



Meeting 3

Individuals with Chronic Conditions

Chair: David Buchner

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

Experts and Consultants



- Invited experts: None
- Consultants: None

Subcommittee Questions

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?

2. 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, as determined from existing systematic reviews and/or meta-analyses?
 - a) Osteoarthritis
 - b) Hypertension
 - c) Type 2 Diabetes

Question 2 – Update: list of chronic conditions considered (not ordered)

1. Hypertension
2. Mood disorders
3. Cancer survivors
4. Neuromotor disease
5. Type 2 diabetes
6. Congestive heart failure
7. Coronary heart disease
8. Osteoarthritis
9. Stroke
10. Asthma
11. Chronic obstructive lung disease
12. Peripheral artery disease
13. Alzheimer's disease
14. Chronic renal disease
15. Cystic fibrosis
16. Anxiety disorders
17. Lipid disorders
18. ADHD
19. Low back pain due to intervertebral disk disease

Question 2 - update on selection of chronic conditions

From October PAGAC meeting:

- Prioritize conditions for review in Question 2 based upon:
 - (1) public health importance as judged by prevalence.
 - (2) amount of evidence as judged by number of articles retrieved in preliminary searches for systematic review and meta-analyses
 - (3) variety of conditions as judged by organ systems involved.
- Led to prioritizing so far:
 - High blood pressure
 - Osteoarthritis
 - Diabetes

Question 2 - update on selection of chronic conditions

- However, for all 19 chronic conditions considered, searches suggested there was (at least) sufficient evidence.
 - (=> criteria #2 above not that helpful)
- There are 10+ chronic conditions with prevalence in adults or children of 5% or higher.
 - => will need to further prioritize among prevalent conditions to a relatively short list that is feasible to review given available resources.
- Additional PAGAC input on priority conditions yesterday. Proposed:
 - #4 priority = asthma in children (pulmonary)
 - #5 priority = stroke in adults (neurological) -- effects of PA that are not part of rehabilitation.
- Priority of obesity as chronic condition discussed but not finalized

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, or socio-economic status?
 - Does the relationship vary based on: frequency, duration, intensity, type (mode), and how physical activity is measured?
- Source of evidence to answer question: TBD

Analytical Framework

Systematic Review Question

Among cancer survivors, what is the relationship between physical activity and (1) all cause mortality; (2) cancer specific mortality, and (3) risk of cancer recurrence or second primary cancer?

