Physical Activity to Prevent Major Mobility Disability: The Primary Results of the LIFE Study

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The LIFE Investigators

www.aging.ufl.edu
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<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Grant Number</th>
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</thead>
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<tr>
<td>2000</td>
<td>First concept for a Phase 3 trial</td>
<td></td>
</tr>
<tr>
<td>2001-2003</td>
<td>Planning grant R21AG19353</td>
<td></td>
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<tr>
<td>2003-2009</td>
<td>LIFE Pilot U01AG022376</td>
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</tr>
<tr>
<td>Sep 2009</td>
<td>LIFE funding U01AG022376</td>
<td></td>
</tr>
<tr>
<td>Feb 2010</td>
<td>Start randomization</td>
<td></td>
</tr>
<tr>
<td>Dec 2011</td>
<td>Randomization complete n=1635</td>
<td></td>
</tr>
<tr>
<td>Dec 2013</td>
<td>Follow-up complete</td>
<td></td>
</tr>
<tr>
<td>May 2014</td>
<td>Publication of the main results</td>
<td></td>
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</table>
HABC – 400 m walk performance and mobility limitation

Newman et al. JAMA; 2006;295:2018
HABC – 400 m walk performance and mobility disability

Newman et al. JAMA; 2006;295:2018
Medicare Current Beneficiary Survey
Ability to walk ¼ mile, health care cost and hospitalization rates

<table>
<thead>
<tr>
<th>Ability to Walk 1/4 Mile</th>
<th>No Difficulty</th>
<th>Difficulty</th>
<th>Unable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out-of-pocket</td>
<td>1.75 (1.60-1.91)</td>
<td>2.03 (1.79-2.26)</td>
<td>1.85 (1.61-2.10)</td>
</tr>
<tr>
<td>Hospitalizations per 100</td>
<td>25.1 (21.8-28.4)</td>
<td>39.2 (34.0-44.3)</td>
<td>47.3 (40.6-54.0)</td>
</tr>
</tbody>
</table>

Hardy et al. J Gen Intern Med Online; 2010:Oct 23
Predicted life expectancy by age and walking speed in men

Studenski et al. JAMA; 2011;305:50
Predicted life expectancy by age and walking speed in women

Studenski et al. JAMA; 2011;305:50
Potential interventions to maintain mobility

- ACE inhibitors
- Albuterol
- ARBs
- Aspirin
- Carnitine
- CoQ10
- Creatine
- Cytokine inhibitors
- DHEA
- Diet – high protein
- Diet – low calorie
- Erythropoietin
- Estrogens

- Growth hormone
- GH secretagogue
- **Health education**
- Myostatin inhibitors
- NSAIDs
- Pentoxiphylline
- **Physical activity**
- Resveratrol
- SARMs
- Statins
- Testosterone
- Thalidomide
- Vitamin D
- Vitamin E
Lifestyle Interventions and Independence for Elders

The LIFE Study

Is a structured \textit{physical activity} or a \textit{health education} program more effective in reducing the risk of major mobility disability in older persons?

Pahor et al. JAMA 2014
- Multicenter, single-blinded, parallel randomized trial
- 8 field centers across the US
- Coordinating Center: University of Florida
- Data Management Quality Control: Wake Forest University
- Duration: February 2010 – December 2013

Stanford, Pennington, Florida, Northwestern, Pittsburgh, Yale, Tufts, Wake Forest.
LIFE Inclusion criteria

- Men and women 70-89 years
- Sedentary lifestyle (<20 min per week in structured PA, <150 min/week in moderate PA)
- Able to walk 400 m
- SPPB score ≤9 (45% <8)
- No major cognitive impairment
- Could safely participate in the intervention (medical history, physical exam and ECG)
- Gives informed consent, lives in the study area and does not plan to move

Pahor et al. JAMA 2014
Primary outcome: Major Mobility Disability

Inability to walk 400 m at usual pace on a 20 m course - 10 laps (40 m per lap)
- Within 15 min without sitting
- Without help of a person or walker
- Use of a cane and stop for up to 1 min was acceptable

Pahor et al JAMA 2014
Other outcomes

• **Secondary outcomes:**
  • ADL disability
  • Cognitive function
  • Injurious falls
  • Major mobility disability or death
  • Persistent major mobility disability
  • Cost-effectiveness

• **Tertiary outcomes:**
  • Cardiopulmonary events
  • Dementia/MCI

Pahor et al. JAMA 2014
Health Education also called Successful Aging intervention

• Health workshops relevant to older adults (e.g., healthful nutrition, how to effectively negotiate the health care system, how to travel safely, recommended screening, etc.)

