Glycemic control, physical inactivity, and skeletal muscle health

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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

Jensen et al. (2004) J. Am. Geriatr. Soc. 52: 80-5

Canadian Diabetes Association

Diabetes

‘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 1 - Inability to regulate blood glucose levels due to deficient insulin secretion from the pancreatic beta cells

Type 2 - Inability to regulate blood glucose levels due to lack of insulin sensitivity in normally insulin-sensitive tissues

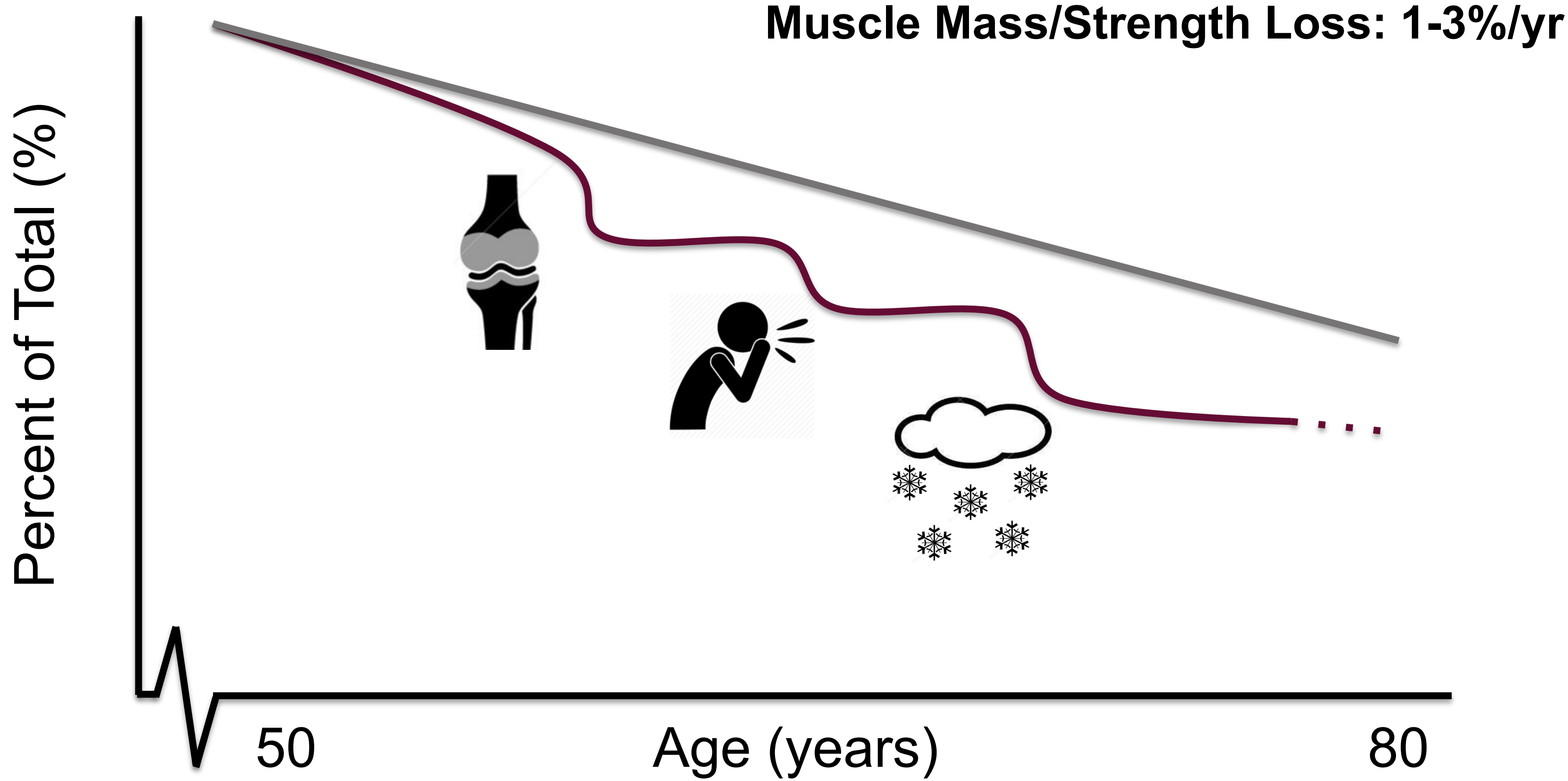
Prevalence of diabetes

Key statistics	2015	2025
Diabetes prevalence (n/%)	3.4 million/9.3%	5 million/12.1%
Prediabetes prevalence (n/ %; age 20+)	5.7 million/22.1%	6.4 million/23.2%
Estimated increase (%)	44% from 2015-2025	

