Glycemic control, physical inactivity, and skeletal muscle health

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Exercise Metabolism Research Group
McMaster University
What I am going to talk about today

1. The loss of skeletal muscle mass and function with age and physical inactivity

2. New insights into the importance of physical activity on glycemic control in older adults

3. Can exercise be used as a tool to improve glycemic control and muscle function
Age-related skeletal muscle loss
Sarcopenia

The loss of muscle mass (myopenia) and strength (dynapenia) with advancing age will affect 250 million people worldwide by 2050

$18.5 billion, which is 1.5% of total U.S health care expenditure in 2000

‘A disease in which the body either cannot produce insulin or cannot properly use the insulin it produces. This leads to high levels of glucose in the blood, which can damage organs, blood vessels and nerves’
Types of diabetes

**Type 2** - Inability to regulate blood glucose levels due to a lack of insulin sensitivity in normally insulin-sensitive tissues.
## Prevalence of diabetes

<table>
<thead>
<tr>
<th>Key statistics</th>
<th>2015</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes prevalence (n/%)</td>
<td>3.4 million/9.3%</td>
<td>5 million/12.1%</td>
</tr>
<tr>
<td>Prediabetes prevalence (n/%; age 20+)</td>
<td>5.7 million/22.1%</td>
<td>6.4 million/23.2%</td>
</tr>
<tr>
<td>Estimated increase (%)</td>
<td>44% from 2015-2025</td>
<td></td>
</tr>
</tbody>
</table>

1 in 10 deaths were associated with diabetes in 2008/2009. Three times more likely to be hospitalized with cardiovascular disease. A third of foot amputations in 2011-2012 were performed on people with diabetes.
Physical inactivity accelerates sarcopenia

Muscle Mass/Strength Loss: 1-3%/yr

English and Paddon-Jones (2010)
Only two weeks of step reduction promotes muscle strength loss

Devries et al. (2015)
Physiol. Rep. 3: e12493
Only two weeks of step reduction promotes muscle mass loss

Breen et al. (2013)
J. Clin. Endocrinol. Metab. 98:2604-2612
Skeletal muscle is a primary site of glucose disposal

Two weeks of step reduction promotes an increase in insulin resistance

12%↑ Fasted state insulin resistance

43%↓ Fed state insulin sensitivity

Breen et al. (2013)
J. Clin. Endocrinol. Metab. 98:2604-2612
‘It’s not about how hard you can hit, it’s about how hard you can be hit but keep moving forward’

Rocky Balboa
Impaired Recovery Following Immobilization

Preliminary data
Experimental design

- n=12
- n=10
- Age: 68±3 yr

Diet: 15% Protein, 30% Fat, 55% Carbohydrate

OGTT Biopsy

OGTT Biopsy

OGTT Biopsy
Results – Daily Step Count

McGlory, von Allmen et al. in preparation
Oral glucose tolerance test
Oral glucose tolerance test response

Glucose/Insulin (arb. units)

Time (min)

Insulin

Glucose

AUC

75g glucose

Chris McGlory, CDA, York University, 28th June 2016.
It’s not just a catabolic crisis!
Exercise works !!
Sakamoto and Holman (2008)
Am. J. Physiol. Endo. Metab.
295:E29-37
Umpierre et al. (2011) JAMA 305: 1790-1799
Diabetes prevention program

3234 non diabetics

- 1700 mg Metformin
- 150 min physical activity/wk + behavior modification
- Placebo

2.8 y follow-up
N. Eng. J. Med. 7:346:393-403
Chris McGlory, CDA, York University, 28th June 2016.