• Short instructor-led program (5-10 min) of gentle stretching or flexibility exercises

• Frequency: weekly during the first 26 weeks, and then monthly (bi-monthly optional)

Pahor et al. JAMA 2014
Physical activity intervention
Center-based in a group setting + home

- Aerobic (walking)
- Strength (lower extremities)
- Balance
- Flexibility stretching
- Behavioral counseling (group and telephone)

Pahor et al. JAMA 2014
Frequency and duration

- Walking 3 to 6 days per week (2 times per week at the center) (minimum walking bout 10 minutes with goal of 30 minutes per bout)
- Strength training 3 times per week (10 minutes per session)

Pahor et al. JAMA 2014
Intensity: moderate

- Walking performed at “12 to 14” (somewhat hard) on Borg scale
- Strength training goal “15 to 16” (hard) on Borg scale

Pahor et al. JAMA 2014
Aerobic

Wake Forest University

University of Florida
Aerobic
Aerobic

Stanford University

Outdoor walking

BP check

Taking a break during the walk
Wide Leg Squat
Toe stand
Knee extension with ankle weights
Assessed for eligibility (n = 14,831)

Total Excluded (n = 13,196)
- Refused (n=4125)
- SPPB too high (n=2654)
- Exercising too frequently (n=2422)
- Plan to move within 24 mos (n=2321)
- Mobility disabled (n=626)
- Morbidity exclusions (n=611)
- Other reasons (n=437)

Randomized (n = 1,635)

Physical Activity intervention (n = 818)
- Received intervention (n = 800)
  - No follow-up for primary outcome (n = 24)
    - 17 withdrawn
    - 2 deceased
    - 5 other
  - Discontinued intervention (n=118)

Analysis

Health Education intervention (n = 817)
- Received intervention (n= 805)
  - No follow-up for primary outcome (n = 14)
    - 10 withdrawn
    - 2 deceased
    - 2 other
  - Discontinued intervention (n=160)

Analysis

Pahor et al. JAMA 2014
**LIFE - Baseline characteristics of the participants**

<table>
<thead>
<tr>
<th></th>
<th>Physical Activity</th>
<th>Health Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=818</td>
<td></td>
<td>N=817</td>
</tr>
<tr>
<td>Age (years)</td>
<td>78.7 ± 5.2</td>
<td>79.1 ± 5.2</td>
</tr>
<tr>
<td>Women</td>
<td>66.9%</td>
<td>67.4%</td>
</tr>
<tr>
<td>Ethnicity: Hispanic</td>
<td>3.8%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Race: Caucasian</td>
<td>73.8%</td>
<td>77.7%</td>
</tr>
<tr>
<td>Race: African American</td>
<td>19.9%</td>
<td>15.3%</td>
</tr>
<tr>
<td>SPPB score</td>
<td>7.4 ± 1.6</td>
<td>7.3 ± 1.6</td>
</tr>
<tr>
<td>SPPB score &lt;8</td>
<td>43.3%</td>
<td>46.2%</td>
</tr>
<tr>
<td>400 m walking speed (m/sec)</td>
<td>0.83 ± 0.17</td>
<td>0.82 ± 0.17</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>30.1 ± 5.7</td>
<td>30.3 ± 6.2</td>
</tr>
</tbody>
</table>

Pahor et al JAMA 2014
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Physical Activity</th>
<th>Health Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>3MSE score</td>
<td>91.5 ± 5.5</td>
<td>91.6 ± 5.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>70.5%</td>
<td>71.5%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>24.4%</td>
<td>26.6%</td>
</tr>
<tr>
<td>Heart attack, MI</td>
<td>7.4%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Stroke</td>
<td>7.0%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Cancer</td>
<td>21.9%</td>
<td>23.6%</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>16.0%</td>
<td>15.2%</td>
</tr>
</tbody>
</table>

Pahor et al JAMA 2014
Attendance to center-based interventions after excluding medical leave

<table>
<thead>
<tr>
<th></th>
<th>25&lt;sup&gt;th&lt;/sup&gt;%</th>
<th>Median</th>
<th>75&lt;sup&gt;th&lt;/sup&gt; %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Activity</td>
<td>50</td>
<td>71</td>
<td>83</td>
</tr>
<tr>
<td>Health Education</td>
<td>63</td>
<td>82</td>
<td>90</td>
</tr>
</tbody>
</table>

Pahor et al JAMA 2014
Accelorometry (Moderate Intensity)

Physical activity

Health Education

P<0.001

Pahor et al JAMA 2014
Major mobility disability events

• 32.5% (532/1635) participants

Persistent mobility disability events

• 17.2% (282/1635) participants

Over an average of 2.6 years of follow-up

Pahor et al JAMA 2014
Events

Physical Activity: 30.1% (n=246/818)
Health Education: 35.5% (n=290/817)

HR=0.82, 95%CI=0.69-0.98
P=0.03

Pahor et al JAMA 2014
Persistent Mobility Disability

Events
Physical Activity: 14.7% (120/818)
Health Education: 19.8% (162/817)