[illegible] with diabetes

www.diabetes.ca

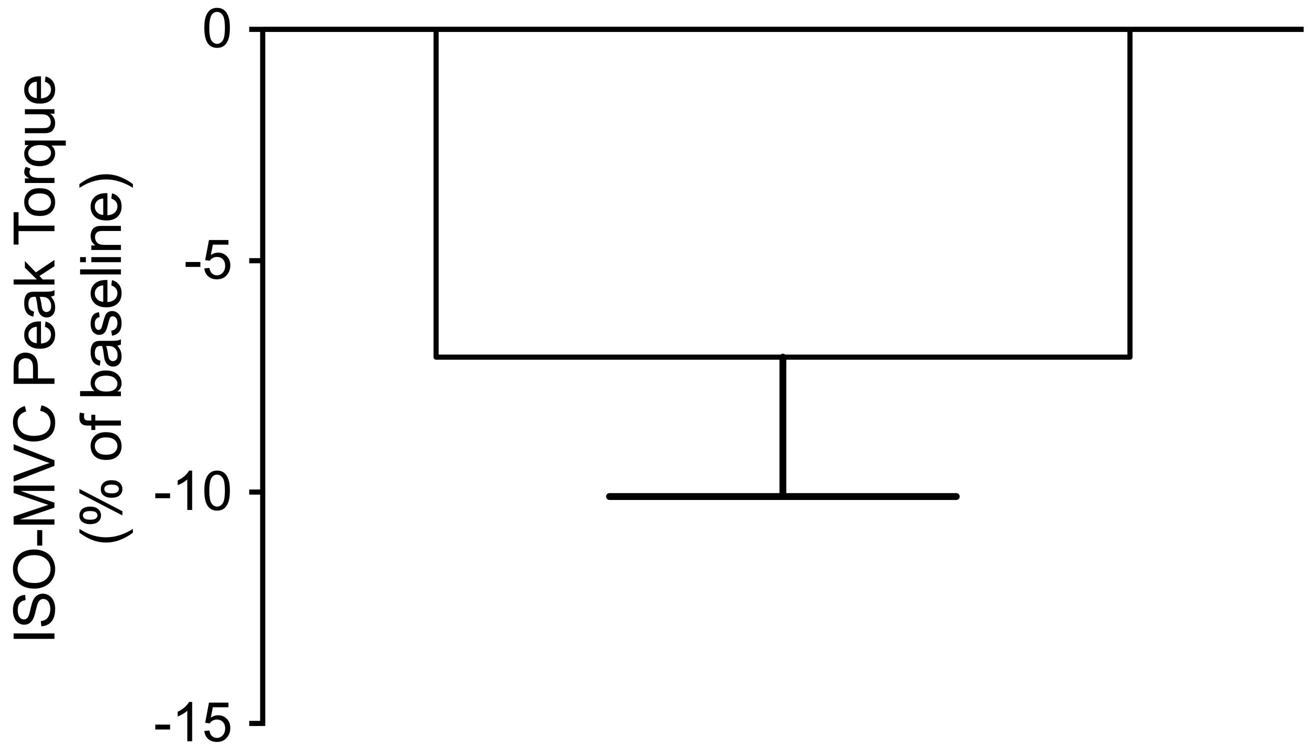
Physical inactivity accelerates sarcopenia



