



Meeting 5

Brain Health

Chair: Kirk Erickson

Members: Chuck Hillman, Rich Macko, David Marquez, Ken Powell

Experts and Consultants



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Subcommittee Questions



1. What is the relationship between physical activity and cognition?
2. What is the relationship between physical activity and quality-of-life?
3. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depressed mood and depression ?
4. What is the relationship between physical activity and sleep?

Question 1

1. What is the relationship between physical activity and cognition?
 - 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?
 - c) Does the relationship exist across the lifespan?
 - d) Does the relationship vary for individuals with normal to impaired cognitive function (i.e., dementia)?
 - e) What is the relationship between physical activity and biomarkers of brain health?

- Source of evidence to answer question
 - Systematic Reviews, Meta-Analyses

Analytical Framework



Systematic Review Question

What is the relationship between physical activity and cognition?

Target Population

People of all ages

Comparison

People who participate in varying levels of physical activity

Intervention/Exposure

All types and intensities of physical activity, including free-living activities, play, and physical fitness

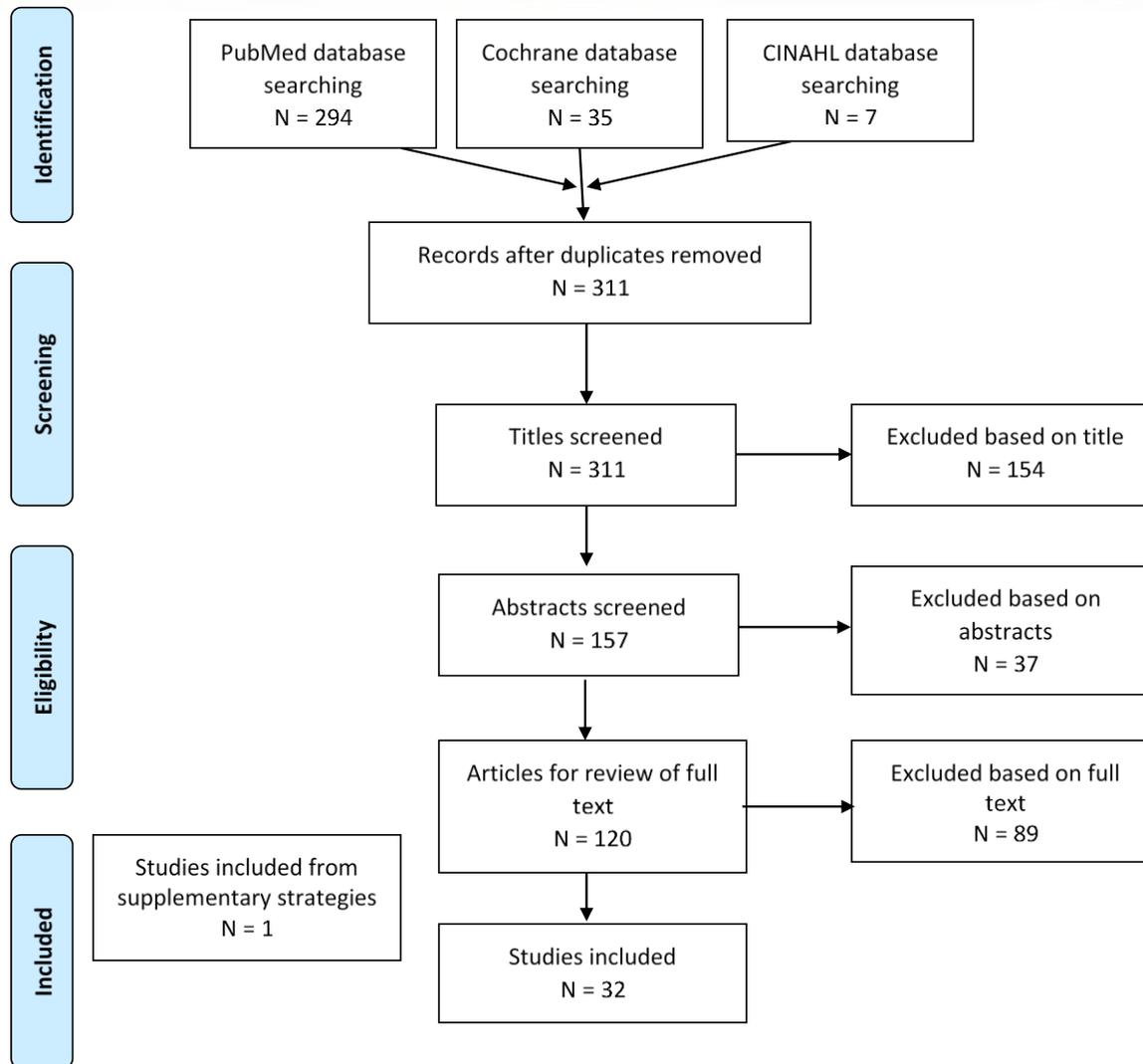
Endpoint Health Outcomes

- Academic achievement
- ADHD
- Alzheimer's disease
- Cognitive decline
- Cognition
- Cognitive function
- Cognitive processing / cognitive processes
- Cognitive impairment
- Cognitive motor / motor cognition
- Dementia
- Impaired cognitive function
- Impaired memory
- Independence / Instrumental ADL / Basic ADL
- Intelligence
- Memory
- Mild cognitive impairment

Key Definitions

- Cognition: The set of mental processes that contribute to perception, memory, intellect, and action. Cognitive function can be assessed using a variety of techniques including paper-pencil based tests, neuropsychological testing, and computerized testing methods. Cognitive functions are largely divided into different domains that capture both the type of process as well as the brain areas and circuits that support those functions. Working memory, visual attention, and long-term memory are all examples of different cognitive domains that are thought to be dependent on overlapping but yet largely separate neural systems.

Search Results: High-Quality Reviews¹



Draft Conclusion Statement

- What is the relationship between physical activity and cognition?
 - Moderate evidence indicates a consistent association between greater amounts of physical activity and cognition across the lifespan and in populations with impaired cognitive function.
- **PAGAC Grade: Moderate**

Modifications of prior grades

- Previous grade and conclusion:
 - Young adults: PAGAC Grade: Moderate
 - Consisted of acute and long-term studies
- New grade and categories:
 - Young adults (just long-term): PAGAC Grade: Grade Not Assignable
 - Only a few low quality studies of longer duration
 - Acute (across the lifespan): PAGAC Grade: Strong
 - This deserves a separate category because it included results across the lifespan (e.g., Ludyga et al., 2016)

Draft Key findings

- Acute exercise effects on cognition:
 - 4 high-quality reviews
 - 3 MA; 1 MR
 - Meta-analyses numbers:
 - Ludyga et al., 2016 (40 experimental studies)
 - Lambourne et al. 2010 (33 studies)
 - Chang et al., 2012 (79 studies)
 - McMorris et al., 2012 (53 studies)
- Preadolescents ES = .54
- Young adults ES = .20
- Older adults ES = .67

Draft Key findings

- Young adults:
 - Memory – 2 RCTs – no significant effects (Roig et al., 2013)
 - Too few studies to establish an effect on executive function (Smith et al., 2010).

