



Meeting 4

Individuals with Chronic Conditions

Chair: David Buchner

Members: Bill Kraus, Rich Macko, Anne McTiernan, Linda Pescatello, Ken Powell

Experts and Consultants



- Consultants:
 - Virginia Byers Kraus, M.D., Ph.D.
 - Duke University School of Medicine

 - Christine M. Friedenreich, Ph.D.
 - Alberta Health Services

 - Ronald J. Sigal, M.D., M.P.H.
 - University of Calgary

Overview: Question #1

1. Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality, (2) cancer-specific mortality, or (3) risk of cancer recurrence or second primary cancer?
 - In March 2017, presented findings for breast cancer and colorectal cancer.
 - Today, findings for prostate cancer are presented.
 - Based upon results of searches, no other cancers have enough evidence to allow review as part of Q1.

Overview: Questions 2-4



Q2-Q4 have similar structure: In people with chronic conditions, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression?

Q2 = Osteoarthritis

Q3 = Hypertension

Q4 = Type 2 diabetes

Questions generally to be answered: “systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports.”

Except made two changes to Q2 on osteoarthritis:

- 1) Added an additional outcome: pain.
- 2) Addressing this question can include de novo evidence reviews (review of original studies)

Made one change on Q3 on hypertension:

- 1) Does effect of PA on progression (assessed by blood pressure) differ by blood pressure?

Question 2 – update on selection of chronic conditions

- Summary from March PAGAC meeting:
 - For a possible Q5, conditions under consideration were:
 - asthma in children
 - stroke in adults
 - Whether to include “obesity” as a possible chronic condition was under discussion.
- Update:
 - Favoring review of stroke in adults for possible Q5 (as time and resources permit) (would need to coordinate with Aging SC)
 - For Q4, it is proposed to review effects of PA on obesity in people with type 2 diabetes.

Question 1

1. Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality, (2) cancer-specific mortality, or (3) risk of cancer recurrence or second primary cancer?
 - Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
 - Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?
- Source of evidence to answer question
 - 1 systematic review
 - 1 meta-analysis
 - 2 source papers identified in meta-analysis

Draft Key Findings: Prostate

- Meta-analysis results:
 - “Highest” vs. “lowest” levels of physical activity were associated with a 38% reduction in risk for prostate cancer-specific mortality (RR 0.62, 95% CI 0.47-0.82)
 - Risk of recurrence was not associated with physical activity (RR 0.77, 95% CI 0.55-1.08)
- Individual cohort results:
 - 4623 Swedish men with localized prostate cancer, followed 10-15 years: ≥ 5 MET-hr/day vs. < 5 MET-hr/day; HR overall mortality = 0.66 (95% CI 0.53-0.83)
 - 2705 men in Health Professionals Follow-up Study, followed median ~ 9 years. ≥ 48 MET-hr/week vs. < 3 MET-hr/week; HR overall mortality 0.38 (95% CI 0.27-0.53, $p < 0.001$)

Draft Conclusion Statement: 1

- Limited evidence indicates an inverse association between “highest” vs. “lowest” levels of physical activity after diagnosis and all-cause mortality among prostate cancer survivors.
 - **PAGAC Grade:** Limited
- Moderate evidence indicates an inverse association between “highest” vs. “lowest” levels of physical activity after diagnosis and prostate cancer-specific mortality among prostate cancer survivors.
 - **PAGAC Grade:** Moderate

Draft Conclusion Statement: 2

- Limited evidence suggests no association between “highest” vs. “lowest” physical activity level and prostate cancer recurrence or progression.
 - **PAGAC Grade:** Limited
- Limited evidence suggests a greater effect of PA on all-cause and prostate-specific mortality with higher amounts of PA, with larger effect on all-cause mortality.
 - **PAGAC Grade:** Limited
- No evidence is available on the association between physical activity and prostate cancer survival or recurrence by age, race/ethnicity, socio-economic status, or weight status.
 - **PAGAC Grade:** Not assignable

Draft Research Recommendations: 1

- Cohort studies of PA and recurrence and mortality in prostate cancer survivors, which consider effects of PA by race/ethnicity, age, SES, weight, and treatment type and completion.
- Randomized controlled trials of PA effect on prostate cancer outcomes, including dose-response trials and trials to elucidate mechanisms of action of PA.
- Studies on PA safety in prostate cancer survivors.

Committee Discussion

1. Among cancer survivors, what is the relationship between physical activity and (1) all-cause mortality, (2) cancer-specific mortality, or (3) risk of cancer recurrence or second primary cancer?
 - Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
 - Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Question 2: Osteoarthritis



2. In persons with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) pain, and (5) disease progression.

When it is determined there is a relationship between physical activity and a health outcome,

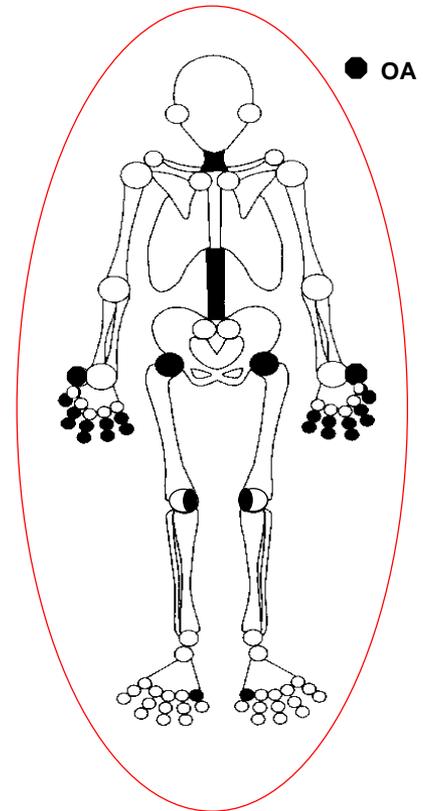
- Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
 - Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?
- Source of evidence to answer question
 - Combination of SR/MA/Existing report and de novo systematic review of original articles
 - De novo for progression outcome only