English and Paddon-Jones (2010)
Curr. Opin. Nutr. Metab. Care. 13:34-39

Only two weeks of step reduction promotes muscle strength loss

Canadian Diabetes Association



Devries et al. (2015)
Physiol. Rep. 3: e12493

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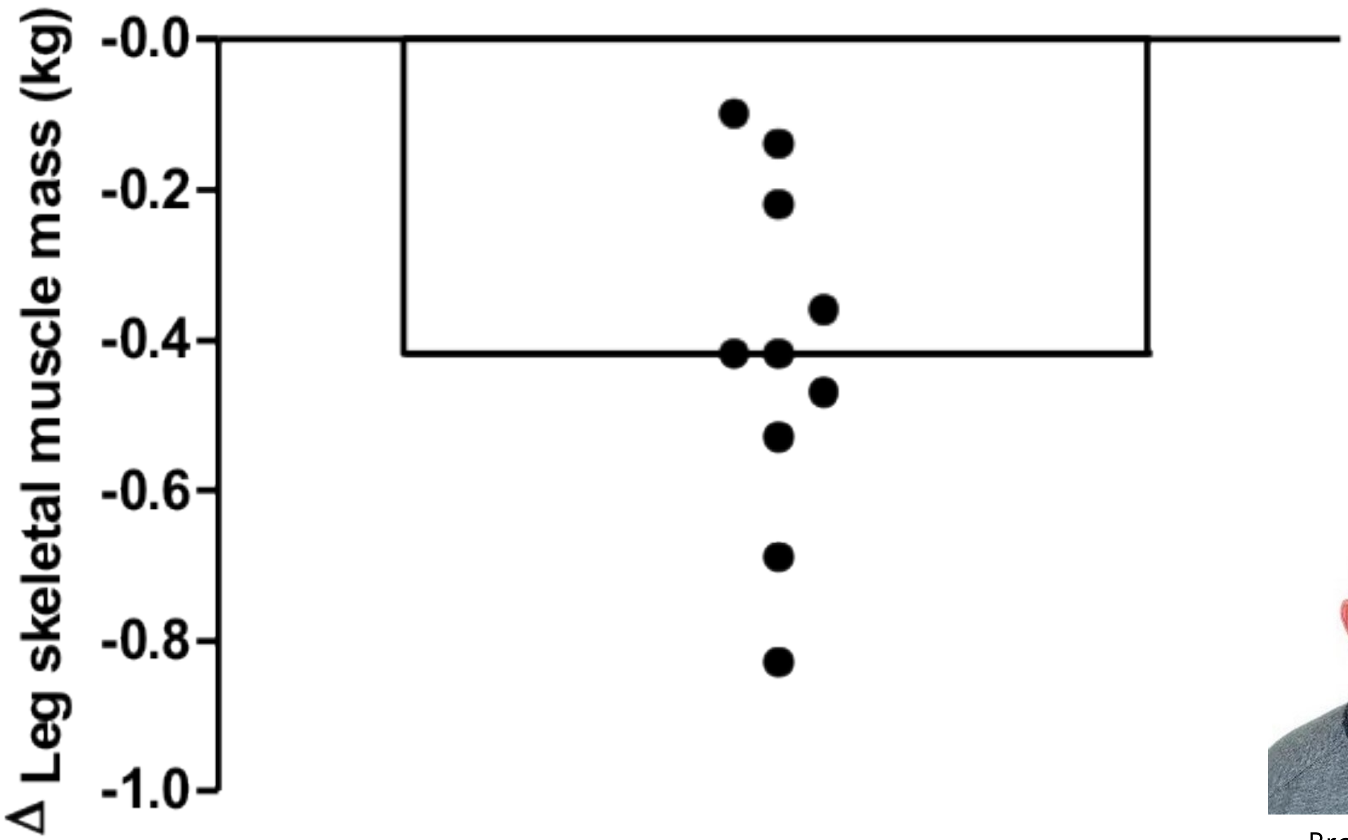
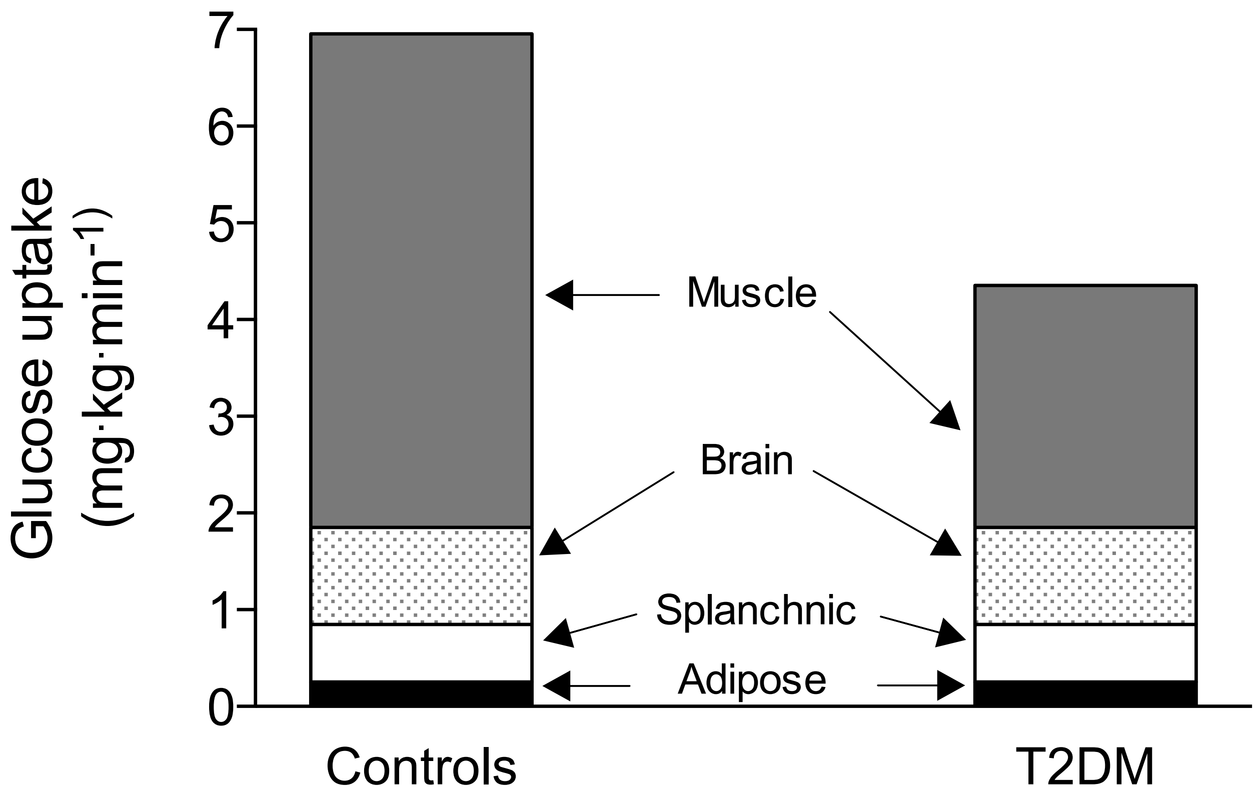
Only two weeks of step reduction promotes muscle mass loss