Draft conclusion statement

- Acute exercise:
 - Strong evidence demonstrates that acute bouts of moderate-intensity exercise transiently improves cognition (i.e., executive function).
- PAGAC Grade: Strong

Draft conclusion statement

- Young adults:
 - Insufficient evidence is available to determine if long-term physical activity improves cognitive function
- PAGAC Grade: Grade Not Assignable

Modifications of prior grades

- Prior grade for conditions of cognitive dysfunction = Moderate
 - This was based on an aggregation of studies examining ALL conditions including dementia, ADHD, schizophrenia, Parkinson's disease, Multiple Sclerosis, stroke.
- New category and definitions:
 - Risk for dementia – Strong
 - Treatment of dementia – Moderate
 - Other conditions associated with cognitive dysfunction - Moderate

Risk for cognitive decline

- Alzheimer's disease
 - Observational studies
 - 9 studies; RR of 0.61 for physically active versus not physically active (Beckett et al., 2015)
 - 38% reduced decline in >33,000 subjects (Sofi et al., 2011)
 - Strong evidence in favor of physical activity associated with a reduced risk of decline
 - There remains poor information about dose-response effects

Treatment of cognition



- Alzheimer's disease and mild cognitive impairment
 - 18 studies of medium quality (Groot et al., 2016)
 - Positive effect of exercise interventions on cognition (SMD=0.42)
 - AD; SMD=0.338
 - AD or non-AD; SMD=0.47
 - Effects were significant at both low and high frequency (Zheng et al., 2016)

Draft conclusion statement

- Risk for dementia:
 - Strong evidence demonstrates that greater amounts of physical activity is associated with a reduced risk of developing dementia.
- PAGAC Grade: Strong

Draft conclusion statement

- Treatment of dementia:
 - Moderate evidence indicates that physical activity improves cognitive function in individuals with dementia.
- PAGAC Grade: Moderate

Draft conclusion statement

- Treatment of conditions associated with cognitive problems
 - Moderate evidence indicates that physical activity improves cognitive function in individuals with conditions that affect cognitive function (e.g., ADHD).
- PAGAC Grade: Moderate

Draft Research Recommendations

- Conduct research in children <6 yrs of age and middle-aged adults
- Longitudinal studies on older adults with multiple comorbidities
- Better understand biomarkers with brain health and the relative role of genetic and environmental risk factors
- Improve understanding of effects of physical activity in individuals with cognitive impairment
- Improve understanding of dose-response relationship
- Improve understanding of impact of sedentary behavior on cognitive outcomes
- Improve understanding of demographic factors on moderating effect of the physical activity-cognition relationship.
- **Conduct studies and analyze data to better understand dose-response effects in the context of dementia and other conditions.**

Question 2

2. What is the relationship between physical activity and quality-of-life?
 - 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?
- Source of evidence to answer question
 - Systematic Reviews, Meta-Analyses, and Pooled Analysis

Analytical Framework

Systematic Review Question

What is the relationship between physical activity and quality-of-life?

Target Population

People of all ages, including healthy people and people with psychiatric disorders or cognitive impairment

Comparison

People who participate in varying levels of physical activity

Intervention/Exposure

All types and intensities of physical activity, including free-living activities, and play

