



Meeting 5

Aging

Chair: Loretta DiPietro

Members: David Buchner, Wayne Campbell, Kirk Erickson, Abby King, Ken Powell

Subcommittee Questions



1. What is the relationship between physical activity and risk of injury due to a fall?
2. What is the relationship between physical activity and physical function among the general aging population?
3. What is the relationship between physical activity and physical function in older people with selected chronic conditions?

Original Physical Activity Types and Populations Being Addressed



Physical Activity Types

- Single component (e.g., strength training, yoga)
- Dual-task (e.g., walking while counting backwards)
- Multiple component (e.g., strength plus balance training)

Populations

- General Aging
- Level of Impairment
 - Healthy aging
 - Visual Impairment
 - Cognitive Impairment
 - Physical Impairment
 - Frailty
- Specific Disease State
 - Alzheimer's Disease
 - Chronic Obstructive Pulmonary Disease
 - Congestive Heart Failure
 - Coronary Artery/Heart Disease
 - Obesity
 - Osteoporosis/Osteopenia
 - Parkinson's Disease
 - Post-Hip Fracture

Revised Physical Activity Types and Populations Being Addressed



Question 2: What is the relationship between physical activity and physical function among the general aging population?

- General Aging
- Physical Activity Types
 - Single component (e.g., strength training, yoga)
 - Dual-task (e.g., walking while counting backwards)
- Impairments
 - Healthy aging
 - Visual Impairment
 - Cognitive Impairment
 - Physical Impairment

Question 3: What is the relationship between physical activity and physical function in older people with selected chronic conditions?

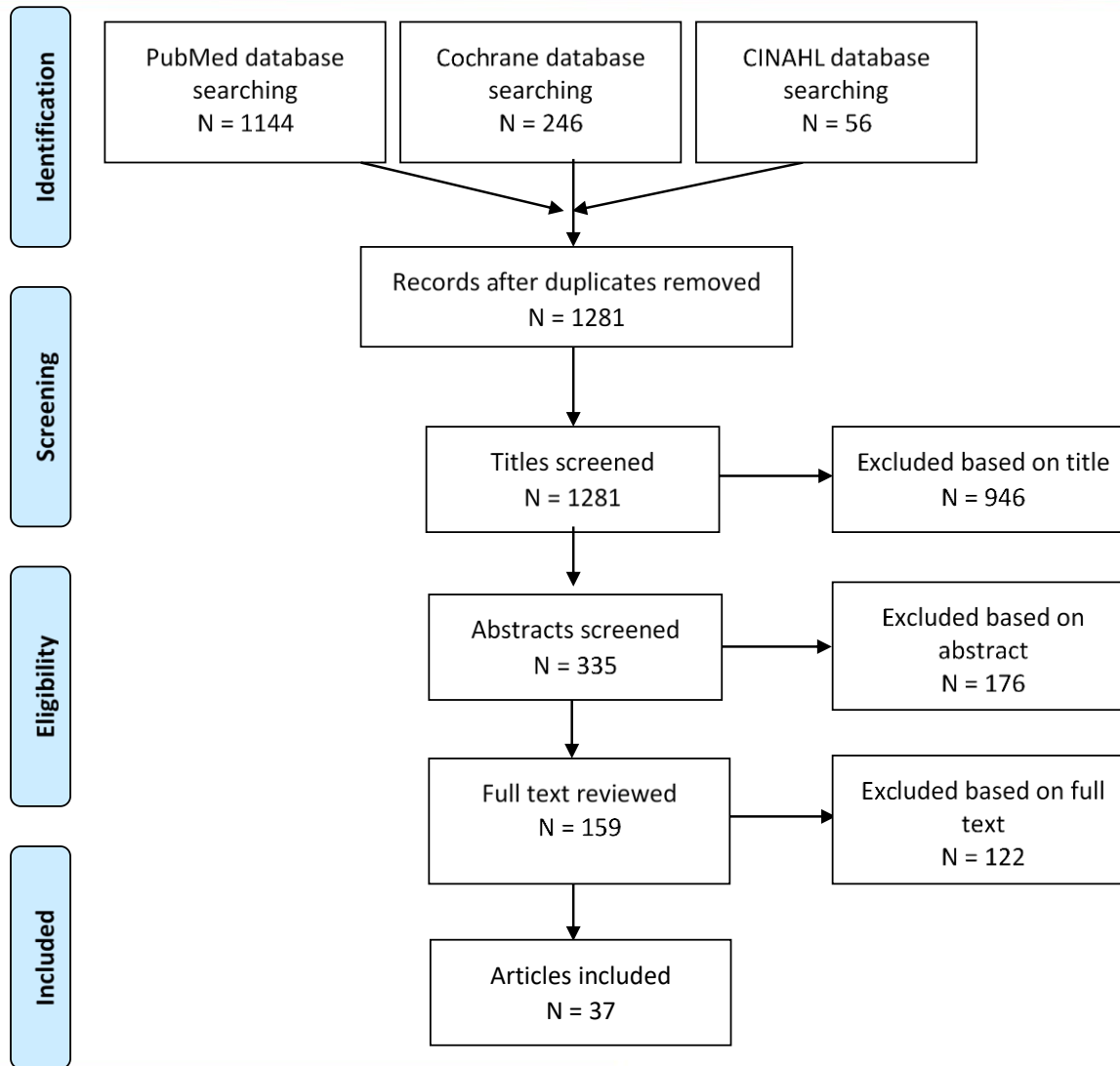
- Cardiovascular Disease
- Chronic Obstructive Pulmonary Disease
- Cognitive Impairment
- Frailty
- Osteoporosis/Osteopenia
- Parkinson's Disease
- Post-Hip Fracture
- Stroke
- Visual impairments

Question 2

2. What is the relationship between physical activity and physical function among the general aging population?
 - 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) What types of physical activity are effective for improving or maintaining physical function?
 - d) What impairments modify the relationship between physical activity and physical function among the general aging population?

- Source of evidence to answer question: Systematic Reviews and Meta-Analyses

Search Results: High-Quality Reviews¹



Description of the Evidence: Meta-analyses and systematic review

- Group 1 (excluded studies of participants with a single chronic condition)
 - Healthy / community living
 - Meta-analysis N=3 [23 RCTs] [37 RCTs & 5 nrCTs] [13 RCTs, 7 nrCTs, 4 single arm]
 - Systematic review N=3
 - All
 - Meta-analysis N=3 [40 relevant RCTs] [19 RCTs] [25 RCTs]
 - Systematic review N=2
- Group 2: included studies of participants with a single chronic condition)
 - Community living
 - Meta-analysis N=3 [28 RCTs] [4 relevant RCTs] [11 RCTs]
 - Systematic review N=0
 - All
 - Meta-analysis N=3 [33 RCTs both reviews led by Liu] [3 relevant RCTs]
 - Systematic review N=4