Question 2: Osteoarthritis: Rationale

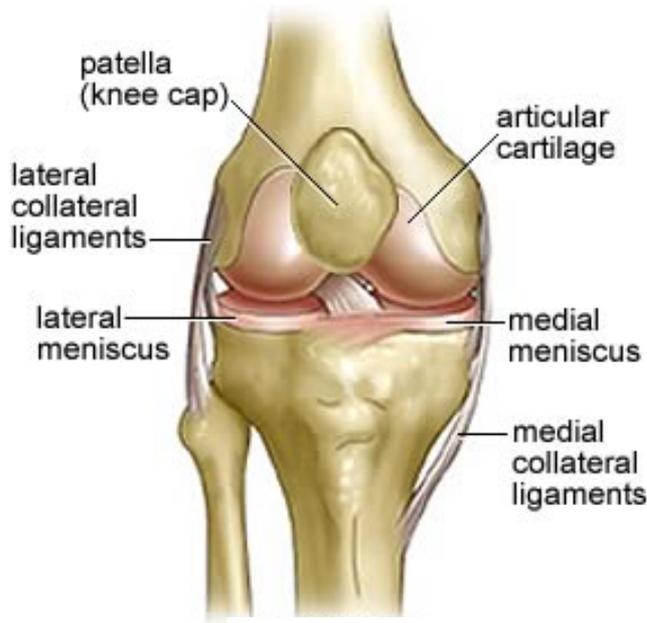
1. OA affects approximately 40% of individuals over 65 years of age in US.
2. Primary source of disability in older people worldwide.
3. OA associated with significant comorbidities: CVD, cardiometabolic disease and excess mortality.
4. Major benefits of PA recognized by OA treatment guidelines.
5. Clarification on appropriate types of PA for progression prevention in OA is important: mode (pool versus land), intensity, duration; can PA provide preventive benefits (e.g. physical function) without increasing disease progression?
6. Potentially great impact of preventive guidelines for people with OA.

Osteoarthritis is a disorder of movable joints occurring idiopathically in characteristic locations and increasing with age.

Osteoarthritis can occur secondarily in ANY joint in response to a joint insult (injury, infection, etc.)



OA is a 'Joint' Disorder



Osteoarthritis involves anatomic, and/or physiologic derangements of all joint tissues (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation, muscle weakness and loss of normal joint function), that can culminate in illness (pain, stiffness, loss of QOL)

Analytical Framework

Systematic Review Question

In people with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) pain, (4) disease progression.

Target Population

Individuals of all ages with osteoarthritis

Comparison

Individuals with osteoarthritis who participate in varying levels or no physical activity

Intervention/Exposure

All types and intensities of physical activity

Endpoint Health Outcomes

- Risk of co-morbid conditions
- Physical function
- Pain
- Health-related quality of life
- Disease progression

Key Definitions

- Risk of co-morbid conditions: The chance of having one or more additional conditions
- Physical function: “Physical function” and “physical functioning” are regarded as synonyms that refer to: “the ability of a person to move around and to perform types of physical activity.”
- Health-related quality of life: “Health-related quality of life (HRQOL) is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning.” Source: HealthyPeople.gov
<https://www.healthypeople.gov/2020/topic-s-objectives/topic/health-related-quality-of-life-well-being>
- Pain
- Disease progression: A change or worsening of a disease over time.

Common Inclusion/Exclusion Criteria

- Language
 - Exclude: Studies that do not have full text in English
- Publication Status
 - Include: Studies published in peer-reviewed journals, PAGAC-approved reports
 - Exclude: Grey literature
- Study Subjects
 - Exclude: Studies of animals only

Inclusion/Exclusion Criteria



- Date of Publication
 - Original Research: 2006 - Present
 - Existing Sources: Include 2011 - Present
- Study Subjects
 - Include: People with osteoarthritis
- Study Design
 - Include: Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports, Randomized controlled trials, Non-randomized controlled trials, Prospective cohort studies, Retrospective cohort studies, Case-control studies, Cross-sectional studies, Before-and-after studies
 - Exclude: Narrative reviews, Commentaries, Editorials
- Exposure/Intervention
 - Include: All types and intensities of physical activity
 - Exclude: Missing physical activity, Therapeutic exercise, Single-acute sessions of physical activity, Physical fitness as the exposure, Physical activity only used as confounding variable
- Outcome
 - Include: Risk of co-morbid conditions, Physical function, Health-related quality of life, Disease progression, Pain

Search Terms: Physical Activity



- Aerobic activity(ies)
- Cardiovascular activity(ies)
- Endurance activity(ies)
- Exercise
- Free living activity(ies)
- Functional training
- Leisure-time physical activity
- Lifestyle activity(ies)
- Muscle stretching exercises
- Physical activity(ies)
- Physical conditioning
- Qi gong
- Recreational activity(ies)
- Resistance training
- Strength training
- Sedentary
- Sedentary lifestyle
- Tai Chi
- Tai Ji
- Walk(ing)
- Yoga