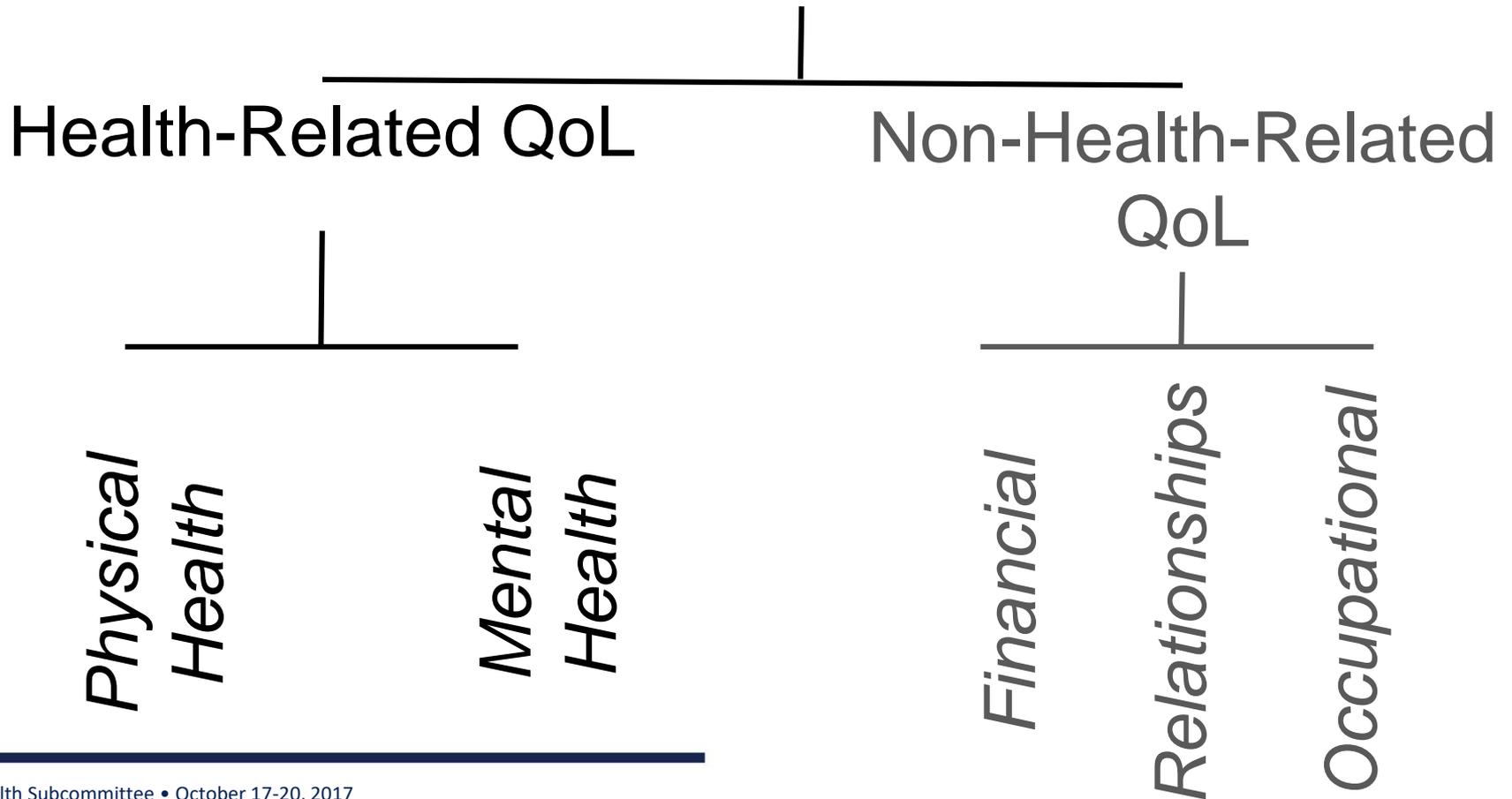
Endpoint Health Outcomes

- Quality of Life
- Life Satisfaction
- Health-Related Quality of Life
- Social Quality of Life

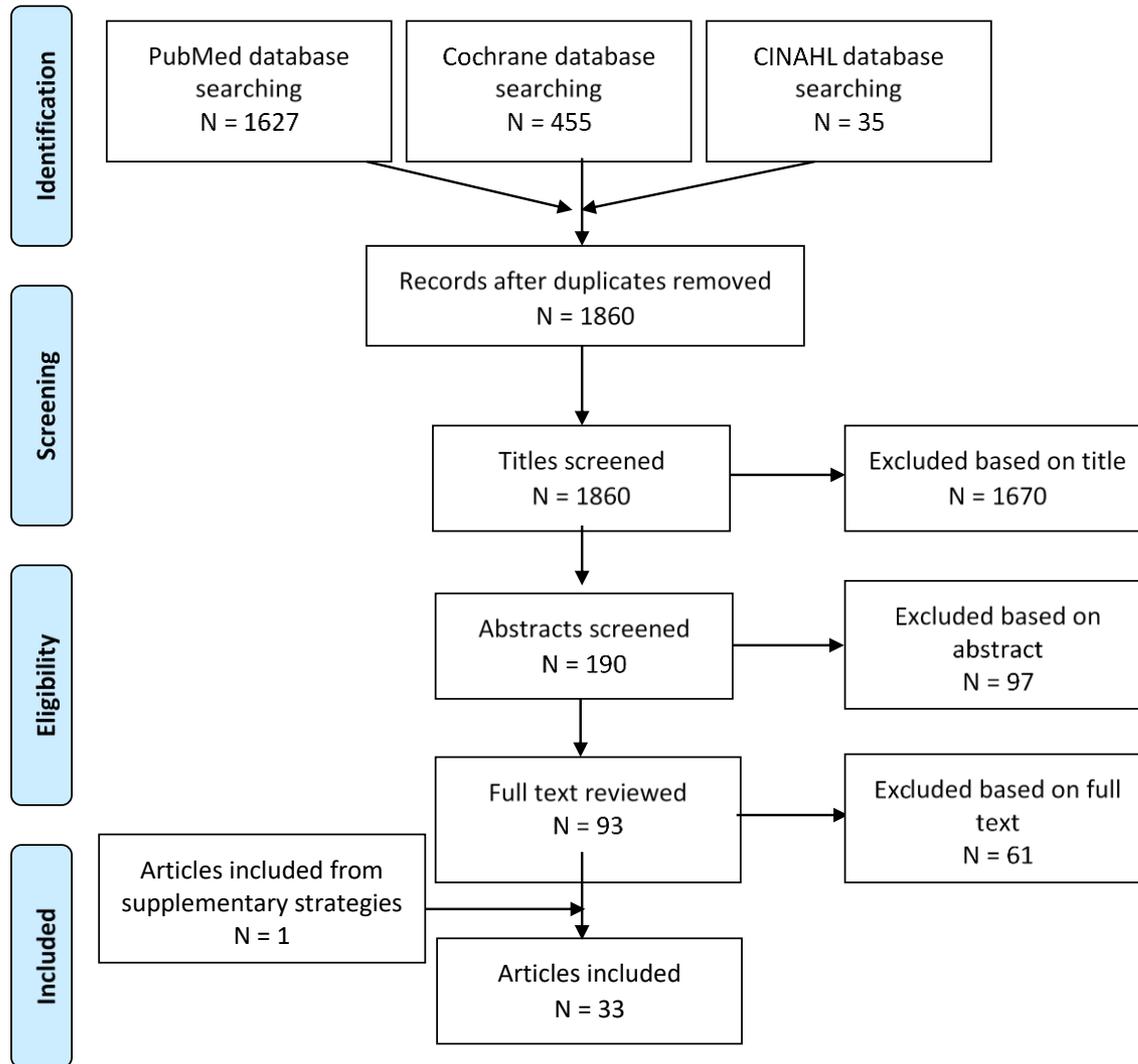
Key Definitions

- Quality of Life: “Quality of life, rather than being a description of patients’ health status, is a reflection of the way that patients perceive and react to their health status and to other, nonmedical aspects of their lives” (Source: Gill TM, Feinstein AR. A critical appraisal of the quality of quality-of-life measurements. *JAMA*. 1994;272:619-626.)

Overall Quality of Life (Satisfaction with Life)



Search Results: High-Quality Reviews¹



Draft Description of the Evidence

- Large heterogeneous literature covering *many* different populations, study designs, and Quality of Life outcomes (momentary to satisfaction with life)
- Largest categories: Older adults & Adults
- 6 'categories':
 - Older adults (11 systematic reviews, 8 meta-analyses, 1 pooled analysis)
 - Adults (6 systematic reviews, 3 meta-analysis)
 - Youth (1 systematic review, 0 meta-analysis)
 - Depression (1 systematic review, 2 meta-analyses)
 - Schizophrenia (0 systematic reviews, 1 meta-analysis)
 - Intellectual Disabilities (1 systematic review, 0 meta-analyses)

Draft Key Findings

- Older Adults (all > 50 yrs)
 - Strong evidence demonstrates that physical activity improves the physical subdomain of HRQoL
 - effect size= 0.41, 95% CI: 0.19 to 0.64 (Kelley, 11 RCTs)
 - Limited evidence suggests that physical activity improves the mental subdomain of HRQoL (effect size = 0.16, 95% CI, -0.81 to 0.5)
 - Limited evidence for frail / institutionalized older adults (only 1 study)
 - Limited evidence in dementia populations.
- Adults (18-65 years)
 - Strong evidence demonstrates that physical activity improves the physical and mental subdomains of HRQoL.
 - Physical health (SMD = 0.22; 0.07 to 0.37)
 - Psychological well-being (SMD = 0.21; 0.06 to 0.36)

Draft Key Findings

- Youth (5-18 years)
 - Limited evidence suggests that lower levels of sedentary time are associated with higher perceptions of global QoL.
 - Of 91 studies, 12 cross sectional and 3 longitudinal provided information about sedentary behavior and well-being or QoL among youth 5 to 18 yrs [Suchert et al., 2015].
 - 9/12 cross-sectional and 2/3 longitudinal reported that lower sedentary time was associated with elevated well-being or QoL.