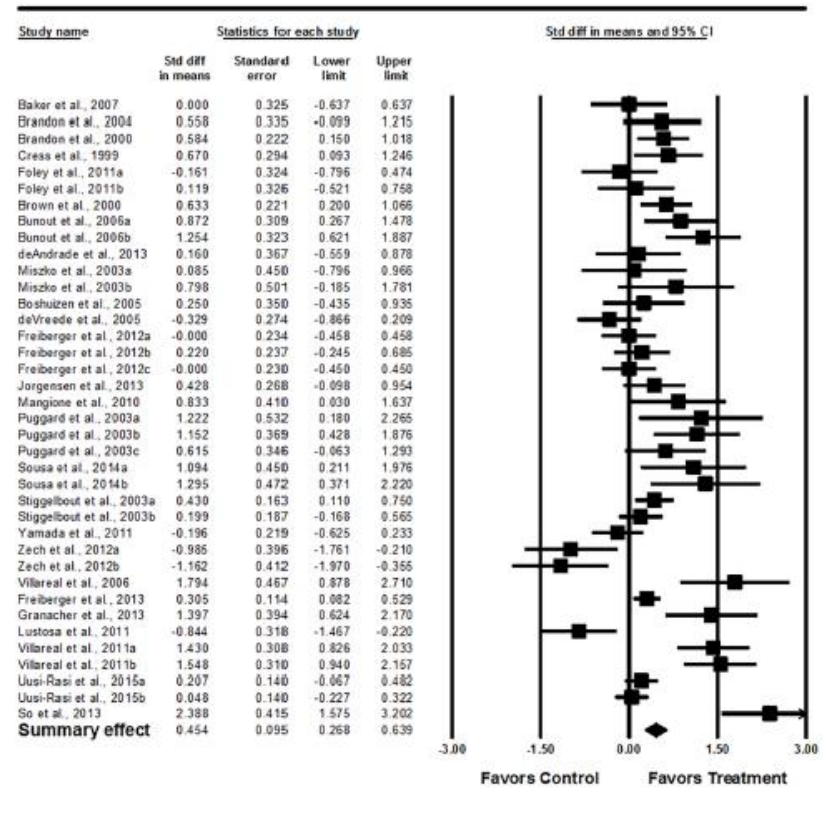
Description of the Evidence: Cohort studies

- Cohort studies of effect of PA on physical function
 - Meta-analysis [1]
 - Systematic review [2,3]
 - Pooled analysis [4]
- Comparisons of types
 - Meta-analyses [5]

1. Tak,2013; 2. Paterson & Warburton,2010; 3. van der Vorst,2016; 4. Morey,2008; 5. Tschopp,2011;

Description of the Evidence: Chase et al, 2017 subgroup/moderate analyses

- **Chase et al, 2017** meta-analysis:
 - Recent (2017)
 - Good quality review (13/17)
 - Large (28 trials involved 31 comparisons)
 - Objective composite measures of PF (SPPB, Up & Go tests, CS-PFP, PPT)
 - Several subgroup analyses and moderator analyses relevant to Q2
- **Summary ES = .45 (.27-.64)**
- Higher quality studies (blinding, randomization method, control group) had smaller effect sizes



SPPB = short physical performance battery; CS-PFP = continuous scale physical performance test, PPT = physical performance test

Description of the Evidence: Quality of meta-analyses

- Quality score total = either 15 or 17 items graded yes, partly, no:
 - Quality of Group 1 meta-analyses: 5 to 16 items scored “yes” out of 15/17
 - Quality of group 2 MA’s: 8 to 14 items scored “yes” out of 17.

Draft Key Findings: Group 1 studies

* = aerobic + resistance+balance

	Aerobic	Resistance / Power	Balance	Combo / Any
Pooled tests				ES=.37 [5]
Usual Gait speed		ES=0.84 [1] MD=0.15 m/s [3] MD=.13 m/s [4] SMD=.25 m/s [6]	MD=.07 m/s [4]	ES=0.84 [1] MD=0.18 m/s [3] *MD=.05 m/s [4] ES=.26 [5]
Any Balance		MD=1.6 sec [6] (OLS)	SMD=1.5 (Berg BS) [2]	ES=.27 [5] (any) MD=-5.3 sec (OLS) MD=1.8 (Berg BS)
Chair rise				ES=.30 [5]
Timed Up & Go		MD=-4.3 sec [6]		MD=-1.6 sec [6]
ADL				ES=.05 (ns) [5]

Note: Effect sizes significant unless marked 'ns'; Berg BS = Berg balance scale; OLS = one leg stand; balance training in [4] were 3 studies with dance-like movements

Draft Key Findings: Group 2 studies

	Aerobic	Resistance / Power	Balance	Combo / Any
Pooled tests		MD= .14 [5]		ES=0.45 [1]
Usual Gait speed		MD=.08 m/s [4]		
Any Balance				MD=1.57 cm [2] (FR)
Chair stand		SMD=-.94 [4]		
Timed Up & Go				
SF-36 PF scale		SMD=.07 ns [5]		g=.41 [3]

Note: Effect sizes significant unless marked 'ns'; FR = functional reach; PF = physical functioning; g = hedge's g; MA's included if ≥ 4 comparisons/studies;

Draft Conclusion Statement: Overall

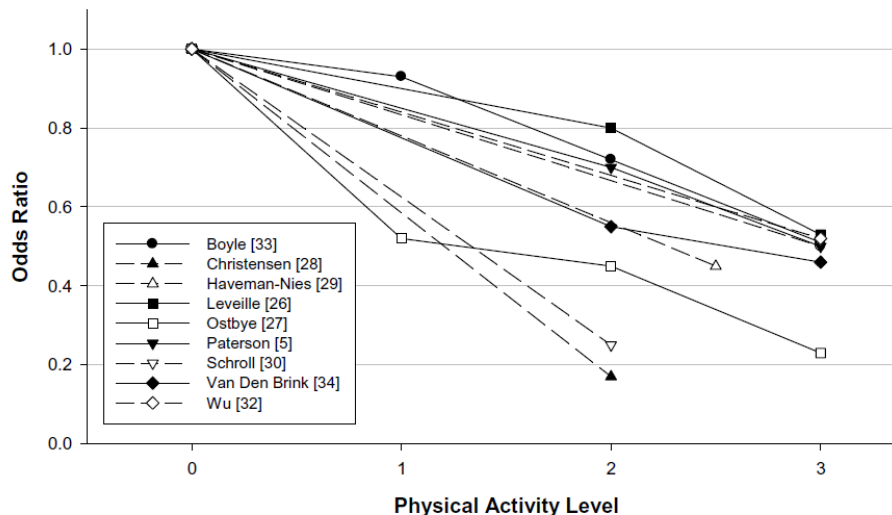
- **Conclusion Statement:**
 - Strong evidence demonstrates that physical activity improves physical function and attenuates the age-related loss of physical function in the general aging population.
- **PAGAC Grade: Strong**

Q2 Draft Key Findings:

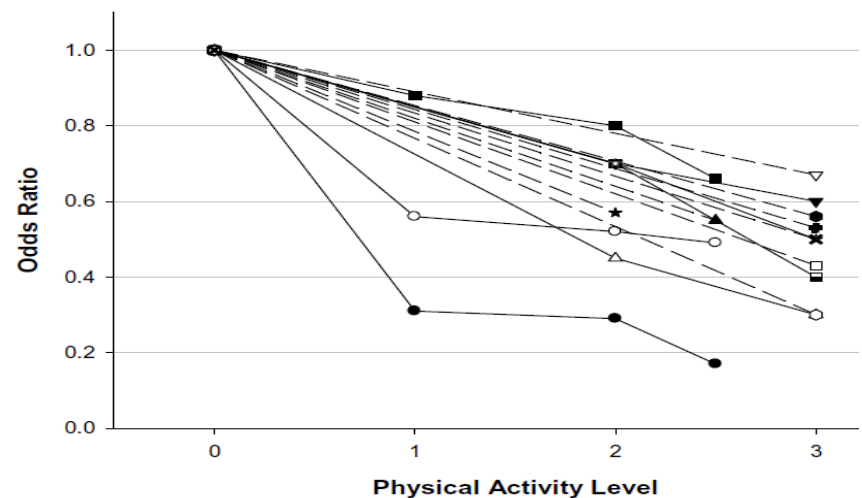
2a. Dose-response

- Data re: Canada's PA guidelines: [Paterson & Warburton, 2010]
- Categories of PA level derived from prospective cohort studies with covariate adjustment in older adults
 - 1 = light activities only occasion walking or gardening
 - 2 = moderate level of activity; volume=3-5 days/week & 30 min/day
 - 3 = vigorous activities and/or high volume of systematic activity

