Midlife Cardiorespiratory Fitness is Associated with Lower Incidence of Depression and Cardiovascular Death With or Without Incident Depression in Later Life

FINANCIAL DISCLOSURE:
No relevant financial relationship exists
Midlife Cardiorespiratory Fitness is Associated with Lower Incidence of Depression and Cardiovascular Death With or Without Incident Depression in Later Life

Benjamin Willis, David Leonard, Carolyn Barlow, Shannon Fitzgerald, Scott Martin, and Laura DeFina
Depression and Cardiovascular Disease

• Depression is associated with cardiovascular disease (CVD)
  – 2014 AHA Scientific Statement
  – Depression = risk factor for adverse outcomes in patients with acute coronary syndrome

• Prevalence of depression increases in the presence of CVD events
  – 1 in 5 patients with CVD is depressed
  – 1 in 3 patients with stroke is depressed
  – Increased CVD mortality risk

Cardiorespiratory Fitness

• Cardiorespiratory fitness (fitness):
  – An objective measure that is a marker of habitual physical activity\(^1\)
  – Higher fitness associated with:
    • Lower incidence of depression\(^2\)
    • Lower CVD mortality\(^3\)

• The joint association of midlife fitness, later life depression, and CVD mortality has not been extensively studied

Hypotheses:

• Midlife fitness would be inversely associated with:
  – Later life incident depression
  – CVD mortality
  – CVD mortality following incident later life depression
Cooper Center Longitudinal Study (CCLS) and Medicare Data

CCLS
- Preventive medical exam
- Started in 1970
- Fitness by max Balke ETT
- Limited morbidity data

Medicare
- Administrative data
- ICD and CPT codes
- Inpatient and outpatient
- Morbidity & mortality

N=19,241
Complete data
First CCLS Exam Prior to Age 65
Medicare Fee for Service 1999-2009

N=17,989
18,890
No prior conditions

351
History of CVD

901 with History of Midlife Depression
Methods: Baseline Examination

• Midlife fitness from CCLS examination:
  • Treadmill time from Balke protocol categorized into age- and gender-specific quintiles
    • Quintile 1: low fit
    • Quintiles 2-3: moderate fit
    • Quintiles 4-5: high fit

• Measured risk factors from CCLS examination:
  • Age
  • Smoking status
  • Systolic blood pressure
  • Body mass index
  • Total cholesterol, fasting glucose
Methods: Outcomes after age 65

- Depression diagnosis ascertained after entry into Medicare.
  - Incident depression diagnoses determined using Centers for Medicare and Medicaid Services (CMS) validated algorithms
  - Based on ICD-9 codes
- CVD death determined from National Death Index (NDI)
  - Based on ICD-9 and ICD-10 codes
Methods: Analysis

• Three transition states defined for analysis:
  – Healthy---->Incident depression
  – Healthy---->CVD death
  – Incident Depression---->CVD death

• Multivariable proportional hazard model
  – Association of fitness with any of the three events
  – Attained age in Medicare used as time scale
  – Models were adjusted for baseline age, year of examination, gender, smoking, fasting glucose, total cholesterol, systolic BP, and BMI
## Results: Cohort Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low Fit N=2959</th>
<th>Moderate Fit N=7230</th>
<th>High Fit N=7800</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Age, years</td>
<td>46.9</td>
<td>49.4</td>
<td>51.6</td>
</tr>
<tr>
<td>Medicare Age, years</td>
<td>74.2</td>
<td>74.5</td>
<td>74.2</td>
</tr>
<tr>
<td>Women, (%)</td>
<td>16%</td>
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<td>99</td>
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117,219 person years of observation: 2701 depression events + 841 CVD deaths
Rates of Incident Depression by Fitness Category

<table>
<thead>
<tr>
<th>Fitness Category</th>
<th>Rate per 1000 person years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Fit</td>
<td>30.7</td>
</tr>
<tr>
<td>Moderate Fit</td>
<td>26.2</td>
</tr>
<tr>
<td>High Fit</td>
<td>22.2</td>
</tr>
</tbody>
</table>

P for trend <0.001
Rates of CVD Death Without Incident Depression by Fitness Category

P for trend <0.001
Rates of CVD Death Preceded by Incident Depression by Fitness Category

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<th>Fitness Category</th>
<th>Rate per 1000 person years</th>
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<tr>
<td>Low Fit</td>
<td>32.9</td>
</tr>
<tr>
<td>Moderate Fit</td>
<td>25.8</td>
</tr>
<tr>
<td>High Fit</td>
<td>16.1</td>
</tr>
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</table>

P for trend <0.001
Transition Model Hazard Ratios

**Healthy**

- High Fit = 0.83 (95% CI 0.73, 0.93)