Draft Key Findings



- Schizophrenia
 - Limited evidence suggests that physical activity improves overall QoL.
 - Effects were of moderate size (Hedges' $g = 0.55$)
 - Effects were of similar size for aerobic (7 trials) and yoga (3 trials) (Hedges' $g = 0.58$)
- Depression
 - Limited evidence suggests that physical activity improves physical function or overall QoL (only 3 reviews; small number of high quality studies with mixed findings)

Draft Conclusion Statement

- Strong evidence demonstrates that physical activity improves quality of life in adults and older adults.
- **PAGAC Grade: Strong**

Draft Conclusion Statement

- Is there a dose-response relationship between physical activity and quality-of-life?
 - Insufficient data available.
- **PAGAC Grade: Grade Not Assignable**
- Does the relationship vary by age, sex, race/ethnicity, socioeconomic status, or weight status?
 - Insufficient data available.
- **PAGAC Grade: Grade Not Assignable**

Draft Research Recommendations

- Include measures of QoL into more RCTs
- RCTs should be conducted with more diverse populations
- Incorporate QoL into prospective studies
- More studies on global QoL, i.e., life satisfaction
- More studies of non-aerobic physical activity and QoL
- Investigate daily physical activity and QoL

Committee Discussion

2. What is the relationship between physical activity and quality-of-life?
 - 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?

Question 3

3. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depressed mood and depression?
 - 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?
 - c) Does the relationship exist across a continuum of mood and affective disorders (i.e., depression)?
 - d) What is the relationship between physical activity and brain structure and function?
- Source of evidence to answer question
 - Systematic Reviews and Meta-Analyses

Analytical Framework



Systematic Review Question

What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depressed mood and depression?

Target Population

People of all ages, including healthy people and people with psychiatric disorders or cognitive impairment

Intervention/Exposure

All types and intensities of physical activity, including free-living activities, sedentary behavior, play, and single, acute bouts of physical activity

Comparison

People who participate in varying levels of physical activity

Endpoint Health Outcomes

- Activation
- Affect
- Affect/Mood Disorders
- Anger
- Anxiety
- Anxiety Disorders
- Arousal
- Bipolar disorder
- Dejection
- Depression
- Dysthymia
- Emotion
- Feeling
- Hostility
- Hypervigilance
- Mood
- Nervousness
- Pleasant
- Pleasure
- Post-traumatic stress disorder (PTSD)
- Symptoms of Anxiety or Mood Disorders
- Tension
- Valence
- Vigor
- Worry

Definitions

- Affect: subjective experience of feeling states defined by independent dimensions of valence (pleasure) and activation.
- Anxiety: unpleasant high activation feeling state characterized by feelings of apprehension, worry, and physical sensations arising from activation of the autonomic nervous system. In the extreme, these feelings can become a clinical disorder.
- Depression: unpleasant low activation feeling state characterized by sadness, or feelings of hopelessness or guilt. In the extreme, these feelings can become a clinical disorder.

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 published since 2006
 - Systematic reviews, meta-analyses, pooled analyses, and reports published since 2006
- **Study Subjects**
 - Include: Human subjects, people of all ages
- **Study Design**
 - Include: Randomized controlled trials, Non-randomized controlled trials, Prospective cohort studies, Retrospective cohort studies, Case-control studies, Before-and-after studies, Time series studies, Systematic reviews, Meta-analyses, Pooled analysis, Reports
 - Exclude: Cross-sectional studies, Narrative reviews, Commentaries, Editorials
- **Exposure/Intervention**
 - Include: All types and intensities of physical activity, including free-living activities, play, sedentary behavior. Studies with single, acute bouts of exercise as the exposure
 - Exclude: Studies that do not include physical activity; Studies with physical fitness as the exposure; Studies of a specific therapeutic exercise delivered by a medical professional (e.g., physical therapist); Studies of multimodal interventions that do not present data on physical activity alone; Studies where physical activity is only used as a confounding variable.
- **Outcome**
 - Activation, Affect, Affect/Mood Disorders, Anger, Anxiety, Anxiety Disorders, Arousal, Bipolar disorder, Dejection, Depression, Dysthymia, Emotion, Feeling, Hostility, Hypervigilance, Mood, Nervousness, Pleasant, Pleasure, Post-traumatic stress disorder (PTSD), Symptoms of Anxiety or Mood Disorders, Tension, Valence, Vigor, Worry