Umpierre et al. (2011) JAMA 305: 1790-1799

### Aerobic training

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Patients</th>
<th>HbA1c Difference, % (95% CI)</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bjorgaas et al. 2005</td>
<td>11</td>
<td>-0.44 (-1.03 to 0.15)</td>
<td>3.46</td>
</tr>
<tr>
<td>Church et al. 2010</td>
<td>72</td>
<td>-0.23 (-0.30 to -0.16)</td>
<td>5.77</td>
</tr>
<tr>
<td>Cuff et al. 2003</td>
<td>9</td>
<td>-0.07 (-0.28 to 0.14)</td>
<td>5.37</td>
</tr>
<tr>
<td>Dela et al. 2004</td>
<td>14</td>
<td>-2.14 (-3.43 to -0.86)</td>
<td>1.38</td>
</tr>
<tr>
<td>Giannopoulou et al. 2005</td>
<td>11</td>
<td>-1.00 (-1.70 to -0.30)</td>
<td>2.96</td>
</tr>
<tr>
<td>Goldhaber-Fiebert et al.2003</td>
<td>33</td>
<td>-1.40 (-2.56 to -0.24)</td>
<td>1.61</td>
</tr>
<tr>
<td>Kadoglou et al. 2007</td>
<td>29</td>
<td>-0.93 (-1.08 to -0.78)</td>
<td>3.55</td>
</tr>
<tr>
<td>Kadoglou et al. 2007</td>
<td>28</td>
<td>-1.02 (-1.59 to -0.45)</td>
<td>4.68</td>
</tr>
<tr>
<td>Kadoglou et al. 2010</td>
<td>22</td>
<td>-0.80 (-1.15 to -0.45)</td>
<td>3.81</td>
</tr>
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<td>Kadoglou et al. 2010</td>
<td>23</td>
<td>-0.59 (-1.11 to -0.07)</td>
<td>1.78</td>
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<tr>
<td>Lambers et al. 2008</td>
<td>18</td>
<td>-0.70 (-1.78 to 0.38)</td>
<td>2.57</td>
</tr>
<tr>
<td>Ligenberg 1997</td>
<td>25</td>
<td>-0.30 (-1.11 to 0.51)</td>
<td>3.64</td>
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<tr>
<td>Middlebrooke et al. 2006</td>
<td>22</td>
<td>0.10 (-0.45 to -0.65)</td>
<td>0.54</td>
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<tr>
<td>Raz et al. 1994</td>
<td>19</td>
<td>-0.30 (-3.53 to 0.93)</td>
<td>2.61</td>
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<tr>
<td>Ribeiro et al. 2008</td>
<td>11</td>
<td>-0.40 (-1.19 to 0.39)</td>
<td>2.88</td>
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<tr>
<td>Sigal et al. 2007</td>
<td>60</td>
<td>-0.50 (-1.22 to 0.22)</td>
<td>4.60</td>
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<tr>
<td>Sridhar et al. 2010</td>
<td>55</td>
<td>-2.76 (-3.13 to -2.39)</td>
<td>0.68</td>
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<tr>
<td>Vancea et al. 2009</td>
<td>14</td>
<td>-0.50 (-2.47 to 1.47)</td>
<td>0.51</td>
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<td>Vancea et al. 2009</td>
<td>9</td>
<td>0.00 (-2.30 to 2.30)</td>
<td>1.43</td>
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<tr>
<td>Verity and Ismail 1989</td>
<td>5</td>
<td>0.50 (-0.75 to 1.75)</td>
<td>59.41</td>
</tr>
</tbody>
</table>

All aerobic training

$I^2 = 92.8\%; P$ for heterogeneity <.001

### Resistance training

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<thead>
<tr>
<th>Source</th>
<th>No. of Patients</th>
<th>HbA1c Difference, % (95% CI)</th>
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<tr>
<td>Castaneda et al. 2002</td>
<td>29</td>
<td>-1.00 (-1.27 to -0.73)</td>
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<tr>
<td>Church et al. 2010</td>
<td>73</td>
<td>-0.15 (-0.22 to -0.08)</td>
<td>5.78</td>
</tr>
<tr>
<td>Dunstan et al. 2002</td>
<td>16</td>
<td>-0.80 (-1.46 to -0.14)</td>
<td>3.17</td>
</tr>
<tr>
<td>Sigal et al. 2007</td>
<td>64</td>
<td>-0.37 (-1.08 to 0.34)</td>
<td>2.92</td>
</tr>
</tbody>
</table>

