Exercise Interventions for the Delayed Progression or Reversal of Frailty
SUMMARY OF ABSTRACTS Exercise Interventions for the Delayed Progression or Reversal of Frailty

Authors: Casey Gray, Charlene Argáez


Acknowledgments:

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.
Research Question
What is the effectiveness of exercise interventions to reverse or delay the progression of frailty in those with frailty?

Key Findings
Ten systematic reviews (two with meta-analyses), ten randomized controlled trials, and four non-randomized studies were identified regarding the effectiveness of exercise interventions to reverse or delay the progression of frailty in those with frailty.

Methods
A limited literature search was conducted on key resources PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by publication type. The search was limited to English language documents published between January 1, 2011 and May 8, 2018. Internet links were provided, where available.

Selection Criteria
One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients with frailty (living in the community, living in long term care, or in acute care)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Exercise interventions</td>
</tr>
<tr>
<td>Comparator</td>
<td>Usual care</td>
</tr>
<tr>
<td></td>
<td>• People who are getting what is currently normal in their setting</td>
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<tr>
<td></td>
<td>• No prescribed change in what they are doing</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Effectiveness and clinical benefit at the patient level, patient centred outcomes. e.g.,</td>
</tr>
<tr>
<td></td>
<td>• Quality of life improvements</td>
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<td></td>
<td>• Improvements on a frailty scale</td>
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<tr>
<td></td>
<td>• Improvements in functional status</td>
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<tr>
<td></td>
<td>• Increased muscle strength or stamina</td>
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<tr>
<td></td>
<td>• Healthcare utilization/need for interventions (need for trip to ER, length of stay)</td>
</tr>
</tbody>
</table>
Study Designs

| Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies |

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, and non-randomized studies.

Ten systematic reviews (two with meta-analyses), ten randomized controlled trials, and four non-randomized studies were identified regarding the effectiveness of exercise interventions to reverse or delay the progression of frailty in those with frailty. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Ten systematic reviews,1–10 (two with meta-analyses),5,8 ten randomized controlled trials,11–20 and four non-randomized studies21–24 were identified regarding exercise interventions for frailty. Detailed study characteristics are provided in Table 2.

Thirteen studies examined multi-component exercise interventions,1,3–5,7,10,12–14,18,21–24 Six studies did not specify the type(s) of exercise examined.2,8,9,11,16,23 Five studies examined a single specific type of exercise: chair based exercise,6 interval-based inspiratory muscle training with a device versus yoga breathing exercises,15 whole body vibration exercises,17 Tai Chi,19 and interactive videogame based dynamic balance exercises.20

Quality of Life Improvements

One systematic review,3, one randomized study,13 and one non-randomized study22 showed a beneficial effect of a multi-component exercise intervention on psychological wellbeing3 and Quality of Life.13,22

In studies that did not specify the type of exercise, there was no difference in quality of life between intervention and comparator groups in one systematic review and one randomized study, and findings were unclear in one systematic review.8,16,9

No studies examined a single exercise type with respect to quality of life.

Improvements on a frailty scale

One systematic review and one randomized study showed a positive effect of multi-component exercise on frailty.4,13

Frailty was reversed with unspecified exercise intervention in one randomized study.11

No studies examined a single exercise type with respect to frailty reversal.
Improvements in functional status

Three systematic reviews and one randomized study had improved physical functioning/performance with exercise versus comparator. Improvements in functional status

Three systematic reviews and one randomized study had improved physical functioning/performance with exercise versus comparator. Improvements in functional status

Mobility was improved with exercise in one systematic review. Evidence was mixed for balance, with unclear findings reported in two systematic reviews, and favourable results in one systematic review. One randomized study showed improved ability to rise from a chair in the exercise group relative to a comparison group. Two systematic reviews and one randomized study showed a positive effect of exercise on gait velocity, and one non-randomized study showed that exercise improved time to complete a 10 min walk. There were mixed findings for activities of daily living, with one SR showing unclear effects, and one non-randomized study showing improvements with exercise intervention versus comparison group. One RCT showed a positive effect of exercise on the swallowing related function of voluntary peak cough flow, but no effect on lip closure force.

Among studies that did not describe the type of exercise examined, systematic reviews showed improved physical performance, balance, and gait speed with exercise versus a comparator. One randomized studies showed improved speed and agility for the exercise intervention group versus the comparator. Findings for activities of daily living and mobility were mixed: activities of daily living were improved in one systematic review, but there was no difference between groups in one randomized study. One systematic review reported improved disability in older people with moderate, but not severe frailty. Finally, timed-up-and-go test of mobility showed no difference between exercise and comparator in one systematic review, however the authors of one randomized study reported non-significant, yet clinically important mobility improvements with exercise.