Target Population

Cancer survivors of all ages

Comparison

Cancer survivors who participate in varying levels of physical activity

Intervention/Exposure

All types and intensities of physical activity

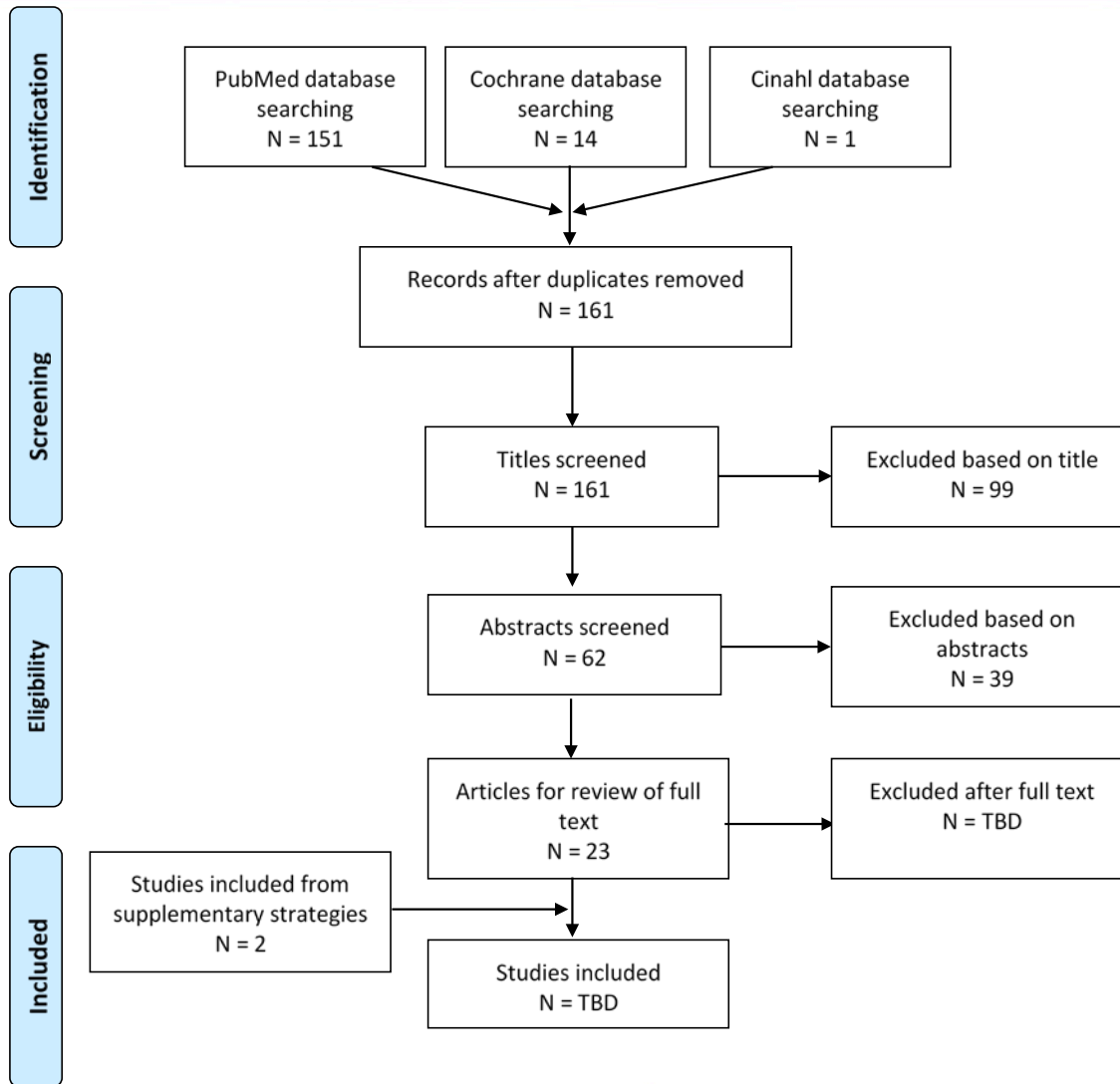
Endpoint Health Outcomes

- All-cause mortality
- Cancer-specific mortality
- Cancer recurrence
- Second primary cancer
- Adverse events related to physical activity

Key Definitions

- Cancer survivor: A person who has been diagnosed with, is undergoing treatment for, or has received treatment for any type of cancer
- Cancer recurrence: Original primary cancer is detected after a remission (when cancer was not detectable)
- Second Primary cancer: A new cancer that occurs sometime after diagnosis of original primary

Search Results: High-Quality Reviews¹ and Reports



Description of the Evidence: Breast Cancer

- Breast Cancer
 - 12 systematic reviews/meta-analyses
 - 1 pooled analysis
 - 1 paper removed because of quality concerns
 - 4 papers removed because they did not report on post-diagnosis PA
 - Remaining: 2 systematic reviews, 6 meta-analyses
 - 5 included studies published between 2014-2016
 - N=3 to 14 studies
 - Mainly considered leisure time PA, some included “total PA”
 - Meta-analyses examined dose-response effects
 - Several examined sub-group effects

Draft Key Findings: Breast (1)

- All-cause mortality*:
 - “High” vs. “Low” PA ~ 40-50% reduction
 - Example of dose response effect from one MA:
 - 5 MET-hr/wk increase: 13% reduction
 - 10 MET-hr/wk increase: 24% reduction
 - 15 MET-hr/wk increase: 34% reduction
- Breast cancer mortality*:
 - “High” vs. “Low” PA ~ 30-40% reduction
 - Example of dose-response relationship from one MA:
 - 5 MET-hr/wk increase: 6% reduction
 - 10 MET-hr/wk increase: 11% reduction
 - 15 MET-hr/wk increase: 16% reduction

* (all effects statistically significant for effects of PA post diagnosis)

Draft Key Findings: Breast (2)

- In general results were strongest for women with estrogen receptor positive tumors, and for Stage 1 (vs. 2-3)
- No difference by menopausal status
- No studies reported on specific race/ethnic groups
- No results controlled adequately for treatment type or amount received

Draft Conclusion Statement



- Conclusion Statement:
 - Physical activity after diagnosis is associated with decreased all-cause and breast-cancer specific mortality in women with breast cancer.
 - A dose-response effect is likely.
 - Risk of recurrence was not addressed in the studies.
- Grade: Moderate

Draft Implications

- Breast cancer survivors should be counseled to engage in regular aerobic physical activity, that is consistent with their abilities and disease status.

