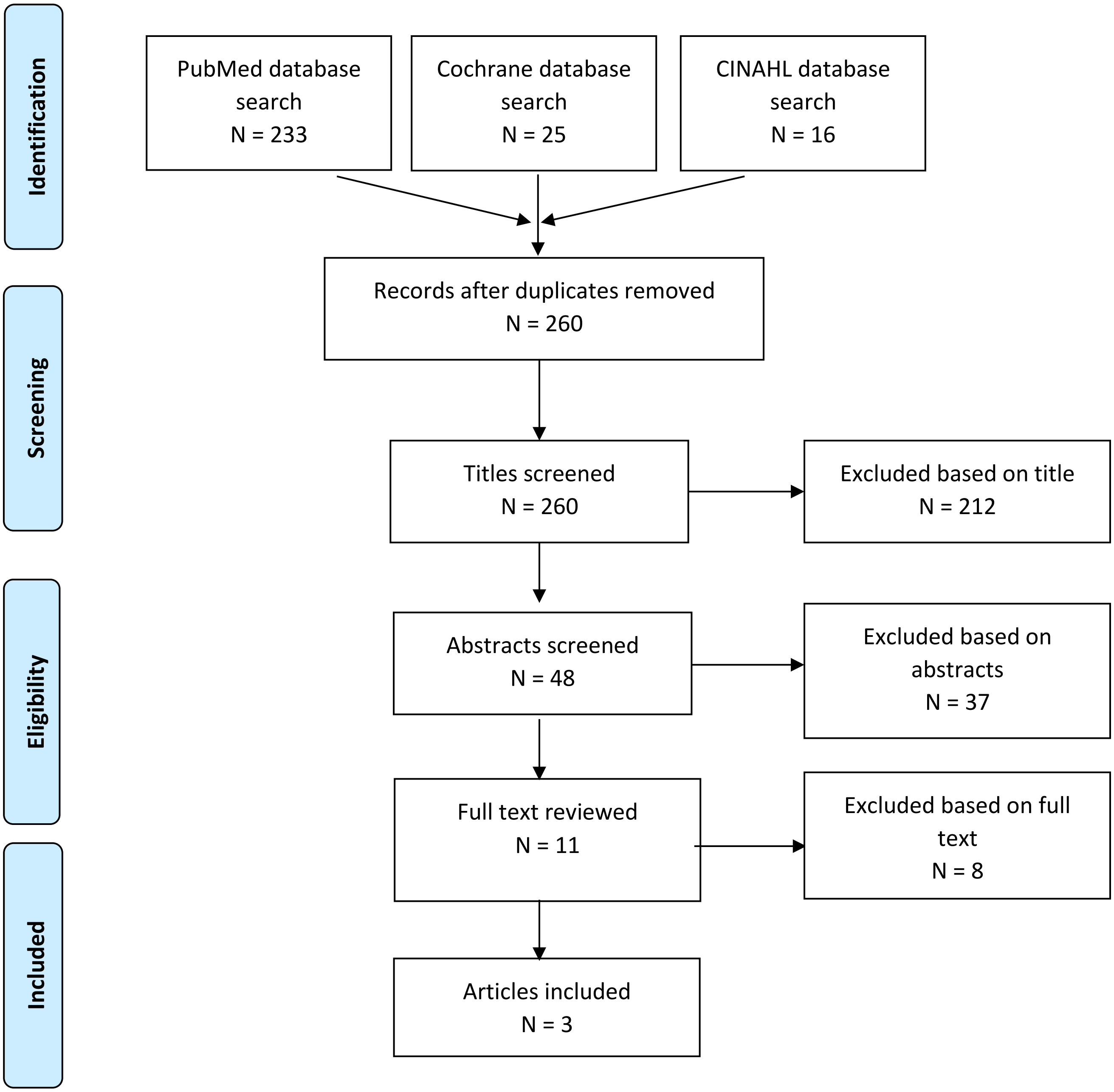
Database: Cochrane; Date of Search: 5/4/17; 25 Results

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

Appendix C: Literature Tree

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



Appendix D: Inclusion/Exclusion Criteria

Exposure Subcommittee
Q6: What is the relationship between high intensity interval training and reduction in cardiometabolic risk?

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 CVD • Studies on high performance athletes	
Comparison	**Include studies in which the comparison is:** • Adults exposed to different intensities of physical activity	
Date of Publication	**Include:** • No date limit	
Study Design/Type of Research	**Include:** • Systematic reviews • Meta-analyses • Report • Pooled analysis **Exclude:** • Original Research articles • Literature reviews	

	• Commentaries	
Size of Study Groups	**Include:** • All	
Intervention/ Exposure	**Include:** • Studies where PA is performed as high-intensity interval training • Studies where the duration of the PA exposure is at least 12 weeks **Exclude:** • Studies examining the metabolic response (e.g., insulin sensitivity, lipid values) to a single dose of PA or acute bouts • Exposure measured by a single measure of physical fitness (cardiovascular fitness, strength, flexibility, walking speed in older adults): Where the measure of physical activity is based only on physical fitness measures (single or combined variables) • Studies that do not include physical activity (or the lack thereof) as the primary exposure variable or used solely as a confounding variable • Studies of a specific therapeutic exercise (range of motion exercise, inspiratory muscle training)	

Outcome	**Include studies in which the outcome is:**
	• All-cause and CVD mortality
	• Cardiovascular Disease (CVD)
	• Type 2 Diabetes
	• Cardiometabolic risk factors:
	  ○ Blood Pressure
	  ○ Blood lipids (total cholesterol, HDL-cholesterol, LDL- cholesterol, triglycerides)
	  ○ Body mass, BMI
	  ○ Waist circumference
	• Cardiorespiratory fitness
	Exclude:
	• Congenital heart disease
	• Studies on progression of CVD	

Multiple Publications of Same Data	**Include:** More than one article per data set. **Note if re-analysis of dataset evaluated for 2008 **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
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	
Bacon AP, Carter RE, Ogle EA, Joyner MJ. VO2max 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	
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. *Sports Med*. 2013;43(10):927-954. doi:10.1007/s40279-013-0066-5.			X		
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		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search
Choi BC, Pak AW, Choi JC, Choi EC. Daily step goal of 10,000 steps: a literature review. *Clin Invest Med*. 2007;30(3):E146-151.				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. *F1000Research*. 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		
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			
Kang M, Marshall SJ, Barreira TV, Lee JO. Effect of pedometer-based physical activity interventions: a				X	

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search
meta-analysis. *Res Q Exerc Sport*. 2009;80(3):648-655. doi:10.1080/02701367.2009.10599604.					
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		
Koichiro A, Hideo M. Potential universal application of high-intensity interval training from athletes and sports lovers to patients. *Keio J Med*. 2016;62(2):19-24. doi:10.2302/kjm.2016-0006-IR.			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				
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 of 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			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search
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):e341-352. 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				
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Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search
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			
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