Physical Activity: Impact on Morbidity and Mortality

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Disclosures

- **Medical/Scientific Advisory Boards**
  - Technogym
  - Cancer Foundation for Life
  - Santech
  - Clarity Project

- **Research Funding**
  - NIH
  - Body Media
  - Coca Cola
  - Department of Defense

- **Royalties**
  - Human Kinetics
Non-Communicable Diseases (NCDs)

- Changing patterns in leisure and work have led to a health crisis
- NCDs cause 65% of all deaths worldwide
- 36.1 million deaths from CVD, Stroke, Diabetes, Cancer & Respiratory diseases.

Economic Burden

- Failure to reduce chronic diseases will result in heavy losses in terms of human life and economic production.

- Current losses:
  - US: $750 billion annually from CVD & diabetes alone.
  - China: $558 billion
  - India: $237 Billion
  - Britain: $33 Billion

- Trends suggest that risk factors and costs are on the rise.
Lancet Physical Activity Series

More of the same is not enough
33 researchers, 16 countries

© 2009 www.outline-world-map.com
EFFECT OF PHYSICAL INACTIVITY ON MAJOR NON-COMMUNICABLE DISEASES WORLDWIDE: AN ANALYSIS OF BURDEN OF DISEASE AND LIFE EXPECTANCY

I-Min Lee, Eric J Shiroma, Felipe Lobelo, Pekka Puska, Steven N Blair, Peter T Katzmarzyk, for the Lancet Physical Activity Series Working Group
Findings

- Between 6-10% of the world’s major NCDs is attributable to inactivity
- By eliminating inactivity, >5.3 M deaths/y may be prevented
- This leads to an increase of 0.68 years in the world’s life expectancy

(For perspective: smoking causes 5 M deaths/y worldwide)
Physical Activity and CRF as Predictors of All-cause Mortality

- 31,818 men and 10,555 women
- 1492 deaths in men during average follow-up of 14.6 years, and 230 deaths in women during average follow-up of 12.8 years
- PA mortality trends not significant after adj for CRF
- CRF trends significant after adj for PA

Lee DC, et al. *BJSM* 2-11; 45:504-10
Aerobics Center
Longitudinal Study
Design of the ACLS

1970  More than 80,000 patients  2005
Cooper Clinic examinations--including
history and physical exam, clinical tests,
body composition, EBT, and CRF

Mortality surveillance to 2003
More than 4000 deaths

1982 ‘86 ‘90 ‘95 ’99 ‘04
Mail-back surveys for case finding and
monitoring habits and other characteristics
All-Cause Death Rates by CRF Categories—3120 Women and 10 224 Men—ACLS

Blair SN. *JAMA* 1989
Does Changing Cardiorespiratory Fitness Reduce Mortality Risk?
Fitness Change Categories

- Unfit was defined as the least fit 20% of men in each age group
- Men were classified as fit or unfit at both examinations
- Change categories
  - unfit at both examinations = never fit
  - unfit at first, fit at second = improvers
  - fit at both examinations = always fit

Blair SN et al. *JAMA* 1995; 273:1093-8
<table>
<thead>
<tr>
<th>Fitness Groups</th>
<th>Age-adjusted Death Rates/10,000 Man-years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CVD</td>
</tr>
<tr>
<td>Never fit</td>
<td>65</td>
</tr>
<tr>
<td>Improvers</td>
<td>31</td>
</tr>
<tr>
<td>Always fit</td>
<td>14</td>
</tr>
</tbody>
</table>

Blair SN et al. *JAMA* 1995; 273:1093-8
Cardiorespiratory Fitness, Risk Factors and All-Cause Mortality, Men, ACLS

Cardiorespiratory Fitness Groups

*Adjusted for age, exam year, and other risk factors

Risk Factors
- current smoking
- SBP ≥ 140 mmHg
- Chol ≥ 240 mg/dl

Deaths/10,000 MY*
- Low
- Mod
- High

# of risk factors
- 0
- 1
- 2 or 3

Blair SN et al. JAMA 1996; 276:205-10
CVD Death Rates* by Fitness Groups, 7,080 Women and 25,341 Men, ACLS

Deaths/10,000 PY

Adjusted for age, exam year, and other risk factors

Blair SN et al. JAMA 1996; 276:205-10
CRF and Other Health Outcomes
CRF and Digestive System Cancer Mortality