Search Terms: Physical Activity

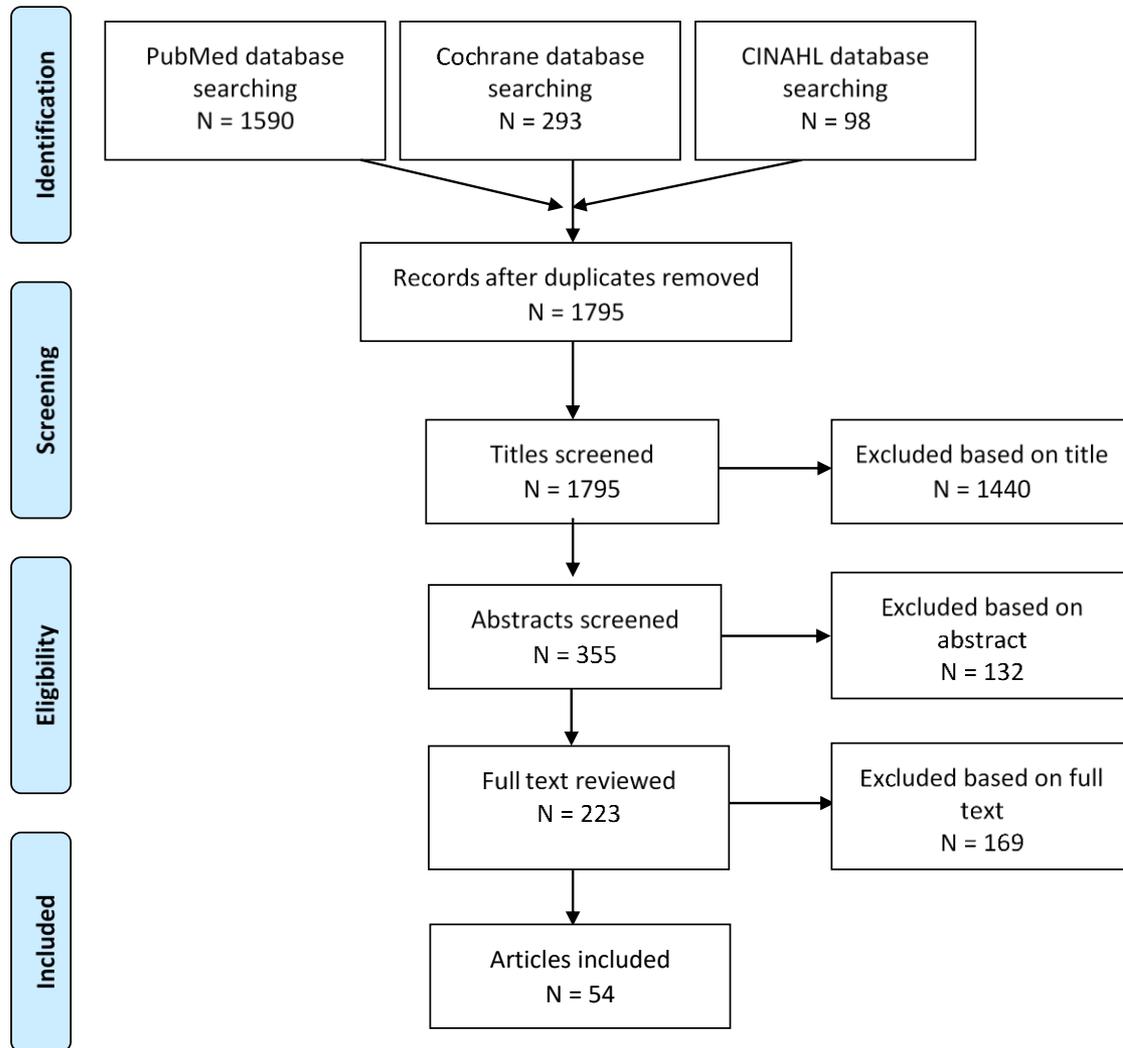


- Aerobic activity(ies)
- Balance training
- Cardiovascular activity(ies)
- Chi kung
- Computer time
- Computer use
- Endurance activity(ies)
- Endurance training
- Exercise
- Free living activity(ies)
- Functional training
- Inactivity
- Lifestyle activity(ies)
- Motor performance
- Motor skill(s)
- Physical activity(ies)
- Physical conditioning
- Physical education
- Physical education and training
- Physically inactive
- Qi gong
- (Recess AND (Child OR Youth))
- Recreational activity(ies)
- Resistance training
- Screen time
- Sedentarism
- Sedentary lifestyle
- Sedentary
- Sitting
- Strength training
- Stretching
- Tai chi
- Tai ji
- Television
- TV viewing
- TV watching
- Video game(ing)
- Walk(ing)
- Yoga

Search Terms: Outcome

- Activate(d), (s), (ation)
- Adjustment disorder(s)
- Affect disorder(s)
- Affect(ive)
- Anger
- Antidepressant
- Anxiety disorder(s)
- Anxiety
- Anxiolytic
- Arousal
- Aroused
- Bipolar disorder(s)
- Dejection
- Depressed(ion)
- Depressive
- Dysthymia
- Dysthymic Disorder
- Emotion(s), (al)
- Feelings
- Hostility
- Hypervigilance
- Mood disorder(s)
- Mood
- Nervous(ness)
- Panic
- Phobia
- Pleasant
- Pleasure(able)
- PTSD
- Tension
- Trauma and Stressor Related Disorders
- Traumatic stress disorder(s)
- Valence
- Vigor
- Worried
- Worries
- Worry

Search Results: High-Quality Reviews¹



Description of the Evidence

- RCTs and acute exercise studies
- Covering normal variations in affect to clinical disorders.
 - Affect: 2 systematic review; 1 meta-analysis
 - Anxiety: 5 systematic reviews; 5 meta-analyses
 - Depression and Depressed mood: 17 systematic reviews; 27 meta-analyses

Draft Key Findings

- Affect:
 - Below the lactate/ventilatory threshold
 - imposed exercise intensity was slightly less pleasant than self-selected exercise ($d = -0.36$)
 - At the lactate/ventilatory threshold
 - imposed exercise intensity was moderately less pleasant than self-selected exercise ($d = -0.57$)
 - Above the lactate/ventilatory threshold
 - imposed exercise intensity was much less pleasant than self-selected exercise ($d = -1.36$)
 - Post-exercise
 - no difference in post-exercise affective valence as a function of interval vs continuous training
 - Oliveira et al., 2015, Stork et al., 2017 (9 studies; $N=207$), Liao et al., 2015 (10 studies; >1000 participants)
 - 10 experimental studies with $N=241$ (Oliveira et al., 2015)

Draft Conclusion Statement

- **Affect:**
 - Strong evidence demonstrates that increasing intensity of physical activity reduces pleasure during exercise.
- **PAGAC Grade: Strong**

Draft Key Findings

- Anxiety
 - Acute bouts of exercise yields a small but significant decrease in anxiety ($g = -0.16$) (Ensari et al., 2015)
 - 36 experimental studies (N=1233)
 - Within 1 meta-analysis of meta-analyses, longer-term exercise interventions reduces anxiety (Overall Cohen's $d=0.34$; RCTs= 0.45):
 - 54 studies (N=47229)
 - at least to the same extent as established treatments
 - to a greater extent than placebo in both “normal” populations
 - in individuals with anxiety disorders or clinical anxiety
 - Limited evidence in individuals with post-traumatic stress disorder
 - In youth:
 - Meta-analysis – all findings favor PA intervention
 - tension/anxiety (-0.36 ; 95% CI: $-0.71, -0.01$),

Draft Conclusion Statement



- For the general population, strong evidence demonstrates:
 - Reduced state anxiety following acute bouts of exercise
 - Reduced trait anxiety following weeks/months of regular exercise.
- Exercise (both acute and chronic) alleviates anxiety symptoms in individuals with anxiety disorders and/or clinical symptoms of anxiety.
- **PAGAC Grade: Strong**

Draft Key Findings

- Depression and Depressed Mood in adults
 - Prevention:
 - Greater amounts are associated with reduced rates of depression (Mammen et al., 2013; 30 observational studies (25 showed effects))
 - <150 minutes/week was associated with prevention; >30 minutes/day reduced odds of developing depression by 48%
 - Treatment:
 - Consistent and large effects
 - -.53 to -1.39 (Josefsson et al., 2014; Stathanopolous et al., 2006)
 - When compared to CBT or medication there are no significant differences
 - Exercise is as effective as these treatments
 - Effect size larger for clinical depression (-1.03) and smaller for depressive symptoms (-.59)
 - Insufficient evidence available for caregivers, people with dementia, alternative modes of activity (e.g., yoga), schizophrenia, or other neurologic/psychiatric conditions.