ADL, IADL, QOL disability indexes
N=9 lines



Odds of functional limitations in
“higher” level functions (e.g., walking a
distance or climbing stairs) (N=15 lines)



Q2 Draft Key Findings:

2a. Dose-response

Balance training frequency vs effect (SMD) on static steady state balance (e.g. one leg stand)

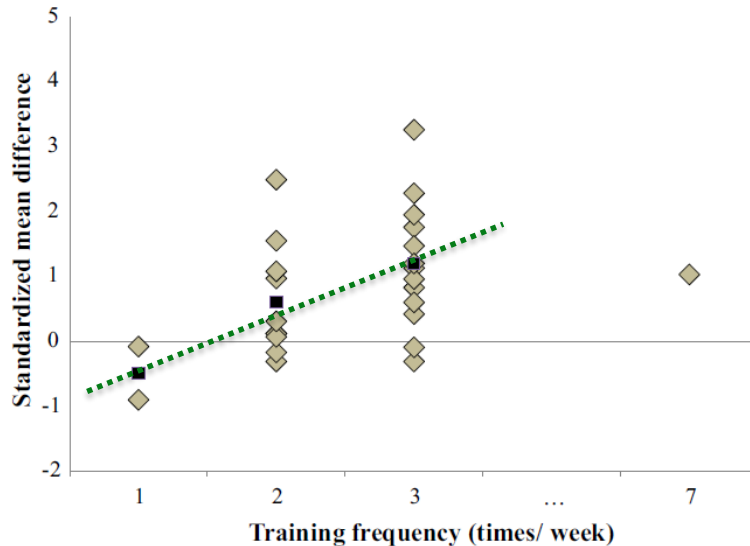


Fig. 8 Dose–response relationships of training frequency on overall balance performance. Each *filled gray diamond* illustrates between-subject standardized mean difference (SMD_{bs}) per single study with passive control. *Filled black squares* represent weighted mean SMD_{bs} of all studies

Note: dotted line added thru weighted SMDs; too few studies for meaningful analysis of other balance outcomes; SSB includes some physiologic measures of balance; authors note there is no standardized measure of “dose” of balance training

Q2 Draft Key Findings:

2a. Dose-response

- Moderator analysis – Chase 2017:
 - Days/week of exercise: $p=.10$
 - Minutes/session: $p<.01$
 - Minutes/week: $p<.01$

 - # repetitions of RT: $p<.01$
 - # sets RT: $p=.09$

RT = resistance training

Draft Conclusion Statement:

2a. Dose-response

- **Conclusion Statement:**

Strong evidence demonstrates an *inverse dose-response relationship* between volume of aerobic physical activity and risk of physical functional limitations in the general population of older adults.

PAGAC Grade: **Strong**

Draft Conclusion Statement:

2a. Dose-Response

- **Conclusion Statement:**

Limited evidence suggests an *inverse dose-response* relationship of volume of muscle-strengthening and frequency of balance activities with risk of physical function limitations in the general population of older adults.

- **PAGAC Grade: Limited**

Q2 Draft Key Findings: 2b. Effect Modification - Individual characteristics

- Moderator analysis [1] Percent sample women – NS
 - Mean BMI of sample – NS
- Meta-regression in cohort MA [2]
 - Effect of age (≤ 75 yrs vs >75 yrs) on relationship of PA with risk of basic ADL disability: $p = ns$.

1. Chase, 2017; 2. Tak, 2013

Draft Conclusion Statement:

2b. Effect Modification

- **Conclusion Statement:**
 - Limited evidence suggests that the relationship between physical activity and physical function does not vary by age, sex, or weight status in the general population of older adults.
- **PAGAC Grade: Limited**

- **Conclusion Statement:**

Insufficient evidence is available to determine if the relationship between physical activity and physical function varies by race/ethnicity and socio-economic status in the general population of older adults.

- PAGAC Grade: **Grade not assignable**

Draft Key Findings:

2c. Types - Aerobic PA (1)

- Systematic review prepared for Canada’s PA Guidelines [1]
 - 35 prospective cohort studies of relatively healthy older adults
 - Abstract conclusion: “There is a consistency of findings across studies and a range of outcome measures...: regular aerobic activity and short term exercise programs confer a reduced risk of functional limitations and disability in older age.”
- Meta-analysis of cohort studies of PA and (adjusted) risk of basic ADL dependency [2]
 - Instruments used to measure PA focused on aerobic PA
 - Low versus moderate-high levels of PA reduced risk of ADL dependency (OR=.507)

Draft Key Findings:

2c. Types - Aerobic PA (2)

- Aerobic activity and physical function:
 - Recent systematic review (2017) in “all” older adults [1]
 - 6 RCTs and 1 nrCT of aerobic PA , with 6 of 7 studies reporting at least one significant effect (no effect sizes provided)
 - *ALL 53 studies used relative intensity to prescribe MVPA*
 - Pooled cohort analysis [2] from RCT data (N=357):
 - Increasing PA over time from less than to above 150 min/week of aerobic PA associated with improvement of ~11 points on SF-36 physical function scale.

1. Bouaziz,2017; 2. Morey, 2008

Draft Key Findings: 2c. Types - muscle strengthening activity

- Power training vs progressive resistance training:
 - 1 meta-analysis [1]
 - Primary analysis of N=6 RCTs showed small advantage of power training (N=230 total participants).
 - Secondary analyses of N=2 to N=7 showed either (1) similar effects of both training types or (2) small advantage of power training on:
 - strength, muscle mass, power, walking speed, balance, self-reported physical function

Draft Conclusion Statement: 2c Types of physical activity

- **Conclusion Statement:**

Strong evidence demonstrates that aerobic, muscle-strengthening, and multicomponent physical activity improve physical function in the general aging population.

- **Grade: Strong**

Draft Key Findings: 2c. Types - Balance training

- One meta-analysis focused on effects of balance training [1].
 - N= 23 RCTs in relatively healthy older adults which included at least one “behavioral balance outcome”
 - Excluded studies of one specific type of training e.g. exergames, water exercise, Tai Chi.
 - Divided balance outcomes into 5 types:
 - Static steady state: SMD = 0.51* (14 comps)
 - Dynamic steady state: SMD = 0.44 (8 comps)
 - Proactive: SMD = 1.74* (7 comps)
 - Reactive: SMD = 1.01 (5 comps)
 - Balance test batteries[^]: SMD = 1.52* (5 comps)

Note: * $p < .05$; [^] = all studies used Berg Balance Scale; comps = # of comparisons in the analysis

Draft Conclusion Statement: 2c. Types of physical activity

- **Conclusion Statement:**
Moderate evidence indicates that activities that improve balance improve physical function in the general aging population.
- **PAGAC Grade: Moderate**

Draft Key Findings: 2c. Types - Flexibility activity

- Flexibility training
 - One MA (3 studies) showing a non-significant trend for flexibility training on gait speed. [Abbema,2016]
 - One systematic review of 22 studies of flexibility training located 3 with physical function outcomes. Abstract stated: “...there is conflicting information regarding both the relationship between flexibility interventions and functional outcomes or daily functioning.” [Stathokostas,2012]

Description of the Evidence: 2c. Types - Tai Chi, Qigong, Yoga

- 1 meta-analysis for effects of Tai Chi (but not Qigong) [1]
 - Of 13 RCTs, 7 were relevant (had no exercise control group), with PEDro quality scores of 6 to 9)
 - Tai Chi interventions varied in forms/types, & included simplified forms.
 - Sample sizes N=18 to N=158; N= 428 total participants; duration 8-52 weeks
- 1 systematic review of effects of Tai Chi or Qigong [2]
 - Of 36 RCTs, 12 were relevant (unselected sample of older adults, no-exercise control group); 5 overlapped with the MA; no quality scores reported..
 - In these 12 RCTs, all interventions were Tai Chi only of various types/forms.
 - 6 of 12 RCTs had sample size >100. N=1551 total participants; duration 8-52 weeks
- 1 meta-analysis of Yoga, regarded as a systematic review [3]
 - Of 6 RCTs, 3 were relevant (unselected sample of older adults, had no-exercise control group), with PEDro scores of 6 to 8; no meta-analysis of just these RCTs
 - Each yoga intervention included at least 10 yoga poses of various types,
 - Sample sizes N=22 to N=135; N=211 total participants.