**Depression**

- High Fit = 0.39 (95% CI 0.31, 0.65)

**CVD Death**

- High Fit = 0.45 (95% CI 0.31, 0.65)

Referent is Low Fit: HR=1.00 for all transitions

Adjusted for Gender, Age, Exam Year, Systolic BP, Glucose, Total Cholesterol, BMI, Smoking, and Gender*Stratum interaction. (Gender*Fitness*Stratum interaction P= 0.4)
### Transition Model: Continuous Fitness

<table>
<thead>
<tr>
<th>Transition</th>
<th>Hazard Ratio Per MET Midlife Fitness</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy to Depression</td>
<td>0.86</td>
<td>(0.81, 0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Healthy to CVD Death</td>
<td>0.84</td>
<td>(0.80, 0.88)</td>
<td>&lt;0.001</td>
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<tr>
<td>Depression to CVD Death</td>
<td>0.95</td>
<td>(0.93, 0.97)</td>
<td>&lt;0.001</td>
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Adjusted for Gender, Age, Exam Year, Systolic BP, Glucose, Total Cholesterol, BMI, Smoking, and Gender*Stratum interaction.
Limitations

• Depression diagnoses not adjudicated diagnoses
  – From administrative Medicare data
  – Chronic Condition Warehouse algorithms are derived from prior research comparing Medicare claims files with clinically adjudicated outcomes
  – Allows long-term follow-up of large population.

• CCLS unique cohort with lower prevalence of traditional risk factors
  – The impact of risk factors in the CCLS is similar to that of risk factors in the general population
Conclusions

• An inverse association exists between midlife fitness and later life:
  – Depression
  – CVD death
  – CVD death even following incident depression

• These findings suggest the importance of fitness in middle-age for prevention of depression and CVD death in older age.
Thank You
Extra Slides
Methods: Medicare ICD-9 Codes for Depression

• Depression diagnosis ascertained after entry into Medicare as a primary outcome.
  – Depression diagnoses based on ICD-9 codes
    • 296.20-296.36 Depressive Disorder
    • 296.50-296.56 Bipolar
    • 296.60-296.66
    • 296.89
    • 298.0
    • 300.4 Dysthymic
    • 309.1 Prolonged Depressive Reaction
    • 311 Depressive Unclassified
CCW Algorithm for Depression Medicare Administrative Data

- Depression: 1 Year DX
- At least 1 inpatient, SNF, HHA, HOP, or Carrier claim with DX codes during the 1 year period.
Fitness In CCLS is Similar to the General Population

Cardiorespiratory Fitness, (VO₂ Max)

CCLS Age 35-44  |  NHANES Age 40-49  |  CCLS Age 45-54

20th %ile  |  50th %ile  |  80th %ile

Wang, *Am J Epidemiol* 2010
Lifetime Risk for CVD Death by Aggregate RF Burden In CCLS is Similar to Other Cohorts

In CCLS is Similar to Other Cohorts

Lifetime Risk for CVD Death by Aggregate RF Burden

CCLS

Pooling Project*

Lifetime risk (%)

45
30
15
0

Attained age (years)

45 55 65 75 85 95

45
30
15
0

Attained age (years)

45 55 65 75 85 95

≥ 2 Major Risk Factors
1 Major Risk Factor
≥ 1 Elevated Risk Factor
≥ 1 Not Optimal Risk Factor
All Optimal Risk Factors

* ≥ 250,000 participants from 17 datasets

Berry, AHA 2007
Midlife Fitness
Hazard of Depression and CVD Death

P for trend = 0.001

Healthy to Depression
Healthy to CVD Death
Depression to CVD Death

Low Fit
Moderate Fit
High Fit

0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6

24
Balke Protocol

- Initial treadmill speed = 88 meter/min (3.3 miles/hour)
- Initial grade = 0% → 2% (Minute 2) → 1% increase every minute
- After 25 minutes, speed is increased 5.4 meters/min each minute
- Test terminated for volitional exhaustion or for medical reasons
- Test time correlates with maximal oxygen uptake ($r = 0.92$)

Pollock, *AHJ* 1976
Cardiorespiratory Fitness (CRF)

- Obtained by maximum Balke treadmill test
- VO$_2$Max estimated from treadmill time
- Cut-points based on age-adjusted CRF.
- Categories based on prior analyses showing highest health risk in quintile 1 or “low fit” category.

Fitness categories$^1$
- Low fit = Quintile 1
- Moderate fit = Quintile 2,3
- High fit = Quintile 4,5

Low Fitness ➔ Higher:
- All-cause mortality
- Cardiovascular mortality
- Cancer mortality
- Cardiovascular disease
- Diabetes mellitus
- Metabolic syndrome
- Depression

$^1$MSSE 2011;43(11):2134-2139.
References


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