- 38,801 men, ages 20-88 years
- 283 digestive system cancer deaths in 17 years of follow-up
CRF was inversely associated with death after adjustment for age, examination year, body mass index, smoking, drinking, family history of cancer, personal history of diabetes
- Fit men had lower risk of colon, colorectal, and liver cancer deaths

• 14,551 women, ages 20-83 years
• Completed exam 1970-2001
• Followed for breast cancer mortality to 12/31/2003
• 68 breast cancer deaths in average follow-up of 16 years
• Odds ratio adjusted for age, BMI, smoking, alcohol intake, abnormal ECT, health status, family history, & hormone use

Sui X et al. *MSSE* 2009; 41:742
CRF and Risk of Incident Hypertension, ACLS Women

- 4,884 healthy women examined at the Cooper Clinic, 1970-1998
- 157 women developed hypertension during average follow-up of 5 years
- Risk adjusted for age, exam year, alcohol intake, smoking, BP, family history of hypertension, waist girth, glucose, & triglycerides

Risk of Developing Hypertension

Barlow CE et al. *Am J Epidemiol* 2006; 163:142-50
Incidence of depressive symptoms by cardiorespiratory fitness categories among women

Cumulative Incidence Rate (%)

Low
Moderate
High
Cardiorespiratory Fitness Level

Linear trend $P < 0.0001$

*Unadj incidence rates

Activity, Fitness, and Mortality in Older Adults
Cardiorespiratory Fitness and All-Cause Mortality, Women and Men \( \geq 60 \) Years of Age

- 4060 women and men \( \leq 60 \) years
- 989 died during \( \sim 14 \) years of follow-up
- \( \sim 25\% \) were women
- Death rates adjusted for age, sex, and exam year

All-Cause death rates/1,000 PY

## Prevalence of Self-reported Functional Limitations by Fitness and Age Groups

<table>
<thead>
<tr>
<th>Fitness Group</th>
<th>40-49</th>
<th>50-59</th>
<th>60+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>18*</td>
<td>23</td>
<td>46</td>
</tr>
<tr>
<td>Moderate</td>
<td>8</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>High</td>
<td>7</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>7</td>
<td>14</td>
<td>24</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>High</td>
<td>3</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

*Prevalence (%)  

Huang et al. MSSE 1998, 30:1430-5
Cardiorespiratory Fitness and Risk of Dementia, ACLS

- 59,960 women and men
- Followed for 16.9 years after clinic exam
- 4,108 individuals died
  - 161 with dementia listed on the death certificate
- Hazard ratio adjusted for age, sex, exam yr, BMI, smoking, alcohol, abnormal ECG, history of hypertension, diabetes, abnormal lipids, and health status

Hazard Ratio

P for trend=0.002

Lui R et al. MSSE 2012
### LIFE-P

#### Serious adverse events

<table>
<thead>
<tr>
<th>Event</th>
<th>Physical activity N=213</th>
<th>Successful aging N=211</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.9%</td>
<td>0.9%</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Life threatening event</td>
<td>1.4%</td>
<td>1.4%</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>20.7%</td>
<td>20.9%</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Significant lab exam</td>
<td>2.8%</td>
<td>3.8%</td>
<td>0.60</td>
</tr>
<tr>
<td>Any SAE</td>
<td>22.5%</td>
<td>23.7%</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Cardiorespiratory Fitness and Health Outcomes in Various Population Subgroups

Such Those with Chronic Disease
Age and exam year adjusted rates of total CVD events by levels of CRF and severity of HTN in 8147 hypertensive men

CVD incidence/1000 man-years

CRF:
- Low
- Moderate
- High

Sui X et al. Am J Hypertension. 2007
Muscular Strength and Health
Muscular Strength and Health Outcomes

Definition of Muscular Strength

- Assessed using resistance weight machines
  - Upper body strength: 1-repetition maximum (1-RM) supine bench press
  - Lower body strength: 1-RM seated leg press
- A combination score = mean of the bench and leg press standardized scores
- Thirds of the age-specific composite score was used for analysis
Thirds of Muscle Strength and Mortality, 8762 Men--ACLS

503 deaths (145 CVD) during average follow-up of 18.9 years

• 8,677 men, 20-82 years
• 18.8 years of follow-up, 211 cancer deaths
• Muscular strength assessed by 1-RM bench press and leg press
• Significant trend across strength categories remained after further adjustment for BMI, % body fat, waist circumference, and cardiorespiratory fitness