Breen et al. (2013)
J. Clin. Endocrinol. Metab. 98:2604-2612

Skeletal muscle is a primary site of glucose disposal



De Fronzo, (1988) *Diabetes*. 37:667-687

Two weeks of step reduction promotes an increase in insulin resistance

Canadian Diabetes Association

12% ↑ Fasted state insulin resistance

43% ↓ Fed state insulin sensitivity

Breen et al. (2013)
J. Clin. Endocrinol. Metab. 98:2604-2612

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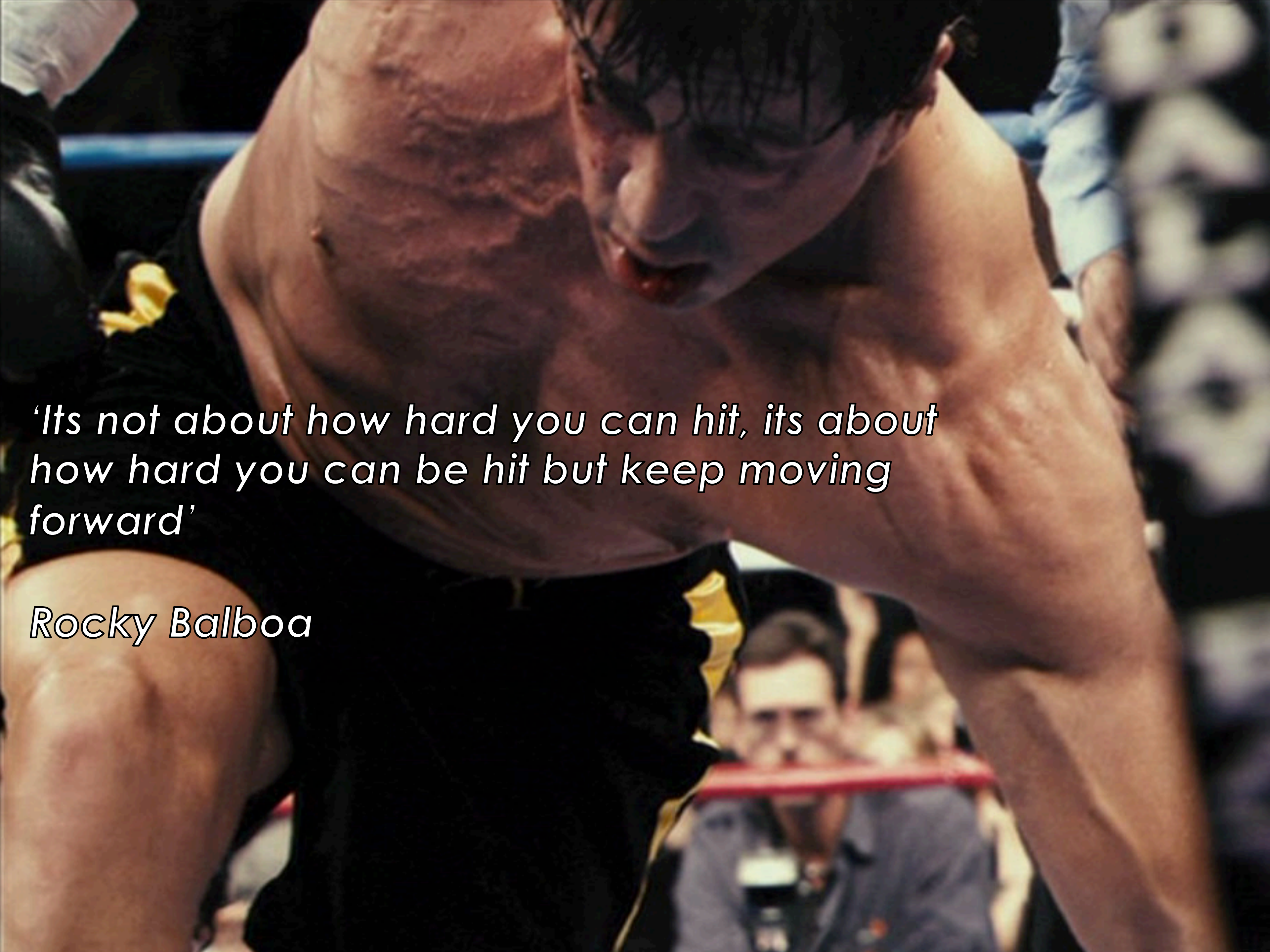
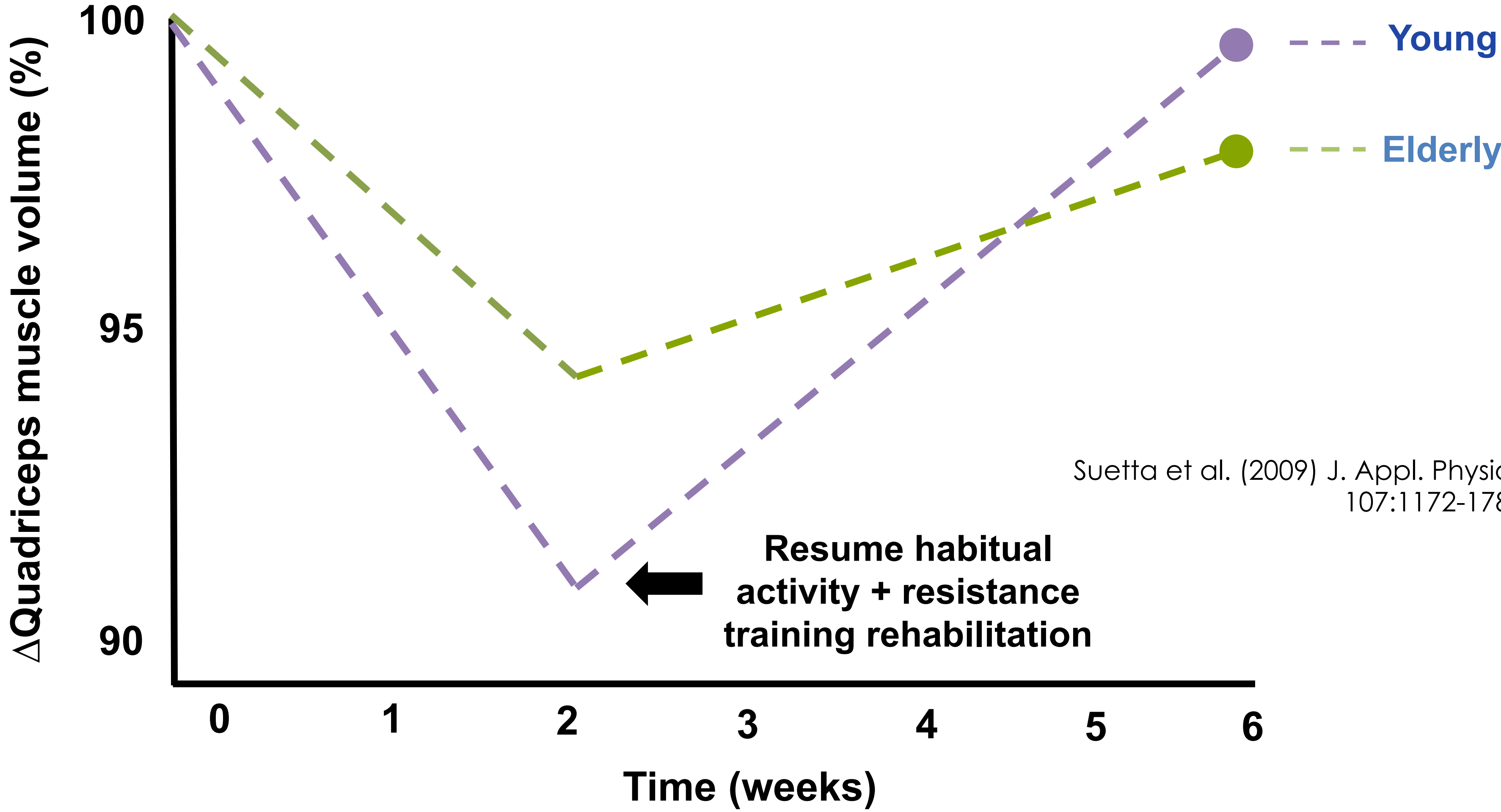