All resistance training

$I^2 = 92.5\%; P$ for heterogeneity <.001

### Combined training

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<tr>
<th>Source</th>
<th>No. of Patients</th>
<th>HbA1c Difference, % (95% CI)</th>
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<tr>
<td>Baldacci et al. 2004</td>
<td>51</td>
<td>-1.24 (-1.88 to 0.60)</td>
<td>3.24</td>
</tr>
<tr>
<td>Church et al. 2010</td>
<td>76</td>
<td>-0.34 (-0.41 to -0.27)</td>
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<td>10</td>
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<td>5.31</td>
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<tr>
<td>Lambers et al. 2008</td>
<td>17</td>
<td>-0.80 (-1.84 to 0.24)</td>
<td>1.86</td>
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<tr>
<td>Loimaala et al. 2003</td>
<td>24</td>
<td>-0.90 (-1.80 to -0.00)</td>
<td>2.26</td>
</tr>
<tr>
<td>Sigal et al. 2007</td>
<td>64</td>
<td>-0.97 (-1.69 to -0.25)</td>
<td>2.86</td>
</tr>
<tr>
<td>Tessier et al. 2000</td>
<td>19</td>
<td>-0.40 (-1.29 to 0.49)</td>
<td>2.28</td>
</tr>
</tbody>
</table>

All combined training

$I^2 = 67.5\%; P$ for heterogeneity = .005

Overall

$I^2 = 91.3\%; P$ for heterogeneity <.001
Sprint interval training vs. continuous exercise

**SIT**: 3 x 20 s sprints, 2 min recovery

**MICT**: 45 min cycling @ ~70% max heart rate

- **SIT**: 9 vs. 10 vs. 6
- **MICT**: 3x/wk, 12 wks training

3 minutes of intense exercise within a 30 minute weekly time commitment

150 minutes of moderate-intensity continuous exercise per week
Sprint interval training vs. continuous

Two weeks of HIIT reduces hyperglycaemia in Type 2 diabetics

**HIIT**: 10 x 60s bouts @ ~90% max heart rate

Little et al. (2011) J. Appl. Physiol. 111:1554-1560
A

CS activity (mmol/kg protein -1/hr -1 )

Pre

Post

* P<0.05

B

Protein content (a.u.)

Complex I NDUF10

Complex II 70 kDa subunit

Complex III Core 2 protein

Complex IV subunit IV

ATP synthase α

Pre

Post

P=0.06

* P<0.05

* P<0.1

GLUT4 protein content (a.u.)

Pre

Post

* P<0.05

Chris McGlory, CDA, York University, 28th June 2016.
Dr. John Holloszy, MD, PhD., 1980s

10 men (7 mild T2D; 3 impaired glucose tolerance)

One size does not fit all

- **PLASMA GLUCOSE (mg·dL⁻¹)**
  - No Exercise
  - 7 days exercise

- **PLASMA INSULIN (µU·ml⁻¹)**
  - No Exercise
  - 7 days exercise

Chris McGlory, CDA, York University, 28th June 2016.
The HERITAGE family study

Boule et al. (2005)
‘Although the effects of structured regular exercise were highly variable, **there were improvements in virtually all IVGTT-derived variables**. In the absence of substantial weight loss, regular exercise is required for sustained improvements in glucose homeostasis’
Resistance exercise attenuates atrophy

Devries et al. (2015)
Physiol. Rep. 3: e12493
Resistance exercise attenuates atrophy

Devries et al. (2015)
Physiol. Rep. 3: e12493
Physical inactivity accelerates sarcopenia

Muscle Mass/Strength Loss: 1-3%/yr

Percent of Total (%)

Age (years)

50  80

English and Paddon-Jones (2010)
What I have told you this morning

1. Brief bouts of physical inactivity have profound negative consequences on skeletal muscle.

2. Older adults do not fully recover glycemic control following brief bouts of physical inactivity.

3. Physical activity and exercise are modifiable risk factors to improve skeletal muscle health.
Its not just all about physiology

‘Tackling physical inactivity and metabolic ill health is multifaceted, complex and will require an interdisciplinary approach’…….

…..but it can be done
Acknowledgements

Mr. Tanner Stokes  Mr. Mark von Allmen  Prof. Stuart Phillips
Thank You!