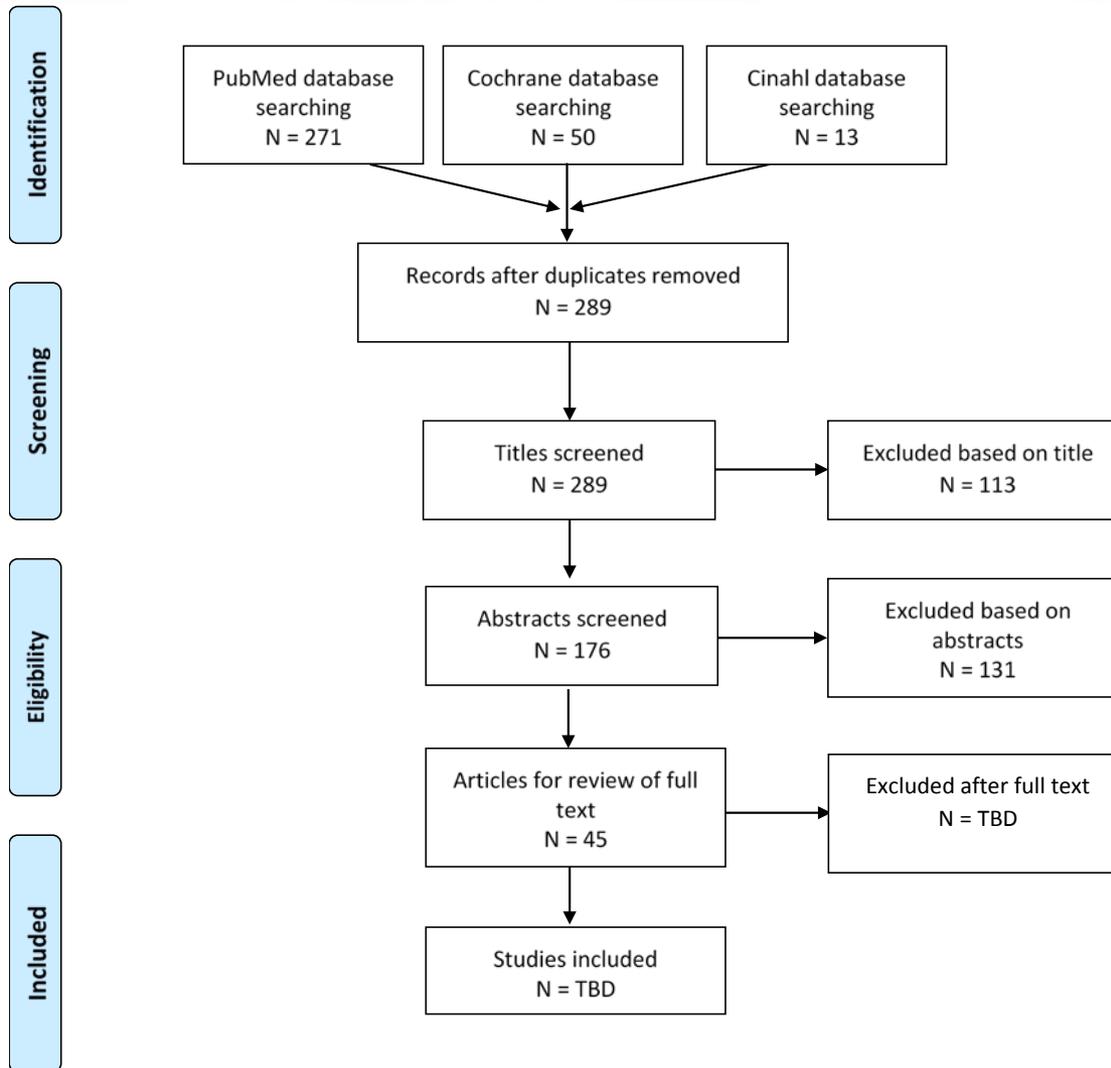
Search Terms: Condition

- Degenerative Arthritides
- Degenerative Arthritis
- Degenerative joint disease
- Osteoarthritic
- Osteoarthritides
- Osteoarthritis
- Osteoarthroses
- Osteoarthrosis
- Osteoarthrosis Deformans
- Osteophytosis
- Wear and tear arthritis

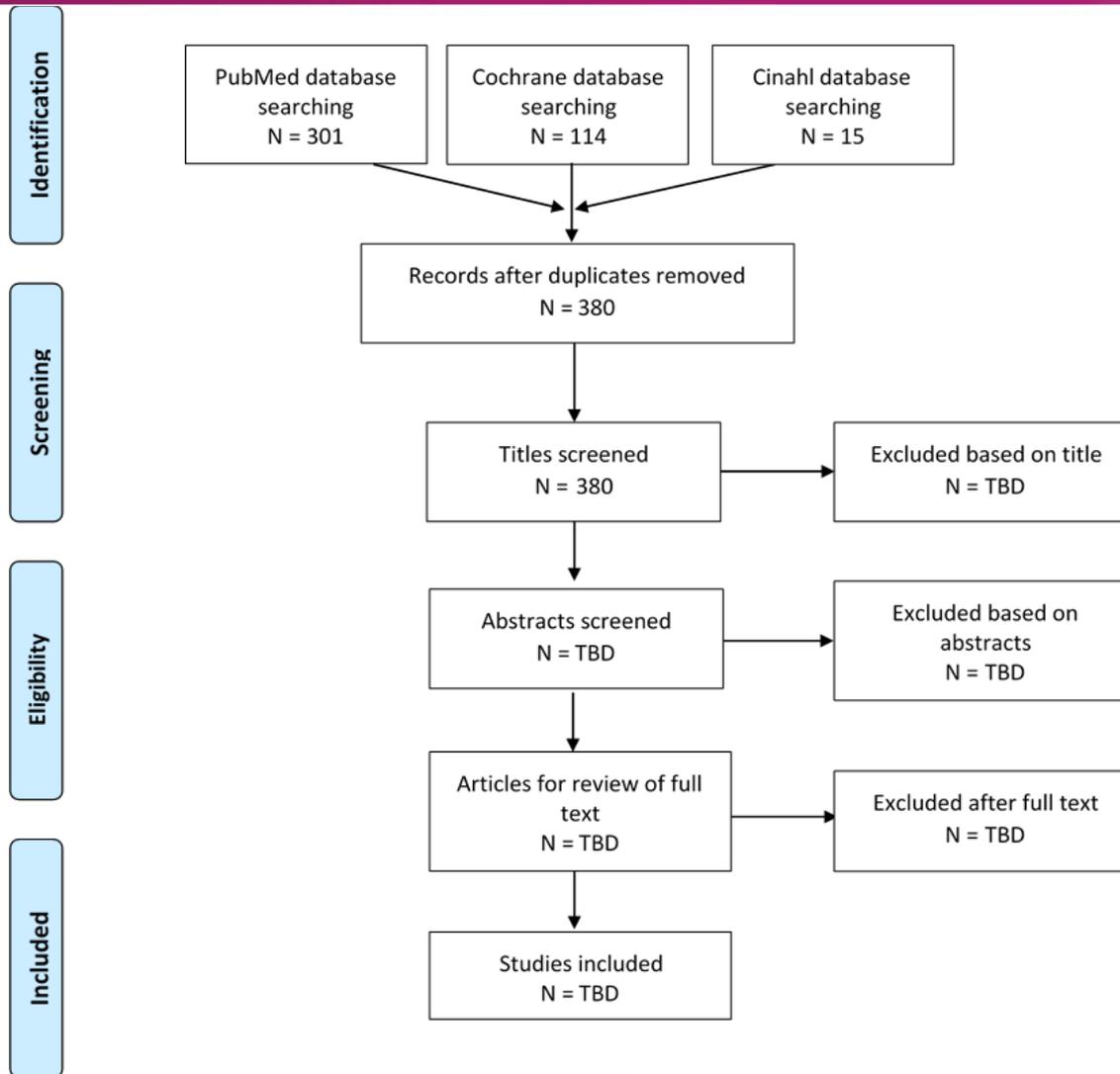
Search Terms: Progression Outcome for Original Research Only

- Acceleration
- Disease Progression
- Progresses
- Progression
- Progressive disease
- Progressive OA
- Progressive Osteoarthritis