‘Its not about how hard you can hit, its about how hard you can be hit but keep moving forward’
Rocky Balboa

Impaired Recovery Following Immobilization



Suetta et al. (2009) J. Appl. Physiol. 107:1172-1780

Preliminary data

Experimental design

n=12

n=10

Age: 68±3yr

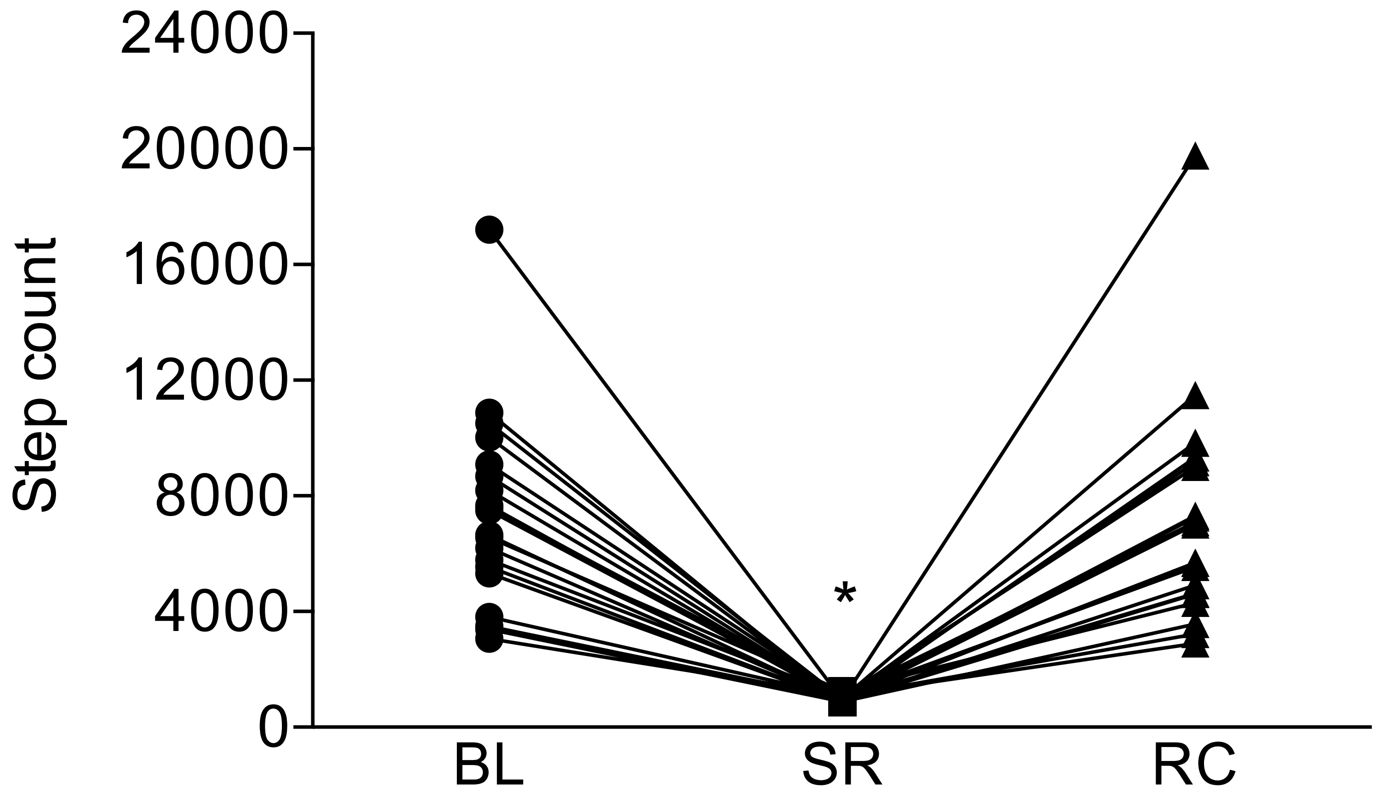
Diet: 15% Protein, 30% Fat, 55% Carbohydrate