Odds of Cancer Death*

* Adj for age, exam yr, smoking alcohol intake, and health status

Strength and Mortality in men with Hypertension

- 1,506 men with hypertension, > 40 yr
- 18.3 years of follow-up, 183 all-cause deaths
- Muscular strength assessed by 1-RM bench press and leg press
- Hypertensive men with high muscular strength had lower risk of mortality

Risk of all-cause death

* Age, physical activity, smoking, alcohol, BMI, health status and family CVD history

Artero EG, et al. JACC 2011; 57:1831-7
Yes, But Those Are Observational Studies, and We Require Randomized Clinical Trial Evidence
Effects of Different Doses of Physical Activity on Cardiorespiratory Fitness Among Sedentary, Overweight or Obese Postmenopausal Women With Elevated Blood Pressure: A Randomized Controlled Trial

Timothy S. Church, MD, MPH, PhD
Conrad P. Earnest, PhD
James S. Skinner, PhD
Steven N. Blair, PED

Low levels of cardiorespiratory fitness are associated with high risk of cardiovascular disease (CVD) and all-cause mortality, and improvements in fitness are associated with reduced mortality risk. Although higher levels of fitness are associated with better CVD risk factor profiles, the fitness-CVD and all-cause mortality relation is only moderately attenuated when traditional risk factors are controlled.

Context Low levels of cardiorespiratory fitness are associated with high risk of mortality, and improvements in fitness are associated with reduced mortality risk. However, a poor understanding of the physical activity–fitness dose response relation remains.

Objective To examine the effect of 50%, 100%, and 150% of the NIH Consensus Development Panel recommended physical activity dose on fitness in women.

Design, Setting, and Participants Randomized controlled trial of 464 sedentary, postmenopausal overweight or obese women whose body mass index ranged from 25.0 to 43.0 and whose systolic blood pressure ranged from 120.0 to 159.9 mm Hg. Enrollment took place between April 2001 and June 2005 in the Dallas, Tex, area.

Intervention Participants were randomly assigned to 1 of 4 groups: 102 to the non-exercise control group and 155 to the 4-kcal/kg, 104 to the 8-kcal/kg, and 103 to the 12-kcal/kg per week energy-expenditure groups for the 6-month intervention period. The training intensity was the heart rate associated with 50% of each woman's peak V̇O₂.

Primary Outcome Measure The primary outcome was aerobic fitness assessed on a 12-stage graded exercise test and quantified as peak absolute oxygen consumption (V̇O₂abs, L/min).

Results The mean (SD) baseline V̇O₂abs values were 1.30 (0.25) L/min. The mean minutes of exercising per week were 72.2 (12.3) for the 4-kcal/kg, 135.8 (19.5) for the 8-kcal/kg, and 191.7 (33.7) for the 12-kcal/kg per week exercise groups. After adjustment for age, race/ethnicity, weight, and peak heart rate, the exercise groups increased their V̇O₂abs compared with the control group by 4.2% in the 4-kcal/kg, 6.0% in the 8-kcal/kg, and 8.2% in the 12-kcal/kg per week groups (P < .001 for each vs control; P for trend < .001). There was no treatment × subgroup interaction for age, body mass index, weight, baseline V̇O₂abs, race/ethnicity, or baseline hormone therapy use. There were no significant changes in systolic or diastolic blood pressure values from baseline to 6 months in any of the exercise groups vs the control group.

Conclusion In this study, previously sedentary, overweight or obese postmenopausal women experienced a graded dose-response change in fitness across levels of exercise training.

Trial Registration clinicaltrials.gov Identifier: NCT00011193
Change in Fitness

<table>
<thead>
<tr>
<th>Study groups</th>
<th>Change in fitness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-1.7</td>
</tr>
<tr>
<td>72 minutes</td>
<td>3.8</td>
</tr>
<tr>
<td>136 minutes</td>
<td>6.7</td>
</tr>
<tr>
<td>192 minutes</td>
<td>9.1</td>
</tr>
</tbody>
</table>
Quality of Life Measures
Exercise Dose and Quality of Life
A Randomized Controlled Trial
Corby K. Martin, PhD; Timothy S. Church, MD, MPH, PhD; Angela M. Thompson, MSPH; Conrad P. Earnest, PhD; Steven N. Blair, PED

Background: Improved quality of life (QOL) is a purported benefit of exercise, but few randomized controlled trials and no dose-response trials have been conducted to examine this assertion.