Search Results: High-Quality Reviews¹



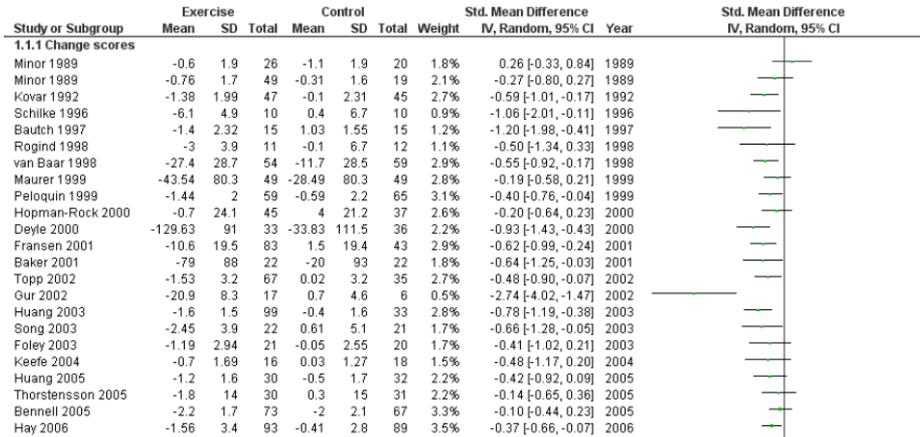
Search Results: Original Research



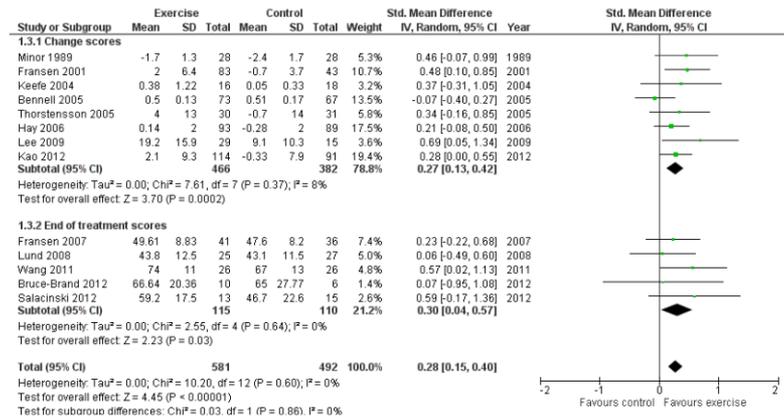
Draft Description of the Evidence

- No summary literature found for outcome of comorbidities.
- Close to finishing final literature selection for outcomes of pain, physical function and QOL.
 - Almost all of the literature controlled clinical studies.
 - Some general observations already present.
 - Dose-response yet to be completed.
- De novo review of outcome of progression ongoing.
- Will show interim results based upon Cochrane 2015 meta-analysis

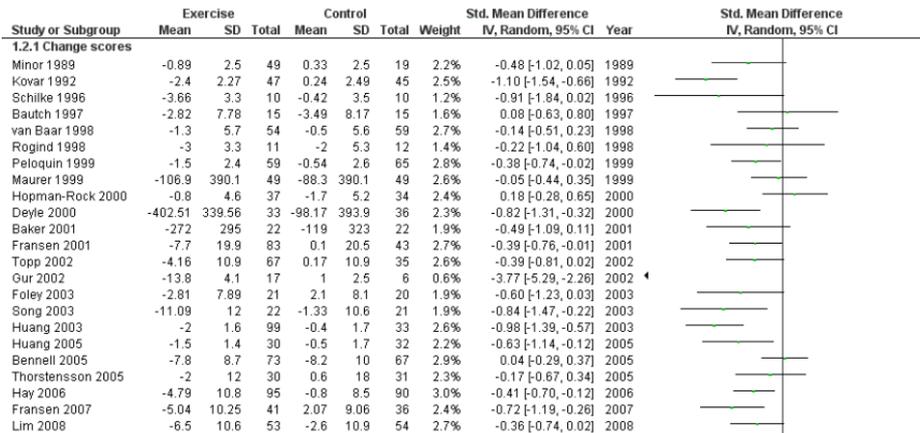
Pain



QOL



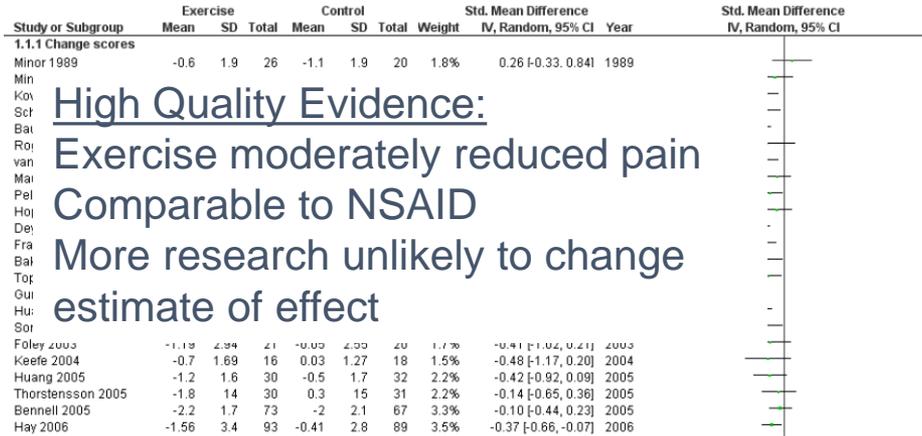
Function



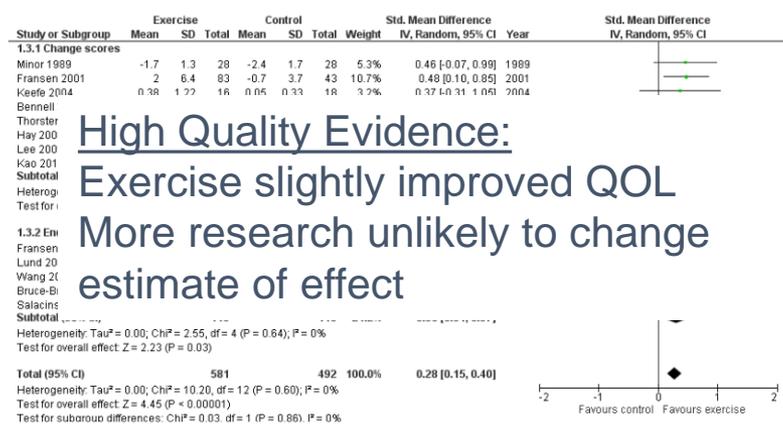
Moderate Quality Evidence:
Unlikely to change

Pain; 3537 (44 studies)