Draft Key Findings: 2c. Types - Tai Chi, Qigong

- 12 RCTs of Tai Chi in the SR:
 - 11 of 12 RCTs positive for 1+ PF outcome
 - All 4 RCTs with self-report PF measures reported significant effects of Tai Chi.
 - 7 of 8 RCTs with performance measures of PF reported at least 1 significant effect of Tai Chi.
 - Breadth of effects: one leg stand, gait speed short and long courses, chair stands, Berg Balance scale, TUG.
- 7 RCTs of Tai Chi in the MA
 - 5 of 7 RCTs positive for 1+ outcome of balance-related physical function.
 - One meta-analysis of 3 studies was negative: no significant effect of Tai Chi on one leg stand

Draft Key Findings – 2c. Types Yoga

- While no MA done of only the 3 relevant RCTs of yoga, data on these RCTs were in analyses (forest plots).
 - Balance
 - In two RCTs, effects on balance were non-significant (ES=.17 & ES=.35).
 - In one RCT, effect on balance was large and significant (ES=0.94)
 - Mobility
 - In one RCT, effect on mobility was non-significant (ES=.39).
 - In one RCT, effect on 4 meter walk was large and significant (ES=0.97)

Draft Conclusion Statement

2c. Types of physical activity

- **Conclusion Statement:**

Limited evidence suggests that activities of Tai Chi improve physical function in the general aging population.

- PAGAC Grade: **Limited**

- **Conclusion Statement:**

Insufficient evidence is available to determine the effects of flexibility activity, qigong, or yoga exercise on physical function in the general aging population.

- PAGAC Grade: **Not assignable**

Description of the Evidence: 2c. Types - Dancing and Active Video Gaming

- 5 Systematic Reviews/ Meta-analyses
 - 3/5 were meta-analyses (Donath, 2016; Rodriques, 2014; Taylor, 2016)
- 2 studies of *dance* interventions
 - Fernández-Arguëlles, 2015 (n=7 RCTs)
 - Keogh, 2009 (3 cross-sectional and 15 training studies)
- 3 studies of *active video gaming* (AVG)
 - Donath, 2016 (n=18 trials);
 - Rodriques, 2014 (n=4 trials);
 - Taylor, 2016 (n=18 RCTs)
- All studies involving healthy, community-dwelling older people

Draft Key Findings: 2c. Types – Dance and Active Video Gaming

- **Dance interventions:**
 - 6/6 studies report improvements in balance (F-A, 2015);
 - 5/5 studies report improvements in gait (F-A, 2015);
 - 6/9 training studies showed improvement in muscle endurance (Keogh, 2009);
- **Active Video Gaming:**
 - Balance: SMD= 0.77 (0.45–1.09)(Donath, 2016);
 - Functional mobility: SMD= 0.56 (0.25–0.78)(Donath, 2016);
 - Balance: MD=0.73; 0.17, 1.29)(Taylor, 2016);
 - 30 sec chair stands: MD=3.99 (1.92, 6.05)(Taylor, 2016)

Draft Conclusion Statement: 2c. Types - Dance and Active Video Gaming

- **Conclusion Statement:**

Limited evidence suggest that dance training improves physical function among the general aging population.

- PAGAC Grade: **Limited**

- **Conclusion Statement:**

Limited evidence suggests that active video gaming improves some domains of physical function among the general aging population.

- PAGAC Grade: **Limited**

Description of the Evidence: 2c. Types - Dual-tasking

- **Dual-tasking**=performing a physical activity while simultaneously performing a cognitive task (e.g., walking while counting backward);
- 4 systematic reviews; 1 meta-analysis
 - 15 RCTs in the MA
 - Primarily community dwelling older adults
 - Included studies with known other conditions (osteoarthritis)
 - Significant variability in how dual-task was defined
 - Most studies included a cognitive task as the secondary task (e.g., verbal fluency)
 - Significant heterogeneity in the types of training: balance, gait, cadence
- Interventions were either physical activity training with a dual-task outcome or dual-task training
 - Durations: 4-25 weeks
 - Frequency: 1-3 times per week
 - Length of sessions: 20-60 minutes
 - Intensity: not well reported.
- **Limitations of the literature:**
 - Quality of studies was poor to moderate; lacked adequate description of training; dual-task calculations; little information about dual-task transfer effects to untrained tasks; low level of precision and rigor

Draft Key Findings: 2c. Types - Dual-tasking

- Small positive effect sizes (but significant) on gait-speed outcomes under dual-task conditions (Plummer et al., 2016)
 - Overall (SMD=0.11)
 - With arithmetic (SMD=0.11)
 - With verbal fluency (SMD=0.09)

- **Conclusion Statement:**
 - Limited evidence suggests that physical activity training or dual-task training modestly improves measures of physical function under dual-task conditions in the general aging population.
- **PAGAC Grade: Limited**

Q2 Draft Key Findings: 2d. Modification by functional impairments

- Average effect size in 33 comparisons in non-frail adults (.35) significantly lower than in frail adults (1.09) ($p < .05$)
- No comparisons found for cognitive impairment or visual impairment

Draft Conclusion Statement: 2d. effect of impairments

- **Conclusion Statement:**
 - Limited evidence suggests that physical activity has a stronger effect on physical function in older adults with limitations in physical function, compared to relatively healthy older adults.
- **PAGAC Grade: Limited**

Draft Conclusion Statement

- **Conclusion Statement:**
 - Insufficient evidence is available to determine whether visual impairments or cognitive impairments modify the relationship between physical activity and physical function among the general aging population.
- **PAGAC Grade: Grade not assignable**