Four studies examined the effect of a single exercise type on functional status. Regarding chair-based exercises, most studies examined in a systematic review showed that exercise improved mobility and function relative to a control group. In a randomized study of older adults with frailty who were unable to perform whole body exercise, yoga respiratory training improved maximum inspiratory and expiratory pressure and maximum voluntary ventilation compared with an inspiratory muscle training group and a non-exercise control group. Compared with usual care and exercises, frail older adults randomized to perform whole body vibration exercises had improved mobility, leg strength and endurance, activities-specific balance confidence score, and general health status. Finally, compared with conventional physical therapy, adults with physical frailty randomized to participate in Tai Chi had a greater improvement in falls.

Increased muscle strength or stamina

Two systematic reviews, one randomized study, and one non-randomized study showed improved muscle strength with multi-component exercise. Studies that examined muscular endurance reported inconsistent findings, with one inconclusive systematic review and one non-randomized study showing improved endurance with multi-component exercise.

A systematic review and a randomized study showed improved muscle strength with exercise (type not specified). One study showed no difference between unspecified exercise and no-exercise conditions for fatigue or physical endurance, however an exercise
+ behavior change enhancement group had greater improvements in physical endurance than the other two conditions.\textsuperscript{23}

One systematic review examined the effect of single type of exercise on muscle strength or stamina. In this review, chair-based exercises led to improved cardiorespiratory fitness relative to a control group in most included studies.\textsuperscript{6}

**Healthcare utilization/need for interventions**

One randomized study showed a decreased number of visits to primary care\textsuperscript{19} and one non-randomized study showed fewer new Long Term Care insurance service requirement certifications\textsuperscript{24} with exercise versus comparison.

When the type of exercise was not specified, one systematic review reported unclear findings with respect to the effect of exercise on hospitalization rates and long term care admission rates.\textsuperscript{9}

A single type of exercise was examined in one randomized study. This study showed that an interactive videogame based dynamic balance exercises group led to greater improvements in balance than a conventional rehabilitation program, however there were no differences between groups for dynamic standing balance control or gait.\textsuperscript{20}

