The Dangers of Too Little Vs. Too Much Exercise

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Exercise and Health

• We know that exercise is a powerful medicine for both the treatment and prevention of chronic disease and reducing the risk for premature death.
  – Proven linear relationship between physical activity and health status.
  – The association between disease and an inactive and unfit way of life persists in every subgroup of the population.

• Too little exercise is THE major public health problem of our time.
Comparing the Danger of *Low Fitness*

Blair; 2008
Low Fitness Kills More People than Smokadiabesity!

Khan; BJSM, 2011
Death Rates by Fitness & BMI Categories

Fitness, Risk Factors and Mortality

The Classification of Risk Factors for Cardiovascular Disease

• Surrogate outcomes of poor lifestyle choices and stress (hypertension, obesity, cholesterol and diabetes), along with smoking are given “causal” risk factor status for CVD.

• Physical inactivity is generally referred to as a “predisposing” risk factor.
  – Suggesting its influence on disease is entirely due to intensification of the causal factors.
  – Result has been disproportionate focus on drugs (mainly lipid and BP) to treat disease.
  – Research has proven this is incorrect.
The Effect of Exercise on CVD Risk

• Even after accounting for traditional CVD risk factors (BP, DM, lipids, weight), the inverse relationship between PA & CVD risk persists.
  – ~59% of the reduction in CVD risk with exercise is due to reducing Inflammation & Clotting (32.6%), BP (27.1%), lipids (19.1%), BMI (10.1%), A1C (8.9%).
  – 41% of risk reduction due to other unknown mechanisms (perhaps endothelium function and remodeling or LV structure and function).
  – Effect of weight loss is only on traditional risk factors.

Mora, Circulation, 2007
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Mora, Circulation, 2007
Irrefutable Evidence that Exercise is Medicine for the Primary and Secondary Prevention of:

- Diabetes mellitus
- Cancer (breast and colon)
- Hypertension
- Depression
- Osteoporosis
- Dementia
- Coronary Artery Disease
- Lower death rate from all causes
What is the Optimal Dose of Exercise?
2018 US Physical Activity Guidelines

• 150 minutes per week of moderate to vigorous PA (like a brisk walk) in adults.
  – 30 minutes walking on 5 days per week.
  – Activity bouts of any duration count!

• 75 minutes per week of vigorous exercise (like running).

• 60 minutes per day in kids (half at vigorous intensity).
Dose-Response Curve for Exercise

- **A** = Sedentary
- **B** = Moderately Active
- **C** = Highly Active

Weekly Exercise Time

Benefit

Low \[\rightarrow\] **A** \[\rightarrow\] **B** \[\rightarrow\] **C** \[\rightarrow\] High

Dose-Response Curve
Exercise is Medicine

Running and Walking are 2 great formulations, but what is the optimal dose of each?
What is the Optimal Dosing Range for Runners?

2 studies shed light on the answer to that question.


Affect of Leisure-time Running on All-cause and Cardiovascular Mortality Risk

• Most data on PA and mortality focused on moderate intensity (walking).
• Examined association of running with all-cause and CV mortality risks in 55,137 adults, 18 to 100 yrs. (mean 44 yrs., 26% female); ACLS data.
  – Compared non-runners to runners in 5 quintiles of distance (miles/wk), frequency (times/wk), amount (MET-min/wk) and speed of running (mph).
  – Also looked at effects of a change in running habits over time in sub-group (20,647) who had ≥2 exams.

HRs of All-Cause and CV Mortality by Running Distance, Frequency, Total Amount, and Speed

**All Cause Mortality**

- **Distance**
  - Hazard Ratio of All-Cause Mortality
  - Hazard Ratio of CV Mortality

- **Frequency**
  - Hazard Ratio of All-Cause Mortality
  - Hazard Ratio of CV Mortality

- **Amount**
  - Hazard Ratio of All-Cause Mortality
  - Hazard Ratio of CV Mortality

- **Speed**
  - Hazard Ratio of All-Cause Mortality
  - Hazard Ratio of CV Mortality
Running Reduced All-Cause and CV Mortality Risk

Hazard Ratios of All-Cause Mortality

Hazard Ratios of Cardiovascular Mortality

Non-runners vs. Quintiles of running characteristics

- Time (min/wk): 0, <51, 51-80, 81-119, 120-175, ≥176
- Distance (miles/wk): 0, <6, 6-8, 9-12, 13-19, ≥20
- Frequency (times/wk): 0, 1-2, 3, 4, 5, ≥6
- Total amount (MET-min/wk): 0, <506, 506-812, 813-1199, 1200-1839, ≥1840
- Speed (mph): 0, <6.0, 6.0-6.6, 6.7-7.0, 7.1-7.5, ≥7.6
HRs of All-Cause and Cardiovascular Mortality by Change in Running Behaviors

Model 1 adjusted for age, sex, exam year and interval btw exams. Model 2 added smoking, alcohol and PA other than running

Running Study Conclusions

• Runners had consistently lower risk of all-cause and CVD mortality compared with non-runners.