Methods: The effect of 50%, 100%, and 150% of the physical activity recommendation on QOL was examined in a 6-month randomized controlled trial. Participants were 430 sedentary postmenopausal women (body mass index range, 25.0-43.0 [calculated as weight in kilograms divided by height in meters squared]) with elevated systolic blood pressure randomized to a nonexercise control group (n=92) or 1 of 3 exercise groups: exercise energy expenditure of +1 (n=147), 8 (n=96), or 12 (n=95) kilocalories per kilogram of body weight per week. Eight aspects of physical and mental QOL were measured at baseline and month 6 with the use of the Medical Outcomes Study 36-Item Short Form Health Survey.

Results: Change in all mental and physical aspects of QOL, except bodily pain, was dose dependent (trend analyses were significant, and exercise dose was a significant predictor of QOL change; P<.03). Higher doses of exercise were associated with larger improvements in mental and physical aspects of QOL. Controlling for weight change did not attenuate the exercise-QOL association.

Conclusions: Exercise-induced QOL improvements were dose dependent and independent of weight change.

Trial Registration: clinicaltrials.gov identifier: NCT00011193
Arch Intern Med. 2009;169(3):269-278

A SEDENTARY LIFESTYLE IS A RISK FACTOR FOR MANY CHRONIC CONDITIONS, INCLUDING DIABETES MELLITUS, HEART DISEASE, STROKE, AND CERTAIN TYPES OF CANCERS.1-3 Regular physical activity and higher levels of cardiorespiratory fitness are associated with lower risk for premature mortality, and exercise training has been demonstrated to improve a number of important risk factors, such as cardiorespiratory fitness,7 weight, high-density lipoprotein cholesterol level, and fasting insulin level.8 Although mood, level of functioning, energy level, and other measures of quality of life (QOL) are purported to be improved by regular exercise, this claim is largely unsubstantiated in populations without significant morbidity. There is strong evidence that regular exercise substantially improves QOL in populations with serious diseases, such as cancer4 or chronic obstructive pulmonary disease,5 but the data are not as supportive in populations without disease. Although many, but not all, epidemiologic studies have found an association between exercise and QOL, the available data from intervention trials fail to consistently find a strong effect of exercise training on QOL.11-13 Furthermore, the data from intervention trials are difficult to interpret because of small sample sizes, inadequate control groups, and poor exercise compliance. In addition, many studies include a weight loss component, making it difficult to separate the benefits of weight loss from the benefits of increased exercise.

To our knowledge, there are no well-controlled, properly powered, randomized controlled trials (RCTs) examining the role of exercise in improving QOL among individuals without significant comorbidities. The Dose-Response to Exercise in postmenopausal Women (DREW) study was designed to examine the health benefits of 50%, 100%, and 150% of the National Institutes of Health Consensus Development Panel's physical activity recommendation among 464 sedentary, overweight or obese postmenopausal women with elevated blood pressure. The primary outcomes of cardiorespiratory fitness and blood pressure have been reported,7 but data on a number of important secondary outcomes also were included a priori in the study design, in-
Change in Physical Health

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>Control</th>
<th>72 minutes</th>
<th>136 minutes</th>
<th>192 minutes</th>
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<tbody>
<tr>
<td>SPH</td>
<td>3.05</td>
<td>7.35</td>
<td>8.56</td>
<td>10.35</td>
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Change in Energy

VT

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<th>Control</th>
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<th>136 minutes</th>
<th>192 minutes</th>
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<tr>
<td></td>
<td>5.21</td>
<td>12.25</td>
<td>11.58</td>
<td>14.42</td>
</tr>
</tbody>
</table>
Exercise Is As Good As Other Treatments for Clinical Depression

Drug therapy and cognitive behavioral therapy produce remission in approximately 40% of clinically depressed individuals.

Improve HbA1c ≥ 0.5% or Decrease DM Medications

P = 0.02

Church et al, JAMA Nov 24 2010
Summary
Attributable Fractions of Health Outcomes
For Low Cardiorespiratory Fitness and
Other Predictors, ACLS

• Attributable fraction (%) is the estimated number of deaths due to a specific characteristic
• Based on strength of association
• Prevalence of the condition
Attributable Fractions (%) for All-Cause Deaths

40,842 Men & 12,943 Women, ACLS

Summary

- Physical inactivity and low fitness are highly prevalent in modern societies
- Inactivity and low fitness are strong determinants of morbidity and mortality due to chronic disease
- Comprehensive programs to increase activity are crucial to the public’s health
Thank you
Questions?