Exercise and Type 2 Diabetes

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COI

- I have no conflicts of interest to declare
Diabetes: A Dangerous Cycle

- Although physical activity is a cornerstone of treatment for T2D, most people with T2D are sedentary.
- Exercise at very low levels feels harder in people with T2D.
- In addition, T2D causes decrease in ability to exercise at high work loads.

Lack of exercise is a proven risk factor for heart disease.

A lack of regular physical exercise is a growing epidemic in the US.

Heart disease is twice as likely to develop in inactive people than in those who are more active.

Physical activity helps maintain weight, improve blood pressure, and prevent or improve diabetes.
Study finds that diet and exercise may prevent Type 2 diabetes

By Sally Quinn
Washington Post Staff Writer

At least 30 million overweight Americans could stymy their risk of developing diabetes by making relatively simple lifestyle changes in their diet and exercise routine, according to a major government study released yesterday.

The Diabetes Prevention Program is the first large study to show that losing weight and exercising can effectively delay diabetes in a wide range of overweight men and women who are at a high risk for Type 2 diabetes. This form of the disease usually sets in later in life and is linked with obesity.

About 28 million Americans have the disease, and 230,000 of them die in Colorado. The disease was once thought to be a middle-aged illness, but an alarmingly high number of children have been diagnosed with it in recent years — mostly because of an increase in childhood obesity.

One-third of the study's participants took a medicine to lower their blood sugar, and the last third changed their eating habits and lowered their body weight by walking 30 minutes a week.

A better life, said Dr. Neal Cole, chief of medicine at Kaiser Permanente. "I'm not talking about joining a health club or running a marathon or losing 50 pounds. It's modest."

The participants who were assigned the super-low-calorie diet instead of the regular diet were also more likely to lose weight. Those who ate the regular diet dropped their chances of getting the disease by 31 percent.

Cole said that dieting could be completely prevented with a combination of medication and lifestyle change.

Doctors don't always recommend dieting and exercise. In some instances, they may recommend medication. In other instances, they may recommend dieting and exercise.
Low cardiorespiratory fitness predicted CVD and all cause mortality in healthy men
- 25,714 people evaluated prospectively
- True whether normal weight, overweight or obese

In men with DM, low CV fitness and physical inactivity predicted mortality
- 1,263 people in a preventive medicine clinic

Figure. Survival curves for all-cause mortality by cardiorespiratory fitness category. Data are from 1263 men with 180 all-cause deaths during 14 777 man-years of observation. The solid line represents fit participants and the dashed line represents unfit participants.
Exercise Duration and \( \text{VO}_2\text{peak} \) in T2D

- **Exercise Duration**
  - Women
  - Men

- **\( \text{VO}_2\text{peak} \)**
  - Women
  - Men

* = \( p < 0.05 \)

Regensteiner et al., 1999; Reusch et al, 2013
What causes the abnormalities?