QOL; 1073 (13 studies)

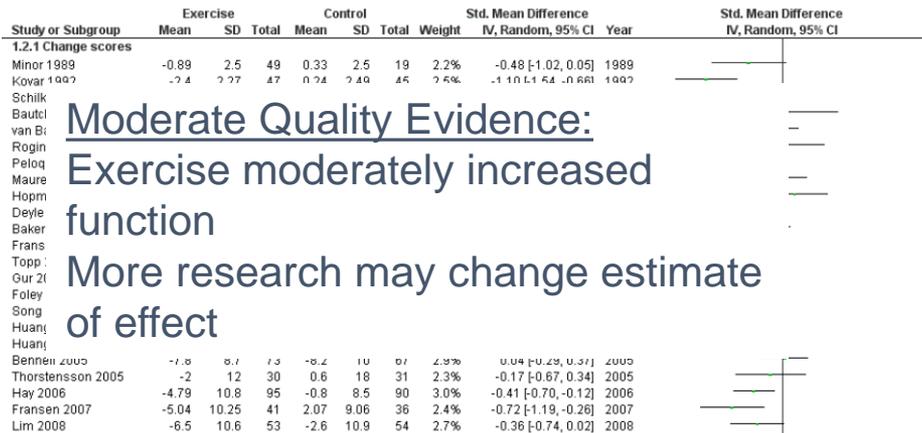


High Quality Evidence:
 Exercise moderately reduced pain
 Comparable to NSAID
 More research unlikely to change estimate of effect



High Quality Evidence:
 Exercise slightly improved QOL
 More research unlikely to change estimate of effect

Function; 3913 (44 studies)



Moderate Quality Evidence:
 Exercise moderately increased function
 More research may change estimate of effect

No evidence of increased dropout
 4607 (44 studies)
 No evidence for increased injuries

Draft Key Findings

- Lack of epidemiologic studies of association of PA with co-morbidities, including mortality.
- PA consistently beneficial for reducing pain & increasing function (WOMAC).
- PA consistently beneficial for improving QOL.
- Effects can be sustained up to 6 months, after cessation of intervention.
- Land-based exercise appears to be as efficacious as water-based exercise.
- PA appears to be as efficacious on pain in OA as analgesics, including opioids.

Draft Conclusion Statement



- Pending

Draft Research Recommendations

- Determine optimal dose, mode, intensity and sustainability for different types and severity of OA.
- More directed research on disease progression: cohort studies with disease status markers.
- Determine capacity of individuals with OA to perform PA at a level able to modify comorbidities.
- Develop predictors of responsiveness.
- Direct comparison of relative effectiveness of PA vs analgesics.

Committee Discussion

Q2. In people with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) disease progression, and (5) pain?

When it is determined there is a relationship between physical activity and a health outcome.

- Is there a dose-response relationship? If yes, what is the shape of the relationship?
- Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
- Does the relationship based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Question 3

3. In people with **hypertension**, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression, as determined from existing systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports?

When it is determined there is a relationship between physical activity and a health outcome (blood pressure),

- Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - Does the relationship vary by age, sex, race/ethnicity, socio-economic status, weight status, or resting blood pressure level?
 - Does the relationship based on: frequency, duration, intensity, type (mode), or how physical activity is measured?
- Source of evidence to answer question
 - SR/MA/Existing Report

Analytical Framework

Systematic Review Question

In people with hypertension, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression, as determined from existing systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports?

Target Population

Individuals of all ages with hypertension

Comparison

Individuals with hypertension who participate in varying levels of physical activity

Intervention/Exposure

All types and intensities of physical activity

Endpoint Health Outcomes

- Risk of co-morbid conditions
- Physical function
- Health-related quality of life
- Disease progression

Key Definitions

- Hypertension or high blood pressure is defined as having blood pressure higher than 140/90 mmHg or being on antihypertensive medications regardless of the BP level.
- Risk of co-morbid conditions: The chance of having one or more additional conditions
- Physical function: “Physical function” and “physical functioning” are regarded as synonyms that refer to: “the ability of a person to move around and to perform types of physical activity.”
- Health-related quality of life: “Health-related quality of life (HRQOL) is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning.” Source: HealthyPeople.gov
<https://www.healthypeople.gov/2020/topic-objectives/topic/health-related-quality-of-life-well-being>
- Disease progression: A change or worsening of a disease over time.

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- Study Subjects
 - Exclude: Studies of animals only

Inclusion/Exclusion Criteria



- **Date of Publication**
 - Original Research: Not applicable
 - Existing Sources: Include 2011 - Present
- **Study Subjects**
 - Include: People with hypertension
- **Study Design**
 - Include: Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports
 - Exclude: Narrative reviews, Commentaries, Editorials, Original research
- **Exposure/Intervention**
 - Include: All types and intensities of physical activity, including acute and chronic activity
 - Exclude: Missing physical activity, Therapeutic exercise, Physical fitness as the exposure, Physical activity only used as confounding variable
- **Outcome**
 - Include: Risk of co-morbid conditions, Physical function, Health-related quality of life, Disease progression