Comment on evidence sources

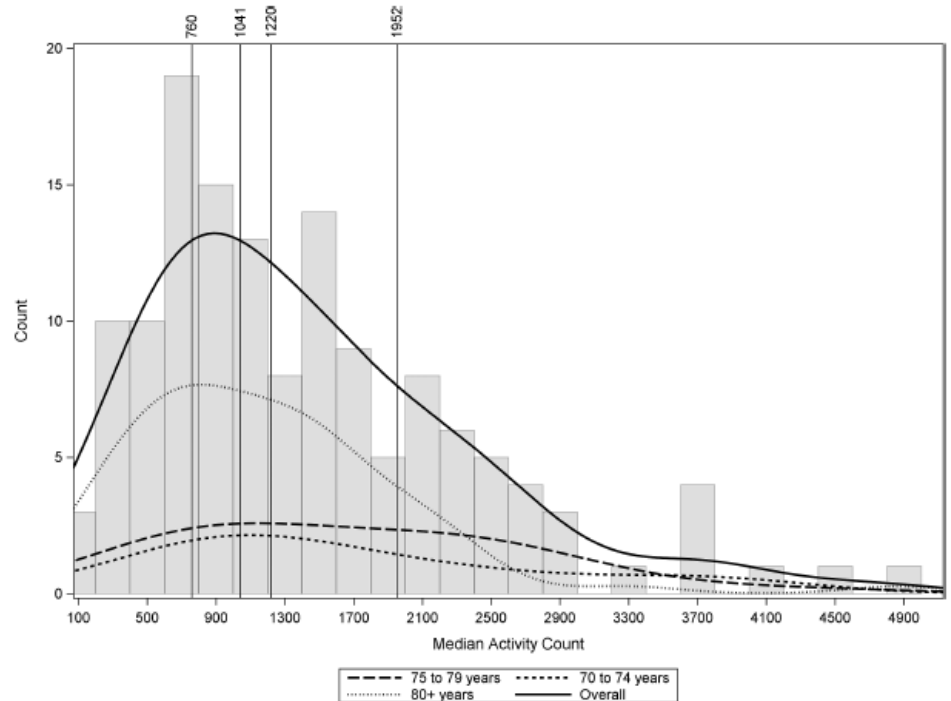
- There is a definitive 2 group RCT of combined exercise on mobility disability = LIFE (Lifestyle Intervention for Elders) study [1]
 - N=1635; average participation 2.6 years; selected for physical functional limitations yet able to walk 400 m.
 - Exercise significantly reduced risk of mobility disability (HR=.82)
- We were unable to locate this study in an evidence table in the included reviews. As the PAGAC search sought only reviews, this study could not be included in the evidence review.
- However, the evidence statements are consistent with the results of LIFE.
 - Strong evidence that physical activity attenuates loss of physical function.
 - In subgroup analyses, the effect of exercise was significant in older adults with lower SPPB scores (HR=.75) and not significant older adults with better scores (HR=.95)
 - Effects of exercise did not differ by sex or age

Draft Research Recommendations

- 1) RCTs comparing various doses of balance training and resistance training on physical function.
- 2) RCTs of yoga and qigong which determine: (1) effects on physical function; (2) types and forms which are effective; and (3) dose-response or minimal effective dose.
- 3) Systematic reporting of adverse effects of physical activity in RCTs and community-based studies of injury risk in older adults, particularly types of PA other than aerobic.
- 4) Meta-analyses which include meta-regression to examine effect of individual characteristics (e.g. age) and level of impairment on variability in results across studies.

Draft Research Recommendations

- 5) Prospective cohort studies of the effects of physical activity on physical function in older adults should include objective measures of the relative intensity of activity (e.g. heart rate monitors) so as to allow more robust analyses of how intensity affects health benefits, and facilitate integration of evidence from RCTs and cohort studies.



Histogram of median accelerometer counts Per minute during structured exercise of the LIFE study. Rejeski et al. J Gerontol 2016

Draft Research Recommendations

- 6) MA's with meta-regressions to determine how much heterogeneity of results can be explained variation in tests used to measure physical function.
 - Comment: need more information on whether variation in results among studies is because some measures are more sensitive in detecting changes in function.

Draft Research Recommendations: Tai Chi, Qigong, Yoga



- 1) RCTs of effects of Yoga and qigong on physical function, including studies of dose-response.
- 2) RCTs to determine the dose response relationship for Tai Chi, including whether minimal effective dose varies by style and forms of Tai Chi.

Draft Research Recommendations: Dual-tasking



- There is a need for studies to clearly describe the dual-task training procedures, the parameters of the secondary task, and whether dual-task costs were reduced by training.
- There is a need for studies to determine whether dual-task training transfers to *untrained* tasks.

Committee Discussion

2. What is the relationship between physical activity and physical function among the general aging population?
 - 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) What type(s) of physical activity are effective for improving or maintaining physical function?
 - d) What factors modify the relationship between physical activity and physical function among the general aging population?

Question 3

3. What is the relationship between physical activity and physical function in older people with selected chronic conditions?
- Source of evidence to answer question: Systematic Reviews and Meta-Analyses

Experts and Consultants



- **Invited experts:** None.
- **Consultants:** Question 3 - Kathleen Janz, PhD and Richard Macko, MD

Analytical Framework

Systematic Review Question

What is the relationship between physical activity and physical function in older people with selected chronic conditions?

Target Population

Adults, 50 years and older with selected chronic conditions (i.e., Alzheimer's Disease, Chronic Obstructive Pulmonary Disease, Congestive Heart Failure, Coronary Artery/Heart Disease, Frailty, Obesity, Osteoporosis/Osteopenia, Parkinson's Disease, or Post-Hip Fracture)

Comparison

Adults, 50 years and older with selected chronic conditions, who participate in varying levels of physical activity, including no reported physical activity

Intervention/Exposure

All types and intensities of physical activity

Endpoint Health Outcomes

- Physical function
- Functional ability
- Move around
- Behavioral ability
- Behavioral disability
- Functional limitations
- Loss of physical function
- Physical disability
- Physical intrinsic capacity

Key Definitions:

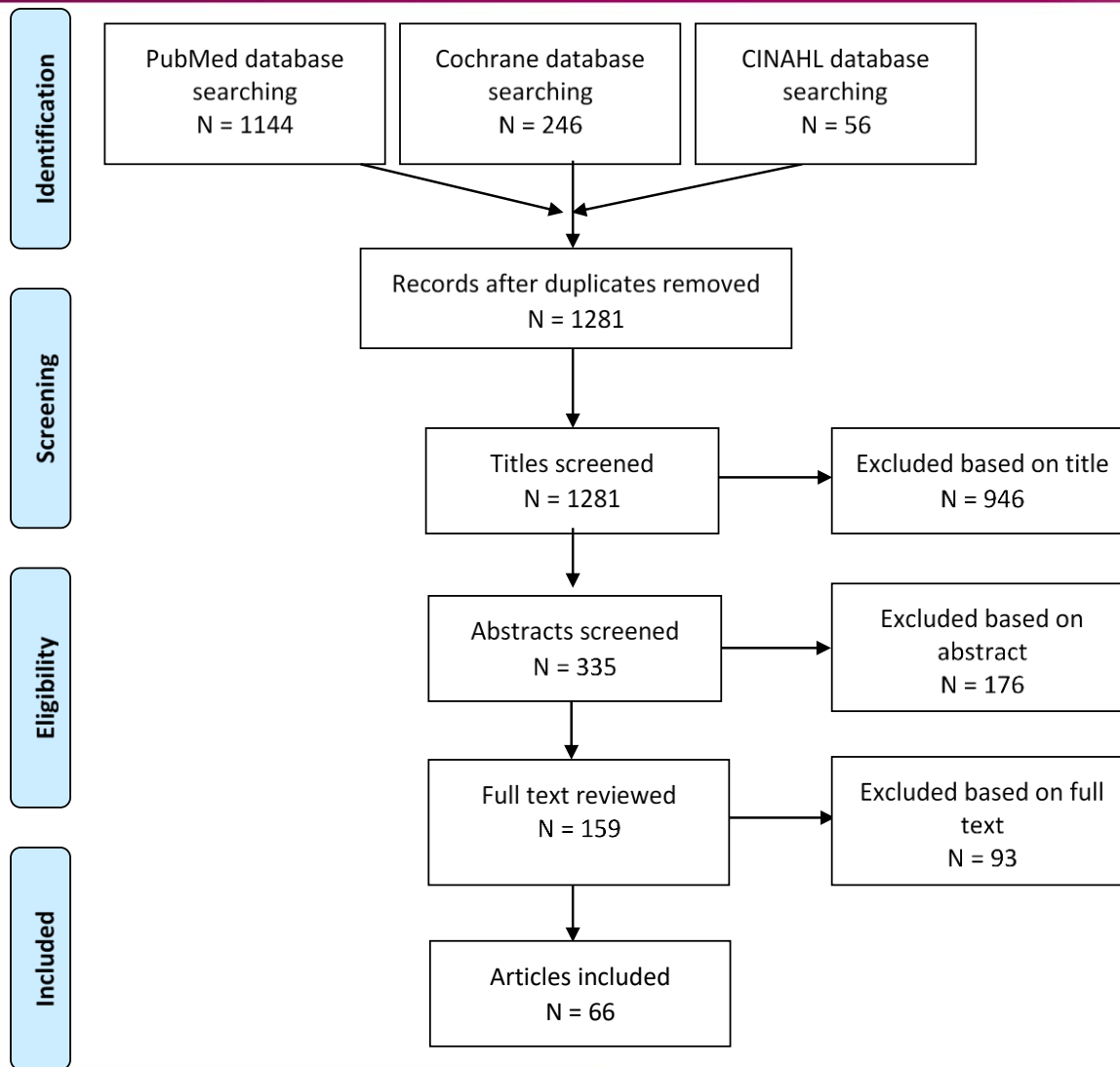
- "Physical function" and "physical functioning" are regarded as synonyms that refer to: "the *ability* of a person to move around and to perform types of physical activity."
- For example, measures of physical function include measures of ability to walk (e.g., usually gait speed), run, climb stairs, carry groceries, sweep the floor, stand up, and bath oneself.
- As measures of behavioral abilities, physical function measures do not include:
 - Physiologic measures, including measures of physiologic capacity (e.g., maximal lung capacities, maximal aerobic capacity, maximal muscle strength, bone density).
 - Measures of the environment or of the host-environmental interaction (e.g., disability accommodation).
 - Measures of what a person usually does (e.g., physical activity level) (as opposed to what a person is capable of doing).