Draft Key Findings Youth

- Depressive symptoms in youth
 - 5/5 of physical activity reported reduction in symptoms (2 SR, 2 MA, 1 RR)
 - Hedge's $g = -0.26$ (95% CI: $-0.43, -0.08$)
 $P=0.004$
 - 1 Review of reviews
 - SMD of $-.62$ (95% CI: $-.81$ to $-.42$)
- Sedentary behavior: 6 studies of 6 reported significantly worse depressive symptoms

Draft Conclusion Statement

- Strong evidence demonstrates that:
 - Greater amounts of physical activity reduces the risk for depression
 - Engaging in physical activity is an effective treatment for depression across the lifespan
 - As effective as other available treatment methods
- **PAGAC Grade: Strong**

Draft Key Findings

- Dose-response
 - Affect: Increasing intensity of physical activity temporarily *reduces* pleasure, but effects only persist while maintaining or increasing intensity
 - Anxiety: Limited evidence for a dose-response relationship for anxiety reduction.
 - Depression: Longer durations at variable levels of intensity reduce depressive symptoms

Draft Conclusion Statement

- Strong evidence demonstrates an acute dose-response of activity intensity such that more intense activities increase displeasure during (but not after) activity
 - **PAGAC Grade: Strong**
- Limited evidence suggests a dose response effect of intensity on anxiety symptoms.
 - **PAGAC Grade: Limited**
- Moderate evidence indicates a dose-response effect of activity on depression/depressive symptoms
 - **PAGAC Grade: Moderate**

Draft Key Findings

- Moderation by age, sex, race/ethnicity, socio-economic status, or weight status?
 - Affect: Insufficient evidence
 - Anxiety: State anxiety reduction appears greater for females, adults >25 yrs of age, and for sedentary individuals. Insufficient evidence is available on other factors.
 - Depression: Moderate evidence that physical activity reduces depressive symptoms more in females than males. Insufficient evidence is available on other factors
 - Females also have higher prevalence

Draft Conclusion Statement



- Moderate evidence indicates that effects of physical activity on anxiety and depression is greater for females than males.
 - **PAGAC Grade: Moderate**

- Insufficient evidence to determine whether age, race, SES, or weight status modify the relationship.
 - **PAGAC Grade: Grade Not Assignable**

Draft Key Findings

- Are effects significant in disorders of anxiety and depression?
 - Major depression - Strong
 - Anxiety disorders - Strong
 - PTSD - Limited
- Depression: Effect sizes are larger for clinical populations (-1.06) than for populations without these clinical conditions (-.53).

Draft Conclusion Statement

- Strong evidence demonstrates that physical activity reduces anxiety and depression in individuals with major depression and anxiety disorders.
- **PAGAC Grade: Strong**

Draft Conclusion Statement

- Does a relationship exist between physical activity and brain structure and function in the context of depression and anxiety?
 - Insufficient amount of evidence available
- **PAGAC Grade: Grade Not Assignable**

Draft Research Recommendations



- **Affect:**
 - Research on resistance training and sedentary behavior reduction.
 - Affective responses to exercise need to be investigated in older adults.
 - Experimental studies of post-exercise affective responses are needed to understand the time course and persistence of affective responses.
 - Individual differences that moderate affective responses need to be investigated
- **Anxiety:**
 - Better designed RCTs for both acute and chronic exercise effects of state and trait anxiety across the age spectrum.
 - More studies comparing effectiveness and dose-response effects of treatments
 - Examination of effects of other physical activity interventions (e.g., yoga, tai chi, qigong, sedentary behavior reduction).
- **Depression:**
 - More research on moderators including demographic factors
 - Better understanding of biological and other mechanisms by which physical activity reduces depressive symptoms in humans
 - More research on the impact of sedentary time on risk for depression

Committee Discussion

3. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depressed mood and depression?
 - 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?
 - c) Does the relationship exist across a continuum of mood and affective disorders (i.e., depression)?
 - d) What is the relationship between physical activity and brain structure and function?

Question 4

4. What is the relationship between physical activity and sleep?

- 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?
 - c) Does the relationship exist for individuals with impaired sleep behaviors or disorders? If yes, for which sleep disorders?
- Source of evidence to answer question
 - Systematic Reviews and Meta-Analyses

Analytical Framework

Systematic Review Question

What is the relationship between physical activity and sleep?

- 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 exist for individuals with impaired sleep behaviors or disorders? If yes, for which sleep disorders?

Target Population

People of all ages, including healthy people and people with sleep disorders, psychiatric disorders, or cognitive impairment

Comparison

People who participate in varying levels of physical activity

Intervention/Exposure

All types and intensities of physical activity, including free-living activities, sedentary behavior, play, and single, acute bouts of physical activity

Endpoint Health Outcomes

- | | | |
|--------------------|--------------------------|--------------------|
| • Sleep Quality | • Sleep Latency | • Total sleep time |
| • Sleep Duration | • Wake-after sleep onset | • Zeitgeber |
| • Sleep-wake cycle | • WASO | |

Key Definitions

Sleep is a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment, which consists of two separate states that are as different from one another as they are from wakefulness: Rapid Eye Movement (REM), and Non-REM. (Kryger 2015, *Principles and Practices of Sleep Medicine*)

Common Inclusion/Exclusion Criteria



- Language
 - Include: Studies published with full text in English
- Publication Status
 - Include: Studies published in peer-reviewed journals, PAGAC-approved reports
 - Exclude: Grey literature
- Study Subjects
 - Include: Human subjects