Draft Research Recommendations 1

- Cohort studies of PA and mortality in breast cancer survivors are needed that take into account additional possible confounders, including treatment type and treatment completion.
- Randomized controlled trials of PA effect on breast cancer outcomes are needed, including dose-response trials and trials to elucidate mechanism of actions of PA

Draft Research Recommendations 2

- Studies of associations of PA and breast cancer survival in specific race/ethnic populations are needed.
- Studies of PA effect on cancer recurrence and second primaries are needed.
- Safety issues for specific patient populations need to be addressed.

Description of the Evidence: Colon Cancer

- Colon Cancer
 - 6 systematic reviews with meta-analyses
 - 1 systematic review with pooled analyses on 3 studies
 - Studies published between 2006-2016
 - N=3 to 11 studies per review
 - All papers included post-diagnosis PA
 - Follow-up from 3.8 - 11.9 years post-diagnosis
 - Mainly considered leisure time PA , some used “total PA” (self-report or interview; MET-hrs/week or total hrs.)
 - Meta-analyses examined PA dose-response
 - Some studies examined sub-group effects

Draft Key Findings: Colon Cancer (1)

- **All-cause mortality:***
 - “Sedentary” vs “low” PA: ~ 23 – 32% reduction
 - “Moderate” vs. “low” PA: ~ 18% reduction
 - “High” vs. “low” PA: ~ 39 - 42% reduction
 - Example of dose-response:
 - 5 MET-hr/week – 15% reduction
 - 10 MET-hr/week – 28% reduction
 - 15 MET-hr/week -- 38% reduction
- **Colon and colorectal specific cancer mortality:***
 - “Sedentary” vs “low” PA: ~ 24 - 30% reduction
 - “Moderate” vs. “low” PA: ~ 18% reduction (trend, 95% CI, 0.61-1.1)
 - “High” vs. “low” PA: ~ 39-44% reduction
 - Increasing PA after diagnosis: ~29% reduction (trend, 95% CI 0.45-1.1)

* (all effects statistically significant for effects of PA post diagnosis)

Draft Key Findings: Colon Cancer (2)

- Associations reported for wide range of duration of follow-up-- from <1 and up to 10 yrs.
- Few studies reported on specific race/ethnic groups
- No results controlled adequately for treatment type or amount received
- Most meta-analyses and studies excluded stage IV

Draft Conclusion Statement: Colon Cancer



- Conclusion Statement:
 - Physical activity after diagnosis is associated with decreased all-cause and colon/**colorectal cancer** specific mortality
 - A dose-response effect is likely
 - Risk of recurrence not addressed in studies.
 - Limited inclusion of minorities
 - Limited with respect to tumor stages (most excluded stage IV, metastatic) and treatment characteristics
- Grade: Moderate

Draft Implications – Colon Cancer



Colon cancer survivors should be counseled to engage in regular aerobic physical activity, that is consistent with their abilities and disease status.

Draft Research Recommendations: Colon Cancer (1)

- (Essentially the same as for breast cancer)
- Cohort studies of PA and mortality in colon cancer survivors are needed that take into account additional possible confounders, including treatment type and treatment completion.
- Randomized controlled trials of PA effect on colon cancer outcomes are needed, including dose-response trials and trials to elucidate mechanism of actions of PA

Draft Research Recommendations: Colon Cancer (2)

- (Essentially the same as for breast cancer)
- Studies of associations of PA and colon cancer survival in specific race/ethnic populations are needed.
- Studies of PA effect on cancer recurrence and second primaries are needed.
- Safety issues for specific patient populations need to be addressed.

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?
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