Search Terms: Physical Activity

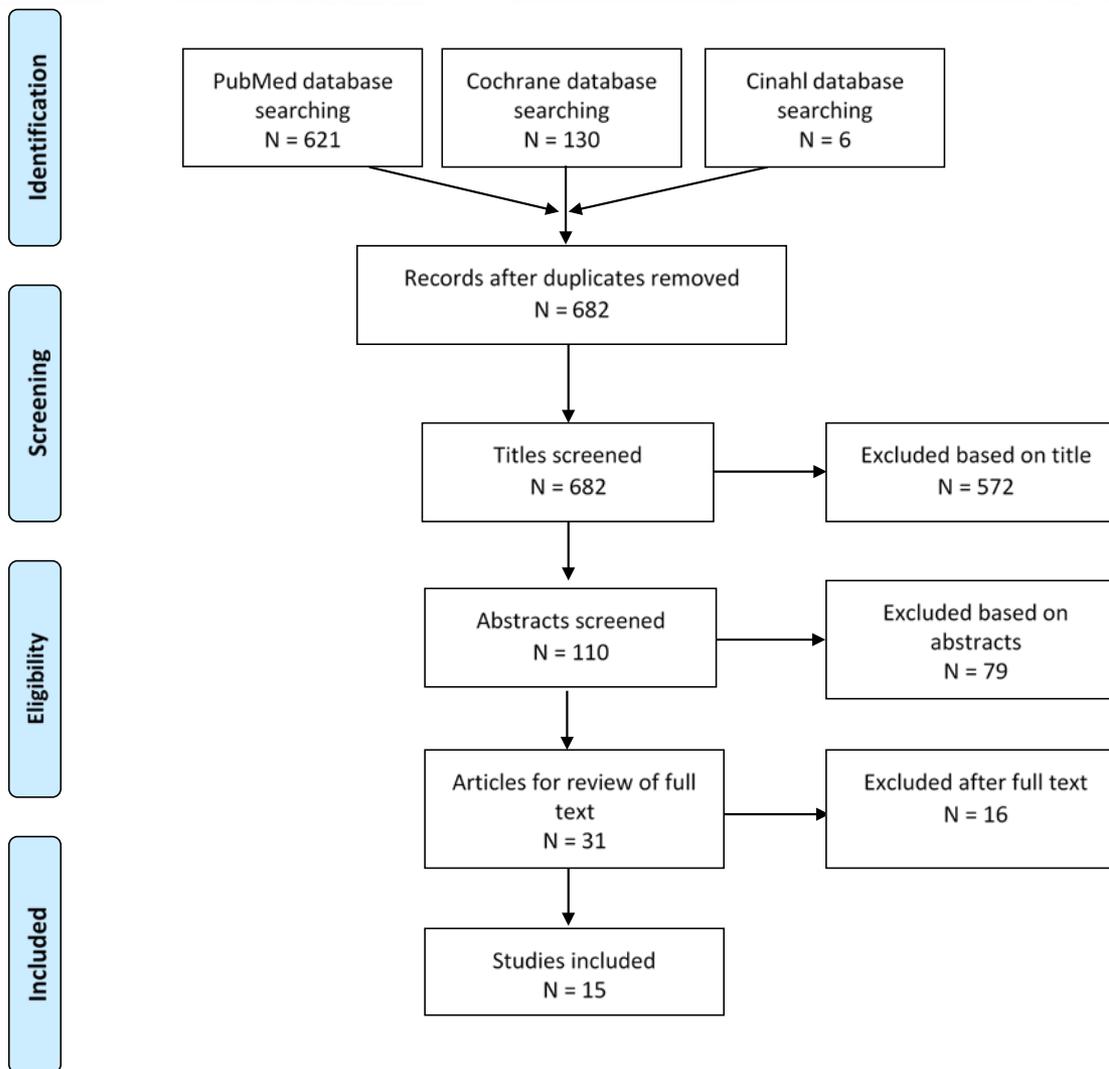


- Aerobic activity(ies)
- Aerobic endurance
- Bicycl*
- Cardiovascular activity(ies)
- Endurance activity(ies)
- Endurance training
- Exercise(s)
- Free living activity(ies)
- Functional training
- Leisure-time physical activity
- Lifestyle activity(ies)
- Muscle stretching exercises
- Physical activity(ies)
- Physical conditioning
- Qi gong
- Recreational activity(ies)
- Resistance training
- Running
- Sedentary lifestyle
- Sedentary
- Speed training
- Strength training
- Tai chi
- Tai ji
- Training duration
- Training frequency
- Training intensity
- Treadmill
- Walking
- Weight lifting
- Weight training
- Yoga

Search Terms: Condition

- Arterial pressure(s)
- Blood pressure(s)
- BP decrease
- BP measurement
- BP monitor(s)
- BP reduction
- BP response
- Diastolic pressure
- Hypertension
- Hypertensive
- Hypotension
- Hypotensive
- Mean arterial
- Normotension
- Normotensive
- Pre hypertension
- Pressure monitor
- Pulse pressure
- Systolic pressure
- Venous pressure

Search Results: High-Quality Reviews¹



Description of the Evidence

- 1 systematic review examined the outcome of cardiovascular mortality based upon 6 large prospective cohort studies [Rossi, 2012].
- 14 meta-analyses * of RCTs examined blood pressure response to PA in sedentary adults with hypertension.
 - All qualifying studies included adults with hypertension or subgroup analyses in people with hypertension*
 - Studies published through 2016.
 - Number of included studies varied: 4 to 93.
 - Total sample size: 125,986; sample ranged from 216-96,073.
 - Method of classifying people as having hypertension in meta-analyses (as well as individual studied reviewed) varied and often did not follow JNC 7 blood pressure classification scheme [Chobanian, 2003],

* [Carlson, 2014; Casonatto, 2016; Conceicao, 2016; Cornelissen, 2011, 2013b; Corso, 2016; Dickinson, 2006; Fagard 2007; MacDonald, 2016; Park, 2017; Wang, 2013; Wen, 2017; Xiong, 2015a,b]

Draft Key Findings

- For outcomes of co-morbidities, physical function, and health-related quality of life:
 - The search strategy did not locate sufficient evidence to address these outcomes.

Draft Conclusion Statement



- *For outcomes of co-morbidities, physical function, and health-related quality of life:*
- Insufficient evidence exists to determine whether a relationship exists between physical activity and risk of co-morbid conditions among adults with hypertension.
Grade: Grade not assignable
- Insufficient evidence exists to determine whether a relationship exists between physical activity and physical function among adults with hypertension.
Grade: Grade not assignable
- Insufficient evidence exists to determine whether a relationship exists between physical activity and health-related quality of life among adults with hypertension.
Grade: Grade not assignable

Draft Key Findings: Progression & CVD mortality

- 1 review of six prospective cohort studies [Rossi, 2012]:
 - Leisure time PA of ≈ 12 MET-hr \cdot wk $^{-1}$ or more reduced cardiovascular mortality 16 percent among men and 22 percent among women [Hu, 2007].
 - Higher amounts of leisure time physical activity equating to ≈ 18 MET-hr \cdot wk $^{-1}$ or more of leisure time physical activity reduced cardiovascular mortality 27 percent among men and 24 percent among women [Hu, 2007].
 - As systolic blood pressure increases, the risk of cardiovascular mortality was reduced 46 percent to 64 percent with higher levels of physical activity versus no physical activity [Vatten, 2006].

Draft Conclusion Statement

- For the outcome of progression:
 - Moderate evidence indicates an inverse, dose-response relationship between physical activity and cardiovascular mortality among adults with hypertension.
Grade: Moderate

Overall Context of PA and blood pressure

- Six meta-analyses were located which examined blood pressure classification as a moderator of the blood pressure response to physical activity:
 - Five reviews * found that PA caused the greatest reduction in blood pressure in people with hypertension.
 - The effect of PA in people with prehypertension was smaller.
 - The effect of PA in people with normal blood pressure was the smallest.