Inclusion/Exclusion Criteria



- **Date of Publication**
 - Original Research: 2006 - Present
 - Existing Sources: Include 2011 - Present
- **Study Subjects**
 - Include: Human subjects, people of all ages
- **Study Design**
 - Include: Randomized controlled trials, Non-randomized controlled trials, Prospective cohort studies, Retrospective cohort studies, Case-control studies, Before-and-after studies, Time series studies, Systematic reviews, Meta-analyses, Pooled analysis, Reports
 - Exclude: Cross-sectional studies, Narrative reviews, Commentaries, Editorials
- **Exposure/Intervention**
 - Include: All types and intensities of physical activity, including free-living activities, play, sedentary behavior. Studies with single, acute bouts of exercise as the exposure. Physical activity as treatment for impaired sleep behaviors.
 - Exclude: Studies that do not include physical activity; Studies with physical fitness as the exposure; Studies of a specific therapeutic exercise delivered by a medical professional (e.g., physical therapist); Studies of multimodal interventions that do not present data on physical activity alone; Studies where physical activity is only used as a confounding variable.
- **Outcome**
 - Include: Sleep quality, Sleep duration, Sleep-wake cycle, Sleep latency, Wake-after sleep onset (WASO), Zeitgeber, Total sleep time

Search Terms: Physical Activity

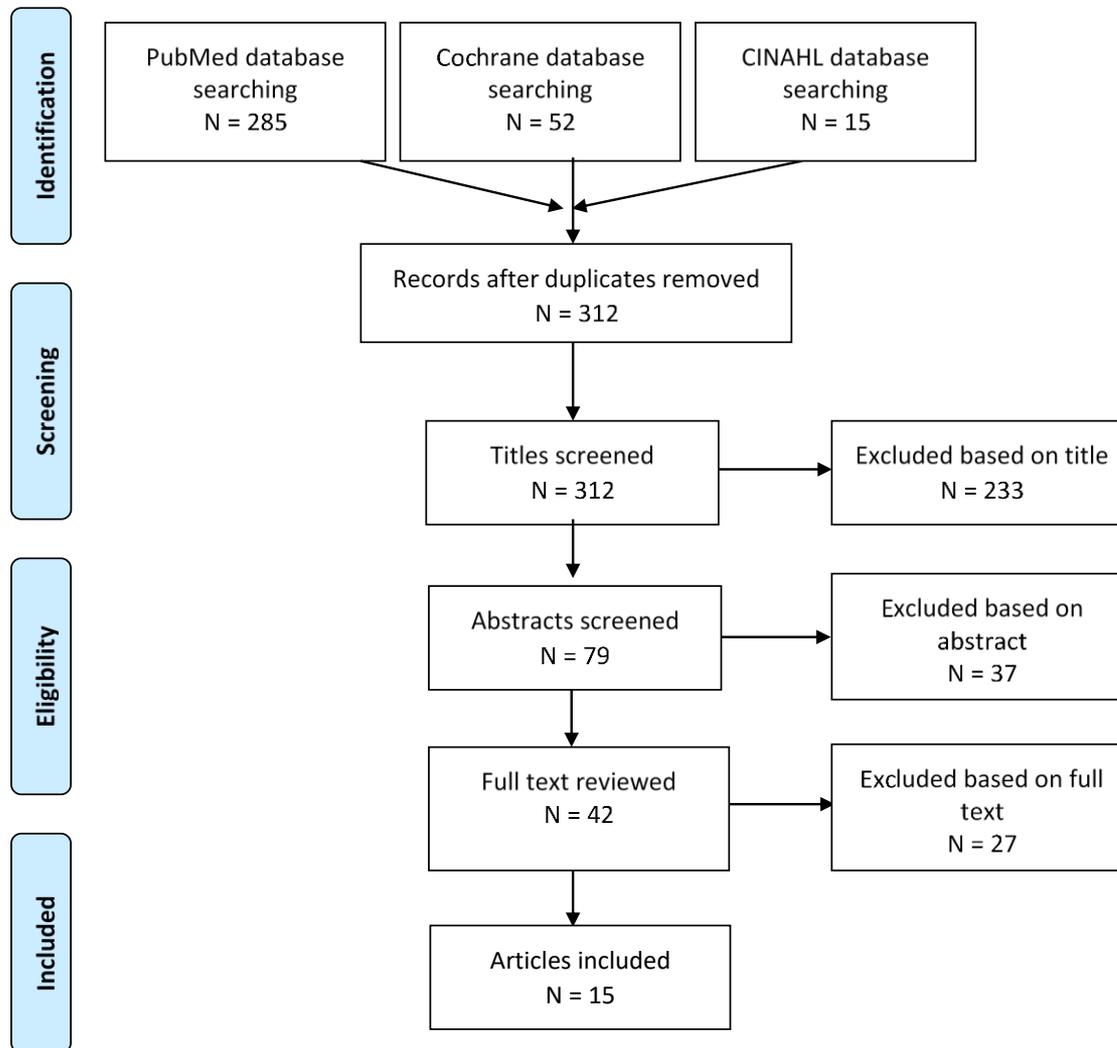


- Aerobic activity(ies)
- Balance training
- Cardiovascular activity(ies)
- Chi kung
- Computer time
- Computer use
- Endurance activity(ies)
- Endurance training
- Exercise
- Free living activity(ies)
- Functional training
- Inactivity
- Lifestyle activity(ies)
- Motor performance
- Motor skill(s)
- Physical activity(ies)
- Physical conditioning
- Physical education
- Physical education and training
- Physically inactive
- Qi gong
- (Recess AND (Child OR Youth))
- Recreational activity(ies)
- Resistance training
- Screen time
- Sedentarism
- Sedentary lifestyle
- Sedentary
- Sitting
- Strength training
- Stretching
- Tai chi
- Tai ji
- Television
- TV viewing
- TV watching
- Video game(ing)
- Walk(ing)
- Yoga

Search Terms: Outcome

- Body clock(s)
- Circadian Clock(s)
- Circadian Rhythm(s)
- Sleep
- Sleep-wake
- Sleep/wake
- WASO (Wake after sleep onset)
- Zeitgeber

Search Results: High-Quality Reviews¹



What is the relationship between physical activity and sleep?

Sleep: Sources of Evidence for General Adult Population



- 10 Review articles
 - 5 meta-analyses
 - 5 systematic reviews
- The reviews include >130 individual research articles.
- Findings consistent across reviews.
- Adults: 66 intervention studies of various designs in N = 2,863 adults aged 18-89 years; 89% without and 11% with sleep problems; 23% high intensity and 23% low intensity PA (Kredlow et al., 2015).