HR=0.72, 95%CI=0.57-0.91
p=0.006

Pahor et al JAMA 2014
## Major Mobility Disability – Subgroup Analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>PA (Events / N)</th>
<th>SA (Events / N)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Interaction P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>246 / 818</td>
<td>290 / 817</td>
<td>0.82 (0.69, 0.98)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>171 / 547</td>
<td>204 / 551</td>
<td>0.82 (0.67, 1.01)</td>
<td>0.95</td>
</tr>
<tr>
<td>Male</td>
<td>75 / 271</td>
<td>86 / 266</td>
<td>0.81 (0.59, 1.11)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity/Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>182 / 604</td>
<td>234 / 635</td>
<td>0.80 (0.66, 0.98)</td>
<td>0.58</td>
</tr>
<tr>
<td>Other</td>
<td>64 / 211</td>
<td>56 / 180</td>
<td>0.90 (0.63, 1.29)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-79</td>
<td>123 / 477</td>
<td>138 / 455</td>
<td>0.85 (0.67, 1.09)</td>
<td>0.76</td>
</tr>
<tr>
<td>80+</td>
<td>123 / 341</td>
<td>152 / 362</td>
<td>0.81 (0.63, 1.03)</td>
<td></td>
</tr>
<tr>
<td>History of CVD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No CVD</td>
<td>155 / 582</td>
<td>187 / 563</td>
<td>0.78 (0.63, 0.97)</td>
<td>0.34</td>
</tr>
<tr>
<td>CVD</td>
<td>91 / 236</td>
<td>103 / 254</td>
<td>0.93 (0.70, 1.24)</td>
<td></td>
</tr>
<tr>
<td>History of Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>114 / 406</td>
<td>126 / 414</td>
<td>0.92 (0.71, 1.19)</td>
<td>0.41</td>
</tr>
<tr>
<td>Impaired FG</td>
<td>59 / 192</td>
<td>68 / 165</td>
<td>0.69 (0.49, 0.99)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>73 / 220</td>
<td>96 / 238</td>
<td>0.78 (0.57, 1.06)</td>
<td></td>
</tr>
<tr>
<td>Gait Speed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.8 m/s</td>
<td>173 / 485</td>
<td>210 / 508</td>
<td>0.81 (0.66, 0.99)</td>
<td>0.63</td>
</tr>
<tr>
<td>0.8+ m/s</td>
<td>73 / 333</td>
<td>80 / 309</td>
<td>0.88 (0.64, 1.22)</td>
<td></td>
</tr>
<tr>
<td>SPPB</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;8</td>
<td>135 / 353</td>
<td>177 / 378</td>
<td>0.75 (0.60, 0.94)</td>
<td>0.19</td>
</tr>
<tr>
<td>8 or 9</td>
<td>111 / 465</td>
<td>113 / 439</td>
<td>0.95 (0.73, 1.23)</td>
<td></td>
</tr>
<tr>
<td>3MSE (post-hoc)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;90</td>
<td>95 / 261</td>
<td>108 / 261</td>
<td>0.88 (0.66, 1.16)</td>
<td>0.58</td>
</tr>
<tr>
<td>90+</td>
<td>151 / 557</td>
<td>182 / 556</td>
<td>0.80 (0.64, 0.99)</td>
<td></td>
</tr>
</tbody>
</table>

Pahor et al JAMA 2014
LIFE – Serious adverse events reported at blinded assessments

<table>
<thead>
<tr>
<th>Event</th>
<th>Physical Activity N = 818</th>
<th>Health Education N = 817</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All serious adverse events</td>
<td>49.4%</td>
<td>45.7%</td>
<td>1.08 (0.98, 1.20)</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>48.4%</td>
<td>44.1%</td>
<td>1.10 (0.99, 1.22)</td>
</tr>
<tr>
<td>Death</td>
<td>5.9%</td>
<td>5.1%</td>
<td>1.14 (0.76, 1.71)</td>
</tr>
<tr>
<td>Persistent disability/incapacity</td>
<td>4.0%</td>
<td>3.2%</td>
<td>1.27 (0.77, 2.10)</td>
</tr>
<tr>
<td>Life threatening event</td>
<td>1.3%</td>
<td>1.0%</td>
<td>1.37 (0.56, 3.40)</td>
</tr>
<tr>
<td>Any other serious events</td>
<td>0.9%</td>
<td>1.0%</td>
<td>0.87 (0.32, 2.40)</td>
</tr>
</tbody>
</table>

Pahor et al JAMA 2014
Take home message

Among older adults at risk of disability, a structured moderate intensity physical activity program, compared with a health education program

• Reduced major mobility disability by 18% and persistent mobility disability by 28%

• Those at highest risk, benefited the most