OGTT
Biopsy

OGTT
Biopsy

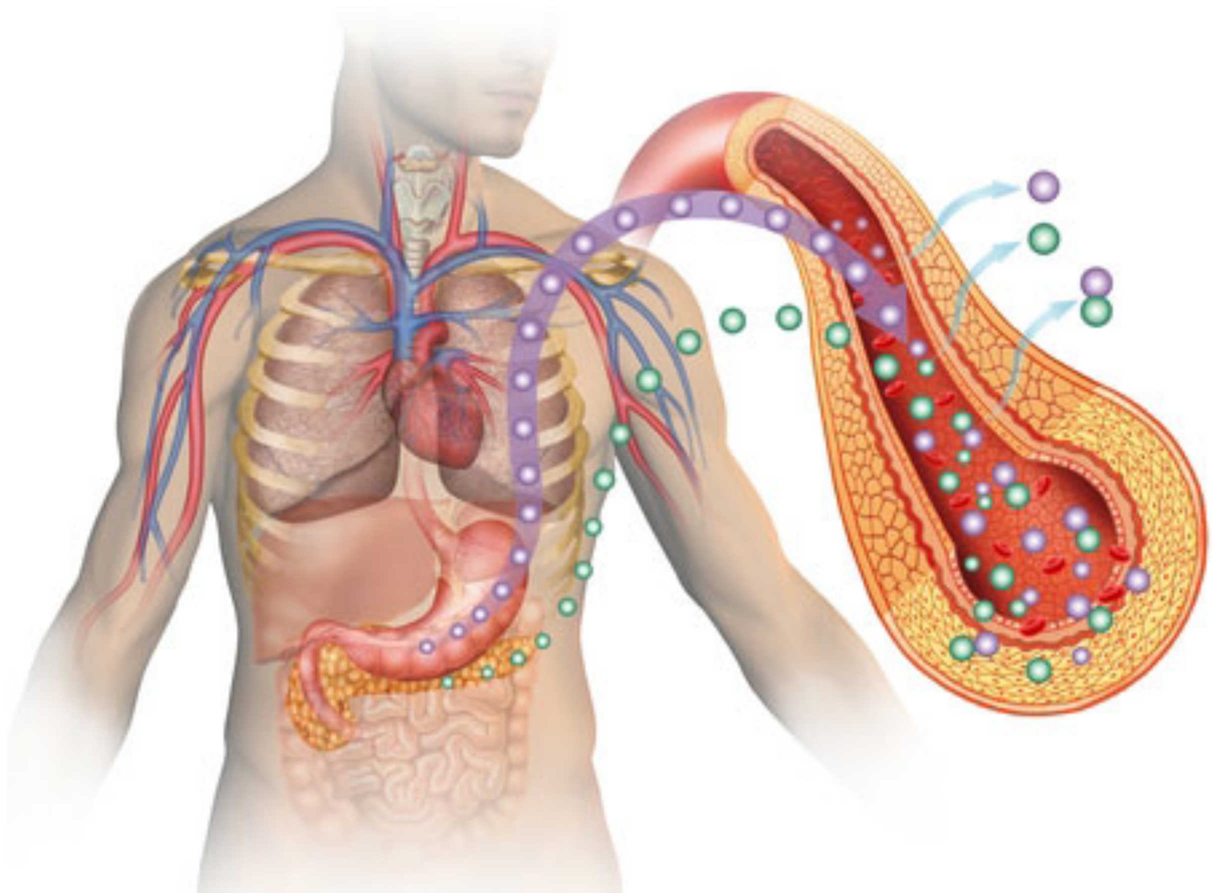
OGTT
Biopsy

Results – Daily Step Count