Physical Activity and Sleep Outcomes



Sleep Outcome	Regular Physical Activity Cohen d effect size, 95% CI	Acute Bouts of Physical Activity Cohen d effect size, 95% CI
Total Sleep Time	d = 0.25, (95% CI, 0.07 to 0.43)	d = 0.22 (95% CI, 0.10 to 0.34)
Sleep Efficiency	d = 0.30 (95% CI, 0.06 to 0.55)	d = 0.25 (95% CI, 0.12 to 0.39)
Sleep Onset Latency	d = 0.35, (95% CI, 0.00 - 0.70)	d = 0.17 (95% CI, -0.02 to 0.32)
Sleep Quality	d = 0.74, (95% CI, 0.48 to 1.00)	Insufficient evidence
Slow Wave Sleep	Higher baseline physical activity is a response modifier for increased slow wave sleep response to an acute bout (d=0.51, P<0.01)	d = 0.19, 95 % CI, 0.02, 0.35, p = .03
Rapid Eye Movement Sleep	Insufficient evidence	d = -0.27, 95 % CI (-0.45, -0.08)

Modified from Kredlow et al. (59 studies; 2,863 adults)

PA and Sleep -General Adult Population



PA Modalities (aerobic; resistance; combined): Similar positive relationship on the majority of sleep outcomes. Limited evidence for differences in a small number of sleep outcomes (slow wave sleep).

PA Dose Characteristics: 30-90 minutes per session, typically 3-to-5 sessions per week, all with similar small-to-moderate positive effect sizes.

Mind-body Exercise Programs (Yoga, Tai Chi, Qigong) show trend toward stronger relationship with sleep outcomes ($d = 0.98$ vs. 0.48); but this does not reach significance, and mind vs. body contributions cannot be separated (small sample sizes).

Draft Conclusion Statement

Strong evidence demonstrates both acute bouts of physical activity and regular physical activity improves sleep outcomes.

- **PAGAC Grade: Strong**

Evidence on PA and Sleep Dose-Response

Sources for Adults: 66 trials (Kredlow et al., 2015)

Length in minutes of acute PA bouts moderates beneficial effects on total sleep time, slow wave sleep, sleep onset latency, stage 4 sleep, REM sleep latency, and REM sleep.

Length in minutes of regular PA modifies sleep onset latency.

PA Intensity: not significantly related to sleep outcomes.

Draft Conclusion Statement

- Moderate evidence indicates more minutes of acute PA bouts and regular PA improves sleep outcomes.
- Positive effects independent of intensity and modality.
- **PAGAC Grade: Moderate**

Evidence - age, sex, race/ethnicity, socio-economic status, weight status

- **Gender/Adults:** Relationships between PA and sleep are strong and consistent across the adult lifespan in men and women.
- **Aging:** Reduced beneficial effects on sleep latency with aging.

PA & Sleep: Vary by age, sex, race/ethnicity, socio-economic status, or weight status

- **1 meta-analysis**
- **1 systematic review**

- **Adolescents & young adults** (14-24 years) 21 studies, 16,549 mostly cross-sectional (healthy; insomnia included but not other conditions) (Bartel et al., 2015)
- **Adolescents:** 41 studies with 32 cross-sectional and 9 trials in 85,561 adolescents; 33 studies including 2 with 9,444 adolescent females examining screen-time sedentary behavior and sleep (Costigan et al., 2013).

- **Children:** Some data but insufficient
- **Race:** Insufficient
- **Socio-economic:** Insufficient
- **Weight Status:** Insufficient

Draft Conclusion Statement

- Moderate evidence indicates that the effects of physical activity on sleep outcomes are preserved across aging and gender, with the exception of sleep onset latency that declines.
PAGAC Grade: Moderate
- Insufficient evidence to examine relationships in adolescents, children, and according to race/ethnicity, socioeconomic, or weight status.
PAGAC Grade: Grade not assignable

Relationships PA and sleep for Persons with Impaired Sleep Behaviors and Disorders



Insomnia: (~30% of U.S. Adults)

- 2 MA and 2 SR

- Adults (18-100 yrs with sleep problems; 16 observational studies, N= 307 to 7888 (Alessi et al., 2011).
- Middle Aged Women- sleep problems primarily insomnia: 4 RCT's, N=660 (Rubio-Arais et al., 2017).
- Middle Aged-Older Adults with sleep problems primarily insomnia, 6 trials with N=305 adults (Yang et al., 2012).
- Middle-Aged and Older adults (5 trials) with N=95 (Passos et al., 2012).

Insomnia/Sleep Problems: Evidence for relationship between PA and Sleep

- **Pittsburgh Sleep Quality Index (PSQI)**- global score on 7 components of sleep quality and patterns improved with SMD = 0.47 (95% CI 0.08 to 0.86). – Yang et al., 2012
- **Reduced sleep latency subscale of PSQI:** SMD = 0.58 (95% CI 0.08 to 1.08). – Yang et al., 2012
- **Reduced medication used to assist sleeping** (3 studies) SMD = 0.44 (95% CI 0.14 to 0.74). - Yang et al., 2012

Overall, moderate effect sizes, but did not significantly effect sleep time parameters of duration, sleep efficiency, sleep disturbance.

Sources:

Obstructive Sleep Apnea

Obstructive Sleep Apnea

- 3 meta-analyses
 - Together include 13 experimental studies (RCT or CT)
- 6 studies (3 RCTs) with N=182 subjects (Iftikhar et al., 2014)
- 80 RCT's with 4,325 adults of all ages (Iftikhar et al., 2017)
 - 5 PA RCTs with 72 subjects in exercise training groups
 - Network analysis comparing treatments to each other

Apnea Hypopnea Index (AHI)

Reduced Apnea Hypopnea Index (AHI) change in mean events/hour -6.27 (-8.54, -3.99).

- **Clinically significant.**
- **Positive effect of PA not different from other OSA therapies.**
- **Positive effects independent of significant loss in weight.**

- **Small-to-moderate effect size improvement in sleep efficiency, and reduced daytime sleepiness (-1.25, 95% CI, -2.397 to -0.0953; reduced daytime sleepiness scores) – Iftikhar et al., 2014**

Draft Conclusion Statement

- Moderate evidence indicates that MVPA improves sleep in individuals that report sleep problems, primarily insomnia, and for obstructive sleep apnea.
- **PAGAC Grade: Moderate**

Draft - Research Recommendations: Sleep

- Understand the relationship between PA and sleep in *children and adolescents* for those with and without sleep disorders.
- Investigate effects of PA on sleep outcomes for persons with sleep disorders beyond insomnia and OSA
- Investigate preventive effects of PA on sleep problems.
- Examine the relationships between PA and sleep outcomes for conditions with sleep problems (e.g., autism).
- Investigate PA and OSA linked to stroke, CVD, diabetes, biomarkers for Alzheimer's disease.
- Investigate the relationship between portable health technologies on relationships between PA and sleep.

Discussion

4. What is the relationship between physical activity and sleep?

- 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?
- c) Does the relationship exist for individuals with impaired sleep behaviors or disorders? If yes, for which sleep disorders?