Are causes:
Peripheral?
Central?
### Demographic Variables

<table>
<thead>
<tr>
<th></th>
<th>Controls (N=10)</th>
<th>Type 2 Diabetes Mellitus (N=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39.3±6.6</td>
<td>42.5±6.3</td>
</tr>
<tr>
<td>Duration of Diagnosed Diabetes (years)</td>
<td>3.6±4.6</td>
<td>3.6±4.6</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>28.3±3.9</td>
<td>31.9±4.3</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>5.0±0.4</td>
<td>6.9±2.3*</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>194±33</td>
<td>188±20</td>
</tr>
<tr>
<td>Metric</td>
<td>Controls (N=10)</td>
<td>T2D (N=10)</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>---------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>$\text{VO}_2\text{max (ml/kg/min)}$</td>
<td>22.3±4.2</td>
<td>18.7±2.3*</td>
</tr>
<tr>
<td>$\text{VO}_2\text{max (ml/min)}$</td>
<td>1639.9±336.8</td>
<td>1519.8±248.6</td>
</tr>
<tr>
<td>Respiratory Exchange Ratio</td>
<td>1.14±0.05</td>
<td>1.18±0.05</td>
</tr>
<tr>
<td>Rate of Perceived Exertion</td>
<td>17.1±1.4</td>
<td>16.6±1.8</td>
</tr>
<tr>
<td>Watts</td>
<td>123±27.5</td>
<td>110±21.1</td>
</tr>
<tr>
<td>HR max (beats/min)</td>
<td>166±15</td>
<td>169±8</td>
</tr>
<tr>
<td>Cardiac Output (Fick) (L/min)</td>
<td>13.1±2.8</td>
<td>12.6±1.6</td>
</tr>
<tr>
<td>Cardiac Index (L/min)(Fick)</td>
<td>7.3±1.4</td>
<td>6.8±0.5</td>
</tr>
<tr>
<td>Arteriovenous oxygen difference</td>
<td>12.8±2.2</td>
<td>12.3±1.3</td>
</tr>
<tr>
<td>Right Atrial Pressure (mmHg)</td>
<td>10.8±3.1</td>
<td>10.7±3.8</td>
</tr>
<tr>
<td>Mean Arterial Pressure (mmHg)</td>
<td>107.6±7.3</td>
<td>117.7±12.6*</td>
</tr>
<tr>
<td>Pulmonary Arterial Pressure (mmHg)</td>
<td>30.3±6.7</td>
<td>34.0±1.5</td>
</tr>
<tr>
<td>Pulmonary Capillary Wedge Pressure (mmHg)</td>
<td>16.7±3.7</td>
<td>23.6±3.9*</td>
</tr>
</tbody>
</table>
T2D has adverse effects on cardiac function

(Regensteiner et al. 2009)
## Nuclear stress (Tc-99m sestamibi) tests

<table>
<thead>
<tr>
<th></th>
<th>Controls (N=7)</th>
<th>Type 2 Diabetes Mellitus (N=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>41±7</td>
<td>43±6</td>
</tr>
<tr>
<td>BMI</td>
<td>28.3±3.2</td>
<td>32.1±5.2</td>
</tr>
<tr>
<td>Total Rest Counts</td>
<td>493.1±138.4</td>
<td>420.0±106.7</td>
</tr>
<tr>
<td>Total Stress Counts</td>
<td>834.8±216.4</td>
<td>656.9±139.4+</td>
</tr>
<tr>
<td>Total Perfusion Reserve (ratio)</td>
<td>1.66±0.33</td>
<td>1.44±0.22</td>
</tr>
<tr>
<td>Resting LV Mass</td>
<td>138.6±22.3</td>
<td>138.1±18.2</td>
</tr>
<tr>
<td>Stress counts/resting myocardial mass</td>
<td>6.60±2.15</td>
<td>4.28±0.75*</td>
</tr>
<tr>
<td>Total myocardial perfusion index</td>
<td>17.5±8.1E⁻⁹</td>
<td>11.0±3.5xE⁻⁹ *</td>
</tr>
</tbody>
</table>
However cardiac abnormalities cannot explain all the exercise abnormality in T2D

- Role of endothelial function
- Peripheral blood flow
- Mitochondrial dysfunction
- Many questions remain
What about T2D in youth?

- Growing problem
- Related to increased obesity/sedentary behavior in adolescents
Insulin Resistance in Adolescents with T2D is Associated with Impaired Exercise Capacity

Nadeau KJ et al. J Clin Endocrinol Metab. 2009
Peak Oxygen Consumption

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Obese</th>
<th>T2D</th>
<th>T1D</th>
</tr>
</thead>
<tbody>
<tr>
<td>3DPAR</td>
<td>1.8 ± 0.32</td>
<td>1.7 ± 0.39</td>
<td>1.8 ± 0.53</td>
<td>1.8 ± 0.26</td>
</tr>
<tr>
<td>RER</td>
<td>1.18 ± 0.07</td>
<td>1.13 ± 0.07</td>
<td>1.13 ± 0.05</td>
<td>1.15 ± 0.05</td>
</tr>
<tr>
<td>Peak Heart Rate</td>
<td>184 ± 11</td>
<td>188 ± 13</td>
<td>183 ± 8</td>
<td>177 ± 15</td>
</tr>
</tbody>
</table>

*p<0.04 vs. controls, #p<0.01 vs. controls, ^p<0.04 vs. obese and T1D

Nadeau et al JCEM 2009
Why Should Kids Exercise?