* [Carlson, 2014; Cornelissen, 2013b; Corso, 2016; Fagard, 2007; MacDonald, 2016] .

Draft Key Findings: Progression and BP

- Three recent meta-analyses of moderate to high quality examined the blood pressure response to aerobic, dynamic resistance, and combined aerobic and resistance exercise training in people with hypertension*: The data available are on the effect of PA on blood pressure across the entire range of blood pressure, not just in people with hypertension. Further, adults with highest blood pressure may not be allowed to exercise until blood pressure is reduced with medications.
 - Published thru 2016
 - Adults with hypertension experienced blood pressure reductions, on average, of 5-8 mmHg.
- * [Cornelissen, 2013b; Corso, 2016; MacDonald, 2016].

Draft Conclusion Statement

- Conclusion Statement: Limited evidence suggests the magnitude of the blood pressure response to physical activity varies by resting blood pressure level, with the greatest blood pressure reductions occurring among adults with hypertension that have the highest resting blood pressure levels.
- Grade: Limited

Draft Key Findings: Progression and BP

- In the few instances in which age, sex, race/ethnicity, socio-economic status, or weight status were examined as moderators of the blood pressure response to exercise training, results were disparate and were not reported by the BP classification of the sample as hypertension, prehypertension, and normal blood pressure.
- In the few instances in which frequency, intensity, and duration were examined as moderators of the blood pressure response to exercise training, results were disparate and were not reported by the BP classification of the sample as hypertension, prehypertension, and normal blood pressure.
- No meta-analyses reported any physical activity measure outside of the structured physical activity intervention.

Draft Conclusion Statement: Progression and BP

- Conclusion Statement: Insufficient evidence exists to determine whether the relationship between physical activity and blood pressure varies by age, sex, race/ethnicity, socio-economic status, and weight status among adults with hypertension.
- Grade: Grade not assignable

- Conclusion Statement: Insufficient evidence exists to determine whether the relationship between blood pressure and physical activity varies by frequency, intensity, and duration of physical activity, or how physical activity is measured.
- Grade: Grade not assignable

Draft Key Findings: Progression and BP

- Effect of Type of Physical Activity on Blood Pressure
 - 3 meta-analyses examined the blood pressure response to aerobic exercise training [Cornelissen, 2013b; Fagard, 2007; Murtagh, 2015],
 - 3 meta-analysis examined the blood pressure response to resistance exercise training [Casonatto, 2016; Cornelissen, 2011; MacDonald, 2016]
 - 1 meta-analysis examined the blood pressure response to combined aerobic and resistance exercise training [Corso, 2016]
 - 1 meta-analysis the blood pressure response to isometric resistance training [Carlson, 2014].
- Of these meta-analyses, 3 recent, moderate to high quality meta-analyses found that blood pressure was reduced by 5 to 8 mmHg among adults with hypertension, 2 to 4 mmHg among adults with prehypertension, and 1 to 2 mmHg among adults with normal blood pressure following exercise training, independent of type (mode) of physical activity.

Draft Conclusion Statement: Progression and BP

- Conclusion Statement: Moderate evidence indicates the relationship between physical activity and blood pressure does not vary by type (mode) of physical activity among adults with hypertension.
- Grade: Moderate

Draft Research

Recommendations: 1

- Conduct randomized controlled trials that examine the influence of age, sex, race/ethnicity, socio-economic status, and weight status on physical activity and blood pressure and other outcomes such as cardiovascular morbidity and mortality, risk of co-morbid conditions, physical function, health-related quality of life, and adverse events related to physical activity participation among adults with hypertension.
- Conduct randomized controlled trials that examine the influence of the frequency, intensity, time, and type (mode) of physical activity on blood pressure and other clinical outcomes such as cardiovascular morbidity and mortality, risk of co-morbid conditions, physical function, health-related quality of life, and adverse events related to physical activity participation among adults with hypertension.
- Conduct randomized controlled trials to examine the influence of complementary and alternative physical activity types (modes), such as yoga and Tai Chi, on blood pressure and other clinical outcomes compared to traditional types (modes) of physical activity among adults with hypertension.

Draft Research Recommendations: 2

- Conduct research that discloses the standard criteria and methods that were used to determine the blood pressure status of the study sample to better isolate samples with hypertension from those with normal blood pressure and prehypertension, and report results separately by blood pressure classification.
- Conduct research that discloses and quantifies medicine use, particularly antihypertensive medication use among samples with hypertension.
- Conduct research that examines both the acute (i.e., short-term or immediate) and the chronic (i.e., long-term or training) blood pressure response to physical activity.

Committee Discussion

3. In people with **hypertension**, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression, as determined from existing systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports?

When it is determined there is a relationship between physical activity and a health outcome,

- Is there a dose-response relationship? If yes, what is the shape of the relationship?
- Does the relationship vary by age, sex, race/ethnicity, socio-economic status, weight status, or resting blood pressure level?
- Does the relationship based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Question 4

4. In people with **type 2 diabetes**, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression, as determined from existing systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports?

When it is determined there is a relationship between physical activity and a health outcome,

- Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
 - Does the relationship based on: frequency, duration, intensity, type (mode), or how physical activity is measured?
- Source of evidence to answer question
 - Systematic Reviews, Meta-Analyses, or Existing Reports

Analytical Framework

Systematic Review Question

In people with type 2 diabetes, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression, as determined from existing systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports?

Target Population

Individuals of all ages with type 2 diabetes

Comparison

Individuals with type 2 diabetes who participate in varying levels of physical activity

Intervention/Exposure

All types and intensities of physical activity, including sedentary behavior

Endpoint Health Outcomes

- Risk of co-morbid conditions
- Health-related quality of life
- Physical function
- Disease progression

Key Definitions

- Type 2 Diabetes is a condition characterized by high blood glucose levels caused by either a lack of insulin or the body's inability to use insulin efficiently. (Source: American Diabetes Association: <http://www.diabetes.org/diabetes-basics/common-terms/common-terms-s-z.html#sthash.ezhRSF7M.dpuf>)
- Risk of co-morbid conditions: The chance of having one or more additional conditions
- Physical function: "Physical function" and "physical functioning" are regarded as synonyms that refer to: "the ability of a person to move around and to perform types of physical activity."
- Health-related quality of life: "Health-related quality of life (HRQOL) is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning." Source: HealthyPeople.gov <https://www.healthypeople.gov/2020/topics-objectives/topic/health-related-quality-of-life-well-being>
- Disease progression: A change or worsening of a disease over time.