Inclusion/Exclusion Criteria



- **Date of Publication**
 - Original Research: Include 2006 - Present
 - Existing Sources: Include 2006 - Present
- **Study Subjects**
 - Include: Adults, 50 years and older
 - Exclude: Nonambulatory only, Hospitalized only, Athletes only
- **Study Design**
 - Include: Randomized controlled trials, Non-randomized controlled trials, Prospective cohort studies, Retrospective cohort studies, Case-control studies, Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports
 - Exclude: Narrative reviews, Commentaries, Editorials, Cross-sectional studies, Before-and-after studies
- **Exposure/Intervention**
 - Include: All types and intensities of physical activity
 - Exclude: Missing physical activity, Single, acute session of exercise, Therapeutic exercise, Physical fitness as the exposure, Only used as confounding variable
- **Outcome**
 - Include: Physical function, functional ability, move around, behavioral ability, behavioral disability, functional limitations, loss of physical function, physical disability, physical intrinsic capacity

Search Results: High-Quality Reviews¹



Description of the Evidence: Cardiovascular Disease

- 3 existing systematic reviews/meta-analyses (Chen, 2016; Wang, 2016, Yamamoto, 2016) and one “integrated “review (Floegel 2016);
- Participants included men and women ages 65 years and older with existing cardiovascular disease (ischemic heart disease, coronary artery disease, cerebrovascular disease, or heart failure) from both community and hospital settings;
- The exposure of interest was all types and intensities of physical activity;
- The outcomes of interest were *performance-based* indices of physical function (6 minute walk test (6MWT), timed-up-and-go (TUG), household and physical activity mobility).

Draft Key Findings: Cardiovascular Disease

- A meta-analysis of 6 RCTs (N=374 CVD patients) reported improvements in the 6MWT among those patients performing traditional Chinese exercises (TCE), compared with those performing aerobic exercise or no exercise (SMD=59.6; 95% CI=5.0 to 114.2 meters)(Wang, et al., 2016);
- Results from a meta-analysis of 3 RCTs (106 heart failure patients) indicated that those performing one hour of Tai Chi on 2-3 times per week over 12 weeks also increased their 6 min walking distance compared with those in usual care or performing aerobic or endurance exercise (SMD=1.58; 95% CI: 0.70-2.45)(Chen, *et al.*, 2016);
- Those people performing RT improved their mobility score compared with those in usual care (SMD=0.61; 95%CI=0.21-1.01) (Yamamoto et al, 2016).

Draft Conclusion Statement: Cardiovascular Disease

- **Conclusion Statement:** Limited evidence suggests that physical activities such as resistance training and complementary/alternative exercise (tai chi, qigong, baduanjin) improve physical function among older people with cardiovascular disease.
- **Grade:** Limited

Description of the Evidence: Cognitive Impairment

- 8 systematic reviews; 5 meta-analyses
 - Included participants that were institutionalized and community dwelling.
 - Most reviews included multiple forms of dementia such as Alzheimer's disease, fronto-temporal dementia, Lewy body
 - Attrition rates are higher in studies with more severe cognitive impairment (Burge et al., 2012; Fox et al., 2014)
 - Reviews included as few as 5 RCTs (Burge et al., 2012) and were as large as 18 (Forbes et al., 2015).
 - ~1400 participants in relevant RCTs
 - Most reviews included approximately 10 RCTs
 - Many different outcomes: gait speed, balance, TUG, etc.
 - ADLs were a common outcome.
- Interventions were almost uniformly multi-modal and included aerobic, resistance, balance, stretching, endurance training
 - Durations: 3 to 12 months
 - Frequency: 2-7 sessions per week
 - Length of sessions: 20-75 minutes
 - Intensity: often not well reported. Most reported light-to-moderate but without any description of how intensity was measured.
- Limitations of the literature:
 - Inadequate blinding; infrequent intent-to-treat analyses; poor description of the physical activity training procedures and monitoring; significant heterogeneity in description of cognitive testing

Draft Key Findings: Cognitive impairment

- Limitations across studies often make it difficult to derive a summary outcome statistic for physical function (Fox et al., 2014)
- Analysis of 6 high quality RCTs:
 - Moderate effect size (0.53) for physical function
 - Moderate/large effect (0.80) for ADLs
 - Effect size of 0.68 in Forbes et al., 2015
 - Effect size of 0.77 in Lewis et al., 2017
- In one high quality study, physical activity delayed deterioration of ADL performance (Burge et al., 2012)

Draft Conclusion Statement: Cognitive Impairment

- **Conclusion Statement:**

Limited evidence suggests that for individuals with cognitive impairment, physical activity programs improve physical function including measures of activities of daily living.

- **PAGAC Grade: Limited**

Description of the Evidence:

COPD = Chronic Obstructive Pulmonary Disease

- No studies of effects of aerobic, resistance, or combined exercise on physical function in older adults with COPD.
- One MA of Tai Chi (1)
 - 12 RCTs—all Tai Chi; Sample sizes N=10 to N=206; N=811 total participants; 10/12 RCTs from China; duration of exercise 6 weeks to 1 year.
- One MA of Tai Chi, qigong, or combined (2)
 - 10 RCTs—7 of qigong and 3 of Tai Chi; Sample sizes N=10 to N=206; N=718 total participants; outcomes assess at either 3 or 6 months.
- Only three RCTs of Tai Chi overlapped between these MAs.

1. Ngai,2016; 2. Ding,2014;

Draft Key Findings: COPD

- In both MAs, a significant effect of exercise on 6MWT (6 minute walk test scored in meters walked);
 - MD = 41.7 meters. (4 RCTs qigong, 1 Tai chi)
 - MD = 29.6 meters. (6 RCTs of Tai chi)
- One MA rated quality of studies in MA as “very low”, and the other as “low”
- Heterogeneity was substantial ($I^2 = 85\%$ and 59%)

Draft Conclusion Statement: COPD



- **Conclusion Statement:**
 - Limited evidence suggests tai chi and qigong might improve one aspect of physical function – walking ability--in older adults with COPD.