• Running even at lower doses or slower speeds was associated with significant mortality benefits.
  – 30-59 min per week (5-10 min per day) gave significant benefit!

• Persistent running over time was more strongly associated with mortality reduction, but any history of running gave benefit.

Coronary Artery Plaque Volume Among Male Marathon Runners.

• Most assume marathon running is good for heart health, but many studies suggest otherwise.
• Observational study comparing coronary calcium scores using high sensitivity CCTA in 2 groups of men average age 56-59 yr:
  – 50 male marathon runners (at least 25 marathons done over 25 years).
  – 23 male sedentary controls matched for age and CAD risk factors.
  – Controls had higher resting pulse, weight and BMI, as well as higher rates of high cholesterol, Hypertension and diabetes.

Schwartz, et al, Mo Medicine; 2014
Results

• Male marathon runners had higher:
  – Total plaque volume (200 vs 126 mm\(^2\))
  – Calcified plaque volume (84 vs 44 mm\(^2\))
  – Non-calcified plaque volume (116 vs 82 mm\(^2\))
  – Lesion area and length, number of lesions per subject, and diameter stenosis did not reach statistical significance

• Despite the fact that the marathon runners showed improvement in traditional CV risk factors (lipids, glucose and BMI)

Marathoners showed increased plaque

Marathon Study Conclusions

• Long-term male marathon runners may have paradoxically increased coronary artery plaque volume.

• This study lends credence to various observational studies showing dramatic mortality reductions in runners compared with sedentary controls, but the effect seems to follow a U-shaped curve.

• Lowest mortality among runners shown with:
  – Jogging 1-2.5 hours per week at moderate pace; benefit goes away >2.5 hrs. (O’Keefe, Heart, 2013).
  – Jogging 5-20 miles per week; benefit goes away beyond 25 miles per week. (O’Keefe, Heart, 2013).
Dose of Jogging and Long-Term Mortality: The Copenhagen City Heart Study

1,098 healthy joggers; 3,950 healthy non-joggers; Prospectively followed 12 years.

*Most favorable mortality - jog 1-2.4 h per week; 2-3x per week; slow to avg. pace

Moderate vs Strenuous PA and CVD Risk

The UK Million Women Study

Prospective cohort study

- 1.1 million women
- Age 50 to 64
- Self reported PA
- 9 years follow-up
  - 49,113 CHD events
  - 17,822 CVA events
  - 14,550 VTE events
- Controlled for BMI, smoking, Etoh and SES.

Armstrong, Circulation; 2015
Moderate vs Strenuous PA and CVD Risk

The UK Million Women Study

Goldilocks Zone

“Sweet Spot”
Strenuous PA; 2-3 times/wk
Moderate PA; 4-6 times/wk

Armstrong, Circulation; 2015
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Armstrong, Circulation; 2015
Risk of A-Fib
(5446 adults >65 yrs)

Mozaffarian; Circulation; 2008.
Dose-Response Curve for Exercise

- A = Sedentary
- B = Moderately Active
- C = Highly Active

Benefit

Weekly Exercise Time

Low A B C High
Are you surprised?

• Life is about moderation – *if a little is good, more is often not better.*

• Is Athletes Heart really a harmless adaptation?
  – LV enlargement, EKG changes (T-inv, Q-waves, RBBB) and arrhythmia (brady, junctional, AV block).
  – After extreme endurance exercise common to see leak of CPK, Troponin and BNP.
  – Evidence of myocardial fibrosis/scarring, potentially dangerous rhythms, and accelerated CVD.

• Pheidippides’ Cardiomyopathy?
My Doctor said "Only 1 glass of alcohol a day". I can live with that.
Are you surprised?