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- Study Subjects
 - Exclude: Studies of animals only

Inclusion/Exclusion Criteria



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 - Original Research: Not applicable
 - Existing Sources: Include 2011 - Present
- Study Subjects
 - Include: People with type 2 diabetes
- Study Design
 - Include: Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports
 - Exclude: Narrative reviews, Commentaries, Editorials, Original research
- Exposure/Intervention
 - Include: All types and intensities of physical activity, including acute and chronic activity
 - Exclude: Missing physical activity, Therapeutic exercise, Physical fitness as the exposure, Physical activity only used as confounding variable, Do not present data on physical activity alone
- Outcome
 - Include: Risk of co-morbid conditions, Physical function, Health-related quality of life, Disease progression

Search Terms: Physical Activity

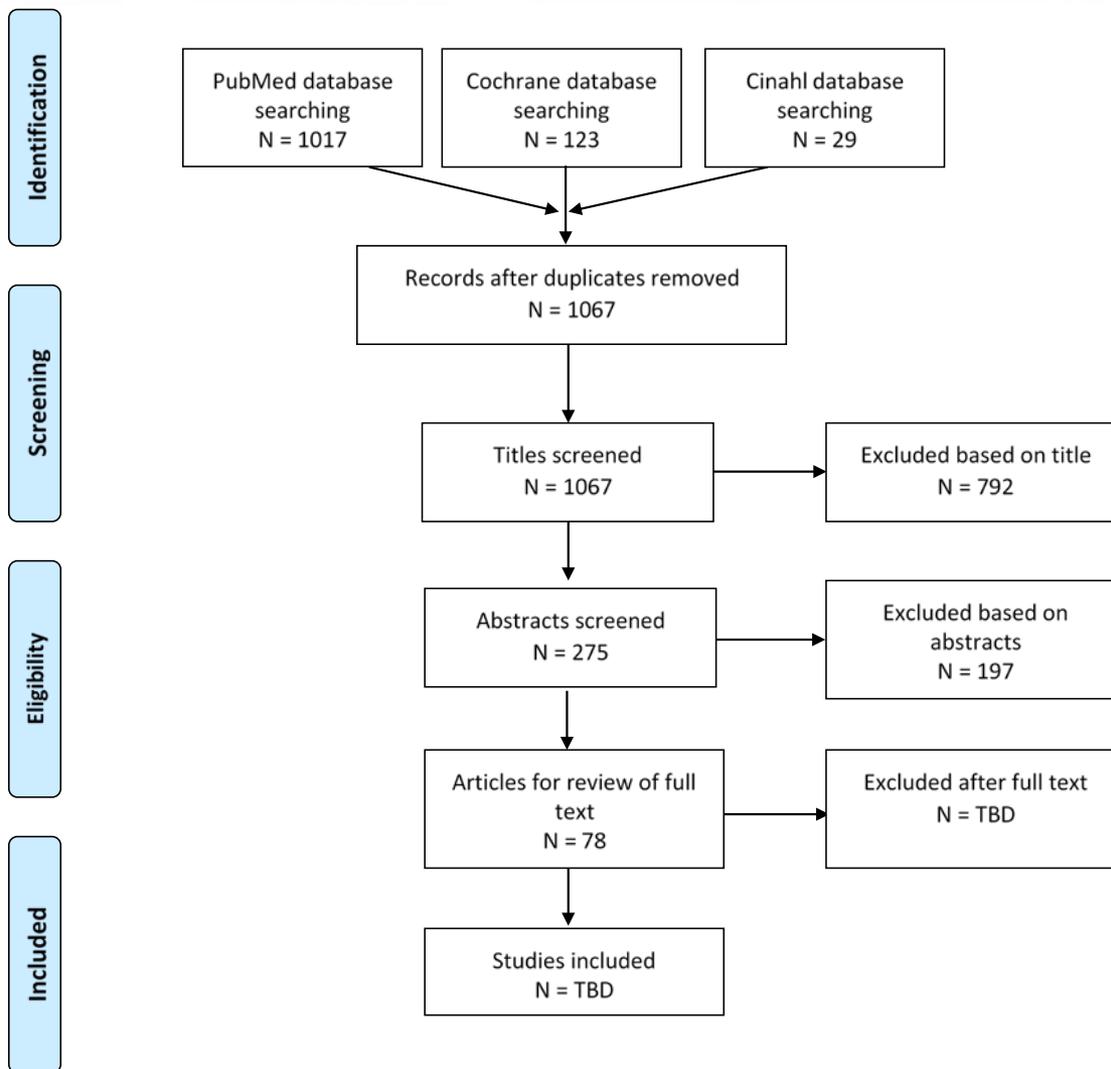


- Aerobic activity(ies)
- Aerobic endurance
- Bicycl*
- Cardiovascular activity(ies)
- Endurance activity(ies)
- Endurance training
- Exercise(s)
- Free living activity(ies)
- Functional training
- Leisure-time physical activity
- Lifestyle activity(ies)
- Muscle stretching exercises
- Physical activity(ies)
- Physical conditioning
- Qi gong
- Recreational activity(ies)
- Resistance training
- Running
- Sedentary lifestyle
- Sedentary
- Speed training
- Strength training
- Tai chi
- Tai ji
- Training duration
- Training frequency
- Training intensity
- Treadmill
- Walking
- Weight lifting
- Weight training
- Yoga

Search Terms: Condition

- Diabetes
- Diabetes mellitus

Search Results: High-Quality Reviews¹



Proposed Review of Progression

- Outcomes regarded as assessing progression:
 - Retinopathy, nephropathy, neuropathy, or diabetes-related foot conditions (e.g. ulceration, amputation)
 - Four indicators of elevated risk of the above: lipids, blood pressure, obesity/adiposity, A1C.
- For example, Q4 review will include effects of PA on A1C levels in people with T2DM.

Committee Discussion

4. In people with **type 2 diabetes**, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, and (4) disease progression, as determined from existing systematic reviews, meta-analyses, pooled analyses, and/or high-quality existing reports?

When it is determined there is a relationship between physical activity and a health outcome,

- Is there a dose-response relationship? If yes, what is the shape of the relationship?
- Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
- Does the relationship based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Next Steps



- Finish written evidence summaries for Q1 (cancer survivors) and Q3 (hypertension).
- Complete review of Q2 (osteoarthritis) and Q4 (type 2 diabetes).
- We propose a Q5: finalize topic and determine resources required.