- Adolescents with diabetes are very sedentary
- Low amounts of moderate and vigorous activity were related to higher CVD risk score in 8-11 year olds.
- Family conflict increases the likelihood of teen depression, but physical activity decreases the likelihood of depression
- Exercise improved executive function and mental functioning central to cognitive development in 7- to 11-year-olds

1. Sigfusdottir ID J Adolesc. 2011
3. Davis CL Health Psychol. 2011
How Much Should Kids Exercise?

- The US. Surgeon General recommends 1 hour of moderate to vigorous physical activity/day for youth
- Physical Activity Guidelines recommend 300 min/wk
Does exercise training benefit T2D?
Physical activity is beneficial for reducing mortality in T2D

- 3,316 persons ages 25-74 years with type 2 diabetes
- Survey between 1972 and 1997 on physical activity, smoking, medical history
- Average follow-up was 18 years
- 1,410 died during follow-up, 903 died of CVD
- Physical during work, leisure time, and commuting defined as light, moderate, hard

Most exercise studies show improved glycemic control from exercise training.

Meta-analysis of 14 exercise trials showed a 0.66% reduction in hemoglobin A$_{1c}$.

*JAMA 2001; Diabetes Care 2013*
Exercise Capacity Improves with Exercise Training

<table>
<thead>
<tr>
<th></th>
<th>Lean Control</th>
<th>Obese Control</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>36±6</td>
<td>37±6</td>
<td>42±7</td>
</tr>
<tr>
<td>Fat Free Mass (kg)</td>
<td>42±7</td>
<td>48±5</td>
<td>47±5</td>
</tr>
<tr>
<td>HgbA1c</td>
<td>6.0±0.6</td>
<td>5.3±0.5</td>
<td>9.0±0.4*</td>
</tr>
</tbody>
</table>

Maximal Exercise Response: exercise training program

<table>
<thead>
<tr>
<th></th>
<th>Lean Control</th>
<th>Obese Control</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO$_2$peak (pre)</td>
<td>25.7±4.9</td>
<td>21.8±2.3</td>
<td>17.3±3.8</td>
</tr>
<tr>
<td>(post)</td>
<td>27.9±5.3*</td>
<td>23.0±2.9*</td>
<td>21.7±5.6*</td>
</tr>
<tr>
<td>Maximal RER</td>
<td>1.13±0.05</td>
<td>1.13±0.08</td>
<td>1.16±0.11</td>
</tr>
</tbody>
</table>

Regensteiner, Diabetes Care 22.1640-1646, 1999; Schmidt et al, 2013
CV adaptations to exercise training in men with T2D

- Men with T2D, age 50±2 yrs, randomly assigned to 24 weeks of exercise 2 times/week (n=12) vs control (n=9)
- Assessed: peak oxygen uptake, BP, transthoracic echo, endurance capacity.

- Schmidt et al, 2013
CV adaptations to exercise training in men with T2D

Among exercisers only:

- LV end diastolic diameter and volume increased (P<0.001) compared to baseline
- LV longitudinal systolic displacement augmented by 23% (P<0.001)
- Global longitudinal 2D strain increased by 10% (P<0.05)
- LV diastolic function and peak diastolic velocity were increased (both P<0.01)
- SBP and DBP reduced by 8% (P<0.01)
- Peak oxygen uptake increased by 12%, (P<0.001)
- Endurance capacity was increased by 42% (P<0.001)
Why does exercise improve exercise abnormalities in T2D?
Mechanisms by Which Exercise Training May Improve Cardiovascular Health in Persons with T2D