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• Pheidippides’ Cardiomyopathy?
Pheidippides

- Hero of ancient Greece ran 26.2 miles from Marathon to Athens to deliver news of military victory over the Persians.
Pheidippides

• Hero of ancient Greece ran 26.2 miles from Marathon to Athens to deliver news of military victory over the Persians.
A Tale of 2 Male Patients;

*Pick the Heart Patient*

- 5’8” Tall
- 158 lbs.
- Never drank alcohol
- Low Fat/High Fiber Diet
- Marathon Runner
- Former smoker

- 5’8” Tall
- 270 lbs.
- Heavy drinker
- High Fat/Low Fiber Diet
- Sedentary
- Heavy cigarette and cigar smoker
Jim Fixx; died age 52 while jogging

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Sometimes you cannot outrun your genes!
MI Risk with *Exercise*

>100 fold increase

2-5 fold increase

* Episode of exercise

Active subject

Sedentary subject

Circulation 2011;124:346-354
What is the Optimal Dosing Range for Walkers?

- 416,175 adults in Taiwan; Followed 8.5 years with activity questionnaires; Correlated with mortality rates
- Compared to inactive group, those doing 92 min per week (~15 min per day) walking:
  - Reduced mortality by 14%
  - 3 years longer life expectancy
  - Every 15 min per day walking, further reduced mortality by 4% (up to 100 min per day)
- Applied to both men and women

Wen CP, et al; Lancet, 2011
How much does walking reduce mortality?

Wen CP, et al; Lancet, 2011
Leisure Time PA and Mortality; A Detailed Pooled Analysis of the Dose-Response Relationship

*Pooled data on 661,137 Men and Women; Median age 62 yrs

Multiples of PA Guidelines

Arem et al; JAMA Internal Medicine; Apr 2015.
How fast do you need to walk; To stay ahead of the Grim Reaper?

• Several studies have shown correlation between walking speed and survival.

• 1705 Australia men, age >70; Measured walking speed at usual pace for 6 m (~20 feet); Speed correlated with mortality rates over 5 yrs:
  – Walking speed of 0.82 m/s (2 mph or 3 kph) was most predictive of mortality (i.e. speed of Grim Reaper)
  – No men walking at speeds > 1.36 m/s (3 mph or 5 kph) were caught by Grim Reaper

• Walking faster protects against mortality!

Association of Fitness With Mortality in Adults Undergoing Ex Treadmill Testing

-122,007 adults with ETT at Clev Clinic
-1991-2014 (23 yrs)
-Fitness inversely a/w all-cause mortality in 5 quintiles of fitness

Mandsager, JAMA 2018
Low Fitness Was Bigger Risk than Hypertension, Diabetes, CAD or Smoking

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>1.41 (1.36-1.46)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CAD</td>
<td>1.29 (1.24-1.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.40 (1.34-1.46)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.21 (1.16-1.25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ESRD</td>
<td>2.78 (2.53-3.05)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Group comparison</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low vs Elite</td>
<td>5.04 (4.10-6.20)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Low vs High</td>
<td>3.90 (3.67-4.14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Low vs Above Average</td>
<td>2.75 (2.61-2.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Low vs Below Average</td>
<td>1.95 (1.86-2.04)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Below Average vs Elite</td>
<td>2.59 (2.10-3.19)</td>
<td>&lt;.001</td>
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<tr>
<td>Below Average vs High</td>
<td>2.00 (1.88-2.14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Below Average vs Above Average</td>
<td>1.41 (1.34-1.49)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Above Average vs Elite</td>
<td>1.84 (1.49-2.26)</td>
<td>&lt;.001</td>
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<tr>
<td>Above Average vs High</td>
<td>1.42 (1.33-1.52)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>High vs Elite</td>
<td>1.29 (1.05-1.60)</td>
<td>.02</td>
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</tbody>
</table>

Mandsager, JAMA 2018
Summary

• Exercise is Medicine that can extend life; Running & walking are great formulations.

• Like any medicine, it has an optimal dosage range, as well as sub-therapeutic and toxic ranges.
  – Running as little as 60 min per week (10 min; 6 days a week) has significant benefits.
  – Walking as little as 92 min per week (15 min; 6 days a week) has significant benefits.
  – Running >2.5 hours per week or >25 miles per week does not seem to provide health benefit and may be harmful.
  – Walking beyond 100 min per day does not seem to add benefit.
  – Extreme endurance exercise may be hazardous to heart.
Summary (continued)

• Various studies support the recommendations from the US Physical Activity Guidelines:
  – 150 min per week of moderate exercise (like brisk walk) and 60 min per day in kids.
  – 75 minutes per week of vigorous exercise (like jogging).

• Biggest benefit is going from sedentary to just moderate amounts of exercise.

• Risk of sudden death goes up with exercise, but especially in sedentary individuals.

• Don’t forget the significant health benefits from strength and flexibility training.
Thank You!

Questions?