### Table 2: Summary of Included Studies on Exercise Interventions for the Delayed Progression or Reversal of Frailty

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention (FITT)</th>
<th>Outcomes</th>
<th>Results</th>
<th>Author Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Reviews and Meta-Analyses</strong></td>
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</tbody>
</table>
| Liberman, 2017\textsuperscript{1} | F: NR  
I: NR  
T: NR  
T: resistance, aerobic, and “other” exercises | Muscle strength, physical functioning | Exercise had moderate-to-large-beneficial effects on muscle strength and physical functioning | “Future studies should focus on the influence of specific exercise modalities and target the frail population more.”\textsuperscript{1} |
| Lozano-Montoya, 2017\textsuperscript{2} | F:NR  
I:NR  
T:NR  
T:NR | Muscle strength, physical performance | Exercise improved muscle strength and physical performance | Exercise interventions improved physical performance in community-dwelling patients aged >65 years with physical frailty and sarcopenia. Muscular strength was improved with multidisciplinary treatment and exercise interventions |
| Silva, 2017\textsuperscript{3} | F: ≥3 times/week  
I: NR  
T: Most interventions included ~60 min per session, over ≥ 6 | Cognition, physical functioning, psychological wellbeing | Compared with the control group, exercise improved cognition, physical functioning, and psychological wellbeing | “Although exercise interventions appear to be effective in managing the various components of frailty and...” |
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<tr>
<td><strong>De Labra, 2015</strong>&lt;sup&gt;4&lt;/sup&gt;</td>
<td>F: NR I: NR T: NR T: Multicomponent aerobic or resistance exercises, physical comprehensiveness TR, strength TR</td>
<td>Falls, mobility, muscle strength, balance performance, change in frailty score</td>
<td>Compared with the control group, exercise improved falls, mobility, and frailty. The effect of exercise on balance was unclear. Effect sizes varied across studies</td>
<td>“This systematic review suggested that frail older adults seemed to benefit from exercise interventions, although the optimal program remains unclear. More studies of this topic and with frail populations are needed to select the most favorable exercise program.”&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Gine-Garriga, 2014</strong>&lt;sup&gt;5&lt;/sup&gt;</td>
<td>F: NR I: NR T: NR T: multicomponent exercises</td>
<td>Physical performance scores, mobility, gait, ADL functional ability</td>
<td>Compared with the control group, exercise improved normal gait speed, fast gait speed, and physical performance scores. The effect of exercise on endurance, balance, and ADL functional mobility was not clear</td>
<td>“Exercise has some benefits in frail older people, although uncertainty still exists with regard to which exercise characteristics (type, frequency, duration) are most effective.”&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Anthony, 2013</strong>&lt;sup&gt;6&lt;/sup&gt;</td>
<td>F: NR I: NR T: NR T: Chair-based exercises</td>
<td>Mobility and function, cardiopulmonary fitness, and mental health</td>
<td>Compared with the control group, most studies showed that exercise improved mobility and function, cardiopulmonary fitness, and mental health.</td>
<td>There is low quality, inconclusive evidence about the effectiveness of chair-based exercises in this population. The literature is inconsistent about the definition and purpose of chair-based exercises.</td>
</tr>
<tr>
<td><strong>Cadore, 2013</strong>&lt;sup&gt;7&lt;/sup&gt;</td>
<td>F: NR I: NR T: NR T: multicomponent exercise TR, resistance TR, endurance TR,</td>
<td>Incidence of falls, gait, balance, and lower-body strength</td>
<td>Compared with the control group, most studies showed the exercise reduced incidence of falls, and improved gait ability, balance, and muscle</td>
<td>“The multi-component exercise intervention composed by strength, endurance and balance training seems to be the best strategy to improve...”&lt;sup&gt;6&lt;/sup&gt;</td>
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<tr>
<td>Chou, 2012&lt;sup&gt;8&lt;/sup&gt;</td>
<td>F: NR</td>
<td>Physical function (TUGT, gait speed, balance, ADL), quality of life</td>
<td>Compared with the control group, the exercise group had improved gait speed, balance, and their performance in ADL. Groups did not differ for TUGT or QoL.</td>
<td>“Exercise is beneficial to increase gait speed, improve balance, and improve performance in ADLs in the frail older adults.”&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Clegg, 2012&lt;sup&gt;9&lt;/sup&gt;</td>
<td>F: NR</td>
<td>Mobility, QoL, ADL, long-term care admission, hospitalisation</td>
<td>Compared with the control group, the exercise group had improved disability in those with moderate but not severe frailty. The evidence was not clear for QoL, long-term care admission rates, hospitalization,</td>
<td>“There is preliminary evidence that home-based exercise interventions may improve disability in older people with moderate, but not severe, frailty. There is considerable uncertainty regarding effects on important outcomes including quality of life and long-term care admission.”&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td>Theou, 2011&lt;sup&gt;10&lt;/sup&gt;</td>
<td>F: various frequencies</td>
<td>Various physical determinants of frailty: various functional outcomes</td>
<td>NR</td>
<td>“Multicomponent training interventions, of long duration (&gt;5 months), performed three times per week, for 30-45 minutes per session, generally had superior outcomes than other exercise programs.”&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ferreira, 2018&lt;sup&gt;11&lt;/sup&gt;</td>
<td>F: NR</td>
<td>Muscle strength, speed, agility</td>
<td>Compared with the control group, the exercise group had improved muscle strength, speed, agility, and reversed frailty</td>
<td>“The 12-week exercise program for frail elderly residents in a long-term care facility was efficient in improving muscle strength, speed, agility.”&lt;sup&gt;11&lt;/sup&gt;</td>
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<tr>
<td>Takatori, 2016</td>
<td>F: 3 times / week I: NR T: 6 months; &quot;brief&quot; session duration T: multi-component home-based exercises targeting prevention of aspiration pneumonia and falls</td>
<td>Prevention of aspiration pneumonia: Voluntary peak cough flow, lip closure force Falls prevention: physical function (TUGT, chair stand, maximal knee extension strength, sit and reach)</td>
<td>Prevention of aspiration pneumonia: Compared with the control group, the exercise group had greater voluntary peak cough flow and did not differ for lip closure force Falls prevention: Compared with the control group, the exercise group had greater improvement in TUGT, Chair Stand Test, maximal knee extension strength, and Sit and Reach Test</td>
<td>&quot;Specifically developed home-based exercise as described in this study is simple and can be performed briefly. Improvements in voluntary peak cough flow and physical function indicate the possible usefulness of such exercise in preventing falls and aspiration pneumonia in community-dwelling frail older adults.&quot;</td>
</tr>
<tr>
<td>Tarazona-Santabalbina, 2016</td>
<td>F: 5 days / week I: NR T: 24 weeks; 65 min per session T: supervised-facility multicomponent exercise program consisting of proprioception, aerobic, strength, and stretching exercises</td>