- Increases aerobic capacity and muscle strength
- Reduces total body and visceral fat; increases lean mass
- Reduces blood pressure
- Lowers blood glucose; increases insulin sensitivity
- Attenuates systemic inflammation
- Improves left ventricular diastolic function
- Decreases arterial stiffness
- Attenuates systemic inflammation
- Reduces left ventricular mass
- Subendocardial ischemia; ischemic preconditioning
- Increased nitric oxide production

Exercise Training
Effective, good evidence
Potential, not yet proven
Prescription for Exercise
2008 Physical Activity Guidelines Advisory Committee Report

Strong evidence for benefit with respect to:

- All-cause mortality
- CHD
- Blood pressure
- Stroke
- **Type 2 diabetes**
- Metabolic syndrome
- Colon cancer
- Breast cancer
- Depression
- Functional health
- Falls
- Cognitive function

Adults who participate in any amount of physical activity gain some health benefits.

A total of 2 hours and 30 minutes (150 minutes) a week of moderate-intensity aerobic activity substantially reduces the risk of many chronic diseases and other adverse health outcomes.

As a person moves from 2 hours and 30 minutes (150 minutes) a week toward 5 hours (300 minutes) a week, he or she gains additional health benefits.

Muscle-strengthening activities involving all major muscle groups should be performed on 2 or more days a week.
Guidelines for Exercise: T2D

- Patients with diabetes should exercise as part of their medical management.
- There is good evidence to suggest benefits of exercise training extend to the cardiovascular consequences of these diseases.
Indications for Cardiac Testing in Patients with Diabetes

- Typical or atypical cardiac symptoms
- Resting ECG suggestive of ischemia or infarction
- Peripheral or carotid occlusive arterial disease
- Sedentary lifestyle or plan to begin a vigorous exercise program
- Two or more of the risk factors listed below
  - Total cholesterol $>240$ mg/dL, LDL cholesterol $>160$ mg/dL, or HDL cholesterol $<35$ mg/dL
  - Blood pressure $>140/90$ mmHg
  - Smoking
  - Family history of premature CAD
  - Positive micro/macroalbuminuria
Exercise Prescription

- **Types and frequency of exercise**
  - Aerobic type 5 times a week
  - Resistance exercise 2 times a week

- **Intensity**
  - Aerobic exercise at 55% to 85% of maximal HR
  - Resistance exercise at 30% to 50% of 1-repetition maximum, 12-15 repetitions, 8 to 10 different exercises
  - Energy expenditure >1000 kilocalories per week

- **Duration**
  - Aerobic for 30 to 45 minutes
  - Resistance takes about 20 minutes
Exercise Precautions

- Medical therapy should be initiated before exercise training if SBP ≥ 160 mm Hg or DBP ≥ 100 mm Hg
- Hypoglycemic reactions in type 2 diabetes are rare
  - Extra carbohydrates may be needed for events > 60 minutes
- Exercise contraindications based on resting blood glucose levels are not definitive
  - 60 mg/dL to 300 mg/dL or 400 mg/dL generally recommended for avoiding hypoglycemia and ketosis
- Extended breath-holding should be avoided to minimize excessive blood pressure responses
- Exercise does not worsen diabetic retinopathy and may delay eye complications by reducing atherosclerotic risk
  - Heavy straining should be avoided
My doctor told me to stop having intimate dinners for four unless there were three other people.

Orson Welles (1915-1985)
Summary

- Exercise is critical for prevention of both diabetes and death
- People with diabetes have defects in functional exercise capacity
- Effects of exercise on the heart and vasculature are still to be defined
What are the keys to exercise?

- Many types of exercise can be helpful including walking, running, swimming and biking.

- It has to be fun!
Walking shoes are 80 bucks
A triple bypass 80 grand
Think of all that cash in hand
And march that tush along
the land
Thank you