- **PAGAC Grade: Limited**

Description of the Evidence: Frailty

- 15 existing systematic reviews and meta-analyses of RCTs.
- 12/15 papers were systematic reviews only
- Most participants included in these studies were all people ages 65 years and older and *all met at least one established criterion for frailty* (most of the MAs included people meeting one or more criteria). The majority of the participants were community-dwelling.
- The exposure of interest was all types and intensities of physical activity, and the outcomes of interest were measures of physical function, such as *performance-based* measures (6MWT, TUG, 30 sec chair stands, gait, balance, strength) or *self-reported* measures of ADLs or QOL.

Draft Key Findings:

Frailty

- Fifteen of the 15 SR/MAs reported that physical activity improved some or all measures of physical function in older people with frailty
- A recent MA (Gine-Garriga, 2014) of 19 RCTs among community-dwelling older adults with frailty reports improvements in normal gait speed (MD=0.07 m/sec; 95% CI: 0.04-0.09) and in fast gait speed (MD=0.08 m/sec; 95% CI: 0.02-0.14) among exercise, compared with control groups. *Overall, exercise decreased the time needed to walk 10 meters by 1.73 sec*
- A meta-analysis of 8 RCTs involving 1068 frail older people reported that the exercise groups increased their gait speed by 0.07 m/sec (95% CI: 0.02-0.11), and improved their Borg Balance Scale (BBS) score (WMD = 1.69; 95% CI: 0.56-2.82) and ADL performance score (WMD=5.33; 95% CI: 1.01-9.64)(Chou, 2012)

Draft Key Findings: Frailty

- *Multi-component exercise training* comprising aerobic, progressive resistance, balance, and functional training appears more effective than single-component training to improve physical function among older people with frailty (Cadore, 2013; Daniels, 2008; Nash, 2012; Theou, 2011; Weening, 2011);
- Theou, *et al.*, (2011) concluded from 47 RCTs that multi-component training of at *least moderate intensity that is performed 3 or more times per week for a duration of 30-45 min per session, over at least 3-5 months* appeared most effective to increase functional ability in older people with frailty;
- In general, greater improvements were observed with greater intensity of exercise (particularly with progressive resistance training) (deVries, 2012; Valenzuela, 2012), greater frequency per week, longer training durations, and greater adherence;
- Only 2/15 SR/MAs considered adverse events from the exercise training protocols (Ginn-Garriga, 2014; Valenzuela, 2012), and neither of these reviews reported any.

Draft Conclusion Statement: Frailty



- **Conclusion Statement:**

Strong evidence demonstrates that physical activity improves measures of physical function in older people with frailty.

- **PAGAC Grade: Strong**

Description of the Evidence: Hip Fracture

- 1 MA was primary source of evidence: (1)
 - Purpose = determine effects of “extended exercise programs” defined as “offered after or extended for more than a regular rehabilitation period.
 - Excluded studies of standard rehabilitation programs.
 - Only studies of community-dwelling older adults (both before and after hip fracture)
 - 11 RCTs of PEDro scores of 5 or higher; sample sizes N=26 to N=180; total participants N=1012; duration of exercise 1 to 12 months; start of exercise = usually a few weeks to a few months after formal rehab ended; exercise = resistance, walking, combined, and other.
- 1 MA was secondary source: (2)
 - Of 13 RCTs, 8 deemed eligible; 7 / 8 RCTs were included in the primary source. Analyses were a source of evidence if they included ONLY (any of) the 8 eligible RCTs

Draft Key Findings: Hip fracture

- Primary source- significant:
 - Balance: ES = .32
 - PPTs: ES = .53
 - TUG: ES = .83
 - Fast gait speed: ES = .42
- Primary source – not significant:
 - Gait speed: ES = .16
 - ADL: ES = .16
 - SF-36 PF: ES = .20
 - 6MWT ES = .22
- Secondary source –all comparisons significant:
 - Berg balance: +3.09 scale pts
 - TUG: -7.14 secs
 - Gait speed (all): +0.07 m/s
 - ADL: ES = .24
 - S-R mobility: ES = .31

Note: The two MAs differed in measures of effect size, how they grouped measures into analyses, and how they analyzed RCTs with more than 2 groups.

PPT = a physical performance test; TUG = time up & go, ADL = activity of daily living; SF36 PF = physical function scale of SF36; 6MWT = 6 minute walk test; S-R = self report

Draft Conclusion Statement: Hip Fracture

- **Conclusion Statement:**

Moderate evidence indicates that, for community dwelling older adults who sustain a hip fracture, extended exercise programs improve physical function.

- **PAGAC Grade: Moderate**

Description of the Evidence: Osteoporosis/Osteopenia

- 4 existing systematic reviews of RCTs (Giangregorio, 2016; Li, 2009; Wilhelm 2012; Zannotto, 2014), one of which included a meta-analysis (Li, 2009);
- Participants included in these studies were all community-dwelling people aged 55 years and older with osteoporosis (with or without fractures);
- These studies involved only RCTs and the exposure of interest was all types and intensities of exercise, and the outcomes of interest were *performance-based* measures of physical function, (gait, balance, strength) or *self-reported* measures of ADLs or QOL.

Draft Key Findings: Osteoporosis/Osteopenia

- Li, et al., (2009) provided the only meta-analysis of 4 exercise RCTs among 256 post-menopausal women with a clinical diagnosis of osteoporosis or osteopenia (with and without fractures) and HRQOL;
- In every RCT, the exercise groups (comprising programs of strengthening, stretching, agility, and/or balance training) showed significant improvements in *self-reported* physical function (SMD=2.77; 95%CI: 2.17, 3.37), compared with the control groups (no exercise or stretching);
- Short duration exercise program (less than or equal to 12 weeks) resulted in significant improvements in (6.54 (95% CI: 0.15, 12.94)) for the physical function domain.
- Importantly, exercise programs that combine strengthening with agility and balance training resulted in significant ($p<0.05$) improvements.

Draft Key Findings: Osteoporosis/Osteopenia

- 4/5 strength training trials included in the Wilhelm, *et al.*, 2012 review demonstrated improvements in physical function and ADLs, with effect sizes ranging from trivial (ES=0.08) to large (ES=1.74). *Those studies reporting greater compliance with the exercise program also reported more positive outcomes.*

Draft Conclusion Statement: Osteoporosis/Osteopenia

- **Conclusion Statement:**

Limited evidence suggests that muscle strengthening and agility (balance) exercises improves physical function in older people who are at risk for fragility fractures due to osteoporosis or osteopenia

- **Grade: Limited**

Draft- Description of the Evidence: Parkinson's Disease



Modality	Studies	Estimated Sample Size
Mixed modality aerobic	35 studies 20 RCTs 18 RCTs 14 RCTs	N = 1,210 N = 901 N = 495
Treadmill	18 RCTs	N = 633
Resistive Training	12 RCTs	N = ~1,000
Tango/Dance	13 studies, 9 RCTs	N = 357
Virtual Reality	8 clinical trials	N = 263
Mind- Body; Yoga, Tai Chi	~29 studies of various designs	N = ~910

Characteristics of Study Population: Parkinson's Disease

- **Disease severity:** mild to moderate (based on Hoehn & Yahr scores 1- 3);
- **Duration of Disease:** typical range 3-11 years.
- **Age:** typical range 57 - 88 years.