<td>Frailty, functionality, cognitive impairment, depression, biological biomarkers of frailty</td>
<td>Compared with the control group, the exercise group reversed frailty and improved functional measurements of frailty, cognitive impairment, depression, QoL, and decreased the number of visits to primary care physician</td>
<td>&quot;We have designed a multicomponent exercise intervention that reverses frailty and improves cognition, emotional, and social networking in a controlled population of community-dwelling frail older adults.&quot;</td>
</tr>
<tr>
<td>Cadore, 2014</td>
<td>F: 2 times / week I: 40% - 60% of 1-repetition maximum T: 12 weeks; T: Multicomponent (muscle power TR, balance, gait retraining)</td>
<td>Gait velocity, balance, ability to rise from a chair, incidence and risk of falls, functional status</td>
<td>Compared with the control group who experienced reduced strength and functional outcomes over the course of the study, the exercise group improved gait velocity, balance, ability to rise from a chair, and had a reduced incidence of falls.</td>
<td>&quot;Routine multicomponent exercise intervention should be prescribed to nonagenarians because overall physical outcomes are improved in this population.&quot;</td>
</tr>
<tr>
<td>Cebria, 2014</td>
<td>F: 5 days / week I: NR T: 6 weeks T: 1) supervised, interval-based inspiratory muscle TR device or Respiratory muscle strength (maximum inspiratory pressure, maximum expiratory pressure) and respiratory muscle endurance (maximum</td>
<td>Compared with interval based inspiratory muscle TR and the control group, the yoga intervention group had improved maximum inspiratory and expiratory pressure, and maximum</td>
<td>Yoga respiratory training was effective and well-tolerated in frail older adults, and may therefore be a useful alternative to inspiratory threshold TR or no training, to improve</td>
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<tbody>
<tr>
<td><strong>2) yoga breathing exercises</strong></td>
<td>voluntary ventilation)</td>
<td>voluntary ventilation.</td>
<td>respiratory muscle when whole body exercise TR is not possible.</td>
<td></td>
</tr>
<tr>
<td>Clegg, 2014</td>
<td>F: NR I: NR T: 12 weeks T: NR</td>
<td>Mobility, measured using the TUGT. Secondary outcomes were ADL, health-related QoL and depression.</td>
<td>Compared with the control group, the exercise group had a non-significant clinically important improvement in TUGT test. There were no differences in ADL, or health-related QoL</td>
<td>The Home-based Older People's Exercise trial pilot study reduced the deterioration in mobility among older people with frailty.</td>
</tr>
<tr>
<td>Zhang, 2014</td>
<td>F: 3-5 times /week I: NR T: 8 weeks; 4-5 min per session T: whole body vibration exercises</td>
<td>TUGT (mobility), leg strength and endurance, lower extremities muscle strength, balance function, balance confidence and General Health Status</td>
<td>Compared with usual care and exercises, the whole body vibration exercise group had improved mobility, leg strength and endurance, bilateral knees extensor strength, activities-specific balance confidence score and general health status</td>
<td>There were no side-effects observed during the TR. Whole-body vibration exercise is a safe and effective method that can improve the mobility, knee extensor strength, balance and the general health status in the frail elderly.</td>
</tr>
<tr>
<td>Gine-Garriga, 2013</td>
<td>F: NR I: NR T: 12 weeks T: Functional circuit training (functional balance and lower-body strength-based exercises)</td>
<td>Self-reported physical function, fear of falling (activities specific balance confidence), physical composite score, mental composite score</td>
<td>Compared with the control group, the exercise group had greater improvements in balance confidence and General Health Status</td>
<td>These data indicate that a FCT program is effective in improving self-reported measures of fear of falling and health status in a group of physically frail individuals.</td>
</tr>
<tr>
<td>Tousignant, 2013</td>
<td>F: NR I: light-moderate intensity T: 15 weeks T: Tai Chi</td>
<td>Fall incidence and severity</td>
<td>Compared with conventional physical therapy, the Tai Chi group had a greater improvement in falls.</td>
<td>Supervised Tai Chi exercises as part of a rehabilitation program seem to be a more effective alternative to the conventional physical therapy exercises for this specific population.</td>
</tr>
<tr>
<td>Szturm 2011</td>
<td>F: 2 times /week I: NR T: 8 weeks; 45 min / session T: interactive</td>
<td>Balance, TUGT (dynamic standing balance control), activities-specific balance confidence,</td>
<td>Compared with a conventional rehabilitation program, the intervention group had greater improvements in balance</td>
<td>Dynamic balance exercises on fixed and compliant sponge surfaces were feasibly coupled to interactive game-based</td>
</tr>
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<tr>
<td>Kato, 2018</td>
<td>F: 7 days / week; I: low to moderate; T: 12 weeks; 20 min / session; T: Marching in place and chair rising movements; gradually increasing speed of movements</td>
<td>ADL, mean power during chair stand, and time to complete a 10-m walk</td>
<td>Compared with the no-exercise comparison group, the exercise group had greater improvements in ADL, mean and relative power during chair stand, and 10-M walk</td>
<td>&quot;The progressive marching in place and chair rising exercise intervention appears to be effective in improving activities of daily living and functional mobility among frail older adults.&quot;</td>
</tr>
<tr>
<td>Hong, 2017</td>
<td>F: 2 times / week; I: NR; T: 8 weeks; T: A community capacity building exercise maintenance program</td>
<td>Muscular strength, static balance, muscular endurance, and health related QoL.</td>
<td>Compared with the physical exercise program comparator, the intervention group had greater improvements in muscular strength, static balance, muscular endurance, and health-related quality of life.</td>
<td>&quot;Results indicated that a community capacity building exercise maintenance program is feasible, and associated with exercise maintenance among frail elderly women.&quot;</td>
</tr>
<tr>
<td>Liu, 2017</td>
<td>F: NR; I: NR; T: 16 weeks; T: Exercise + behavior change enhancement; Exercise + health talks</td>
<td>Fatigue, physical endurance</td>
<td>Combined (exercise + behavior change enhancement); exercise (exercise + health talks); and comparison (health talks alone) groups did not differ for fatigue.</td>
<td>&quot;A trend of greater improvement in physical endurance was observed in the combined group than in the other two groups.&quot;</td>
</tr>
<tr>
<td>Yamada, 2017</td>
<td>F: 1 or 2 times/week; I: light; T: Unclear number of years; 60 min / session; T: group-based self-based New Long Term Care Insurance service requirement certifications (indicator for health)</td>
<td>new Long Term Care Insurance service</td>
<td>Compared with the control group, the self-management exercise group had fewer new Long Term Care Insurance service</td>
<td>&quot;These results indicate the usefulness of self-management group exercise to reduce the incidence of disability in...&quot;</td>
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<td></td>
<td>management multi-component exercise (aerobic, strength TR, flexibility and balance)</td>
<td>services use</td>
<td>requirement certifications during the 4 years of the study.</td>
<td>older adults. Thus, increasing self-management group activities in each community should be encouraged.</td>
</tr>
</tbody>
</table>