Representative (Pooled) Effect Sizes for Physical Activity on Physical Function for Persons with Parkinson's Disease

Physical Function	Improvement vs. Control, Effect size (SMD, 95% CI)
Gait Velocity	0.33 (95% CI 0.17 to 0.49)
6 minute-walk	0.72 (95% CI 0.08 to 1.36)
Timed Up and Go	0.46 (95% CI, 0.08 to 0.76)
Balance	0.36; (95% CI, 0.08 to 0.64)
UPDRS Motor	0.48; (95% CI, 0.21 to 0.75)
Strength	0.61 (95% CI, 0.35 to 0.87)

Effect sizes for 6 physical function outcomes range from small to moderate. Positive values signify improvement vs. control conditions.

Draft Conclusion Statement: Parkinson's Disease

- **Conclusion Statement:**

Strong evidence demonstrates a relationship between greater physical activity and a number of physical function outcomes, including walking, balance, strength, and disease specific (UPDRS) motor scores for individuals with Parkinson's Disease

- PAGAC Grade: **Strong**

Evidence: Effects of Strength Training and Intensive Mobility Training on Physical Function after Stroke



Strength Training: N=5 studies; N=240 individuals (Eng, Pang 2017)

- **Walking velocity:** non-significant effect ($d=-0.11$ (95% CI, -0.46 to 0.24). No effect on stair-climbing.

Intensive Mobility Training: N=10 studies; N=436 persons

- **Walking velocity:** moderate effect size; $d=0.45$ (95% CI, 0.14 to 0.77)
- **Walking Endurance:** small effect size $d = 0.20$ (95% CI, -0.03 to 0.44)
- **Walking velocity:** small increase in walking velocity of 0.23 m/s (95% CI, 0.18 to 0.27).

Evidence: Effects of Treadmill Training on Physical Function for Persons with Stroke

17 controlled studies (N=752)

- **Walking Velocity:**
 - Sub-acute and chronic stroke:** small effect $d=0.23$ (-0.14 to -0.59);
 - Chronic stroke:** small effect $d=0.31$ (-0.06 to -0.69);
- **Walking endurance:**
 - Moderate effect size $d=0.70$ (0.29 – 1.10);
- Effect sizes for treadmill are not different compared to other over-ground physical therapy mobility training modes.

Walking Training with Cuing of Cadence vs Walking Alone: 7 trials, 211 Individuals (Nascimento 2015)

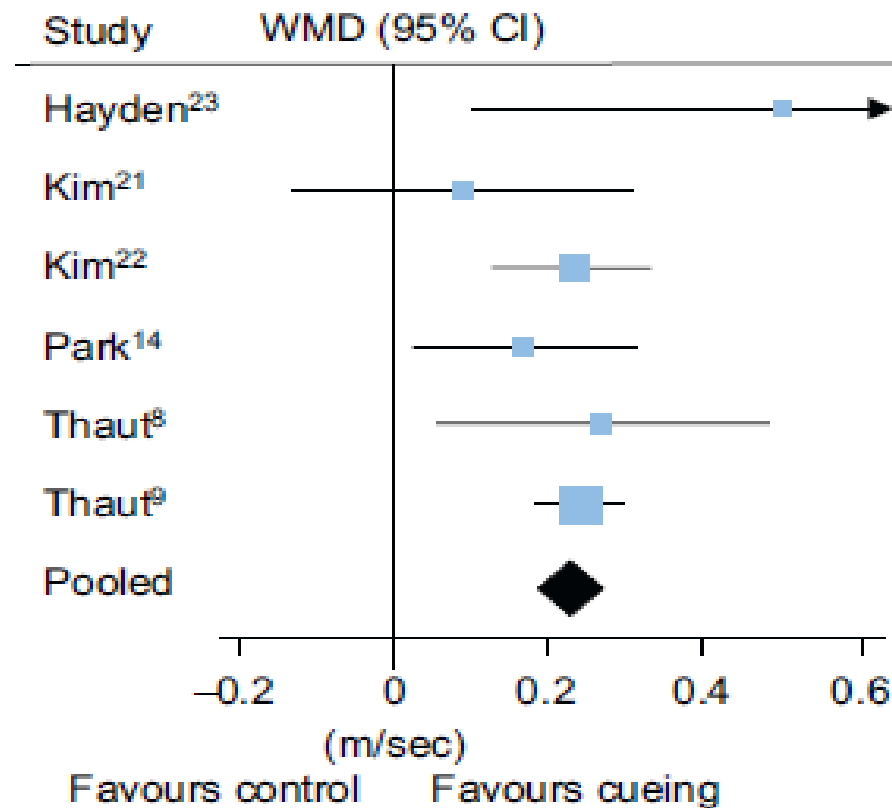


Figure 2. Mean difference (95% CI) of walking training with cueing of cadence versus walking training alone for walking speed (n = 171).

Body Weight Supported Treadmill Rehabilitation after Stroke

LEAPS Study (Duncan et al. *NEJM* 2011)

Groups: Early Locomotor (N=139), Late Locomotor (N=143), or Home Exercise (N=126)

- Higher functional level of walking (home -> limited community) in 52% for all groups.
- All groups had similar improvements in walking endurance from baseline to 1-year.
- Falls: Early locomotor 41%; Late locomotor 33%; Home Exercise 28%

Limitation – All groups received physical therapy.

Conclusions- Treadmill locomotor training not superior to home administered physical therapy exercises; all are effective. Falls is a concern in those with greater gait deficits and this is a greater issue in early locomotor training; a time period when deficits are often worse

Conclusion Statement:

Moderate evidence suggests that mobility-oriented physical activity improves walking function for individuals after a stroke.

PAGAC Grade: Moderate

Description of the Evidence: Visual Impairment

- One systematic review / meta-analysis (1)
 - Included 4 RCTs of small/moderate size
 - Purpose was to assess effect of fall prevention exercise programs, as older adults with visual impairment can be at higher fall risk.

Draft Key Findings: Visual Impairment

- There were no relevant findings in the review:
 - 2 RCTs reported physical function outcomes, but did not have a no-exercise control group.
 - 2 RCTs had a no-exercise control group, but did not report measures of physical function (only physiologic outcomes)

Draft Conclusion Statement: Visual Impairment

- **Conclusion Statement:**
 - Insufficient evidence is available to determine the effect of physical activity on physical function in older adults with visual impairment.
- **PAGAC Grade: Grade not assignable**

Draft Research Recommendations

- Large RCTs are needed to determine the effects of Tai Chi, qigong, dance, active video gaming, and yoga on physical function in older adults with chronic conditions;
- Such studies should address: a) the types or modes that are most effective for specific conditions; and b) the *minimal effective doses* of these activities;
- RCTs and/or meta-regression analyses are needed to establish dose-response effects of aerobic and resistance exercise on physical function for people with frailty, following hip fracture, Parkinson's, and after stroke.

Research Recommendations



- Randomized studies are needed to investigate the optimal dose and mode of physical activity that are necessary to improve and maintain *balance function* and reduce injury-related falls and fractures in persons with frailty, hip fracture, Parkinson's Disease, and stroke;
- Randomized studies are needed to determine effects of physical activity on ADL mobility, instrumental ADL's, free-living physical/ ambulatory activity and social participation for persons with these same conditions;
- Studies of physical activity and physical function are needed across the spectrum of cognitive dysfunction and dementia.

Research Recommendations



- Randomized studies are needed to investigate the potential for physical activity to function as a moderator of *disease progression* and to alter biomarkers, as well as genetic and environmental factors, for disease progression in persons with chronic disease;
- Large cohort and experimental studies are needed to determine the dose-intensity and *timing* of physical activity necessary to improve physical function across the spectrum of chronic disease conditions;
- Large observational or experimental studies with adequate statistical power are needed to determine whether the relationship between physical activity and physical function in older people with specific chronic diseases vary by race/ethnicity, socio-economic status, and sex across the aging spectrum.

Committee Discussion

3. What is the relationship between physical activity and physical function in older people with selected chronic conditions?