References Summarized

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses

   PubMed: PM27755209

   PubMed: PM28490866

   PubMed: PM28555710

   PubMed: PM26626157

   PubMed: PM24291597


Randomized Controlled Trials


PubMed: PM24030238

This randomized controlled trial examined the effects of multicomponent training on muscle power output, muscle mass, and muscle tissue attenuation; the risk


PubMed: PM23835773


PubMed: PM24742587


PubMed: PM23864514


PubMed: PM23740589


PubMed: PM23167499


PubMed: PM21799138

Non-Randomized Studies

Marching and Chair Rising


PubMed: PM29706704

Type Not Specified


PubMed: PM28991596

PubMed: PM27162189

Multi-Component


PubMed: PM28505140
Appendix — Further Information

Systematic Reviews – Mixed Population

Frail and Pre-Frail

PubMed: PM29521871

Systematic Review – Mixed Intervention

PubMed: PM28579766

Review Articles – Systematic Methods Not Specified

PubMed: PM28181204

PubMed: PM24666003

Randomized Controlled Trial – Mixed Intervention

PubMed: PM28085913

Accessed May 24, 2018

Randomized Controlled Trials – Mixed/Co-Morbid Population

Frail and Pre-Frail


PubMed: PM25659147


PubMed: PM28120633


PubMed: PM28295912


PubMed: PM26159634


PubMed: PM24903908


PubMed: PM24374288


PubMed: PM22929394

Frail with Chronic Obstructive Pulmonary Disease
   PubMed: PM27715322

Frail with Dementia

   PubMed: PM24243397

Randomized Controlled Trial – Other Population

Frailty Not Specified

   PubMed: PM25387728

Non-Randomized Studies – Mixed Population

Frail and Pre-Frail

   PubMed: PM27363692

   PubMed: PM26963483

   PubMed: PM27160666

   PubMed: PM24397847
Non-Randomized Studies – Other Population

General Population


PubMed: PM23525478

Non-Randomized Studies – Mixed Intervention

Physical and Social Activity


PubMed: PM25472546