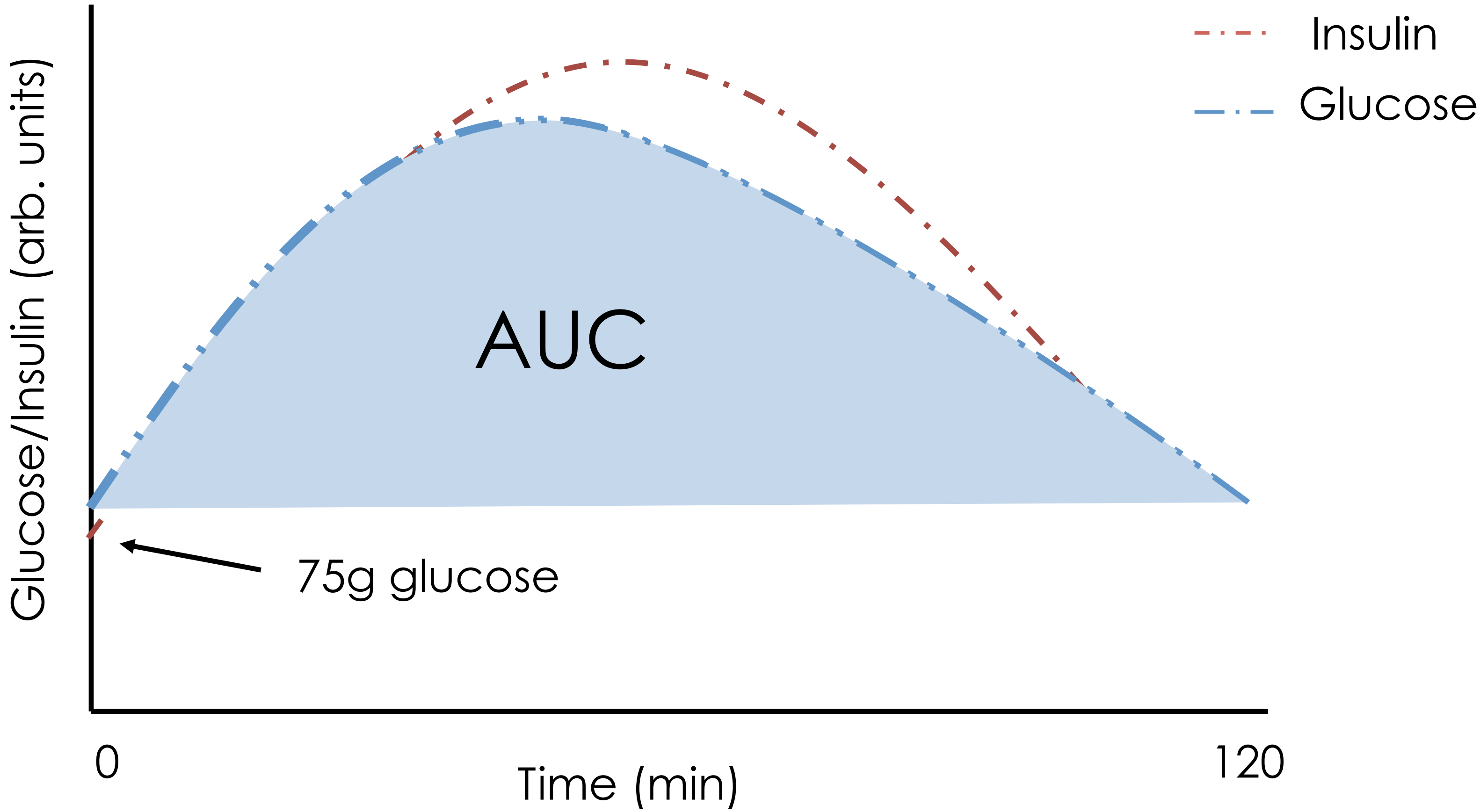


McGlory, von Alllmen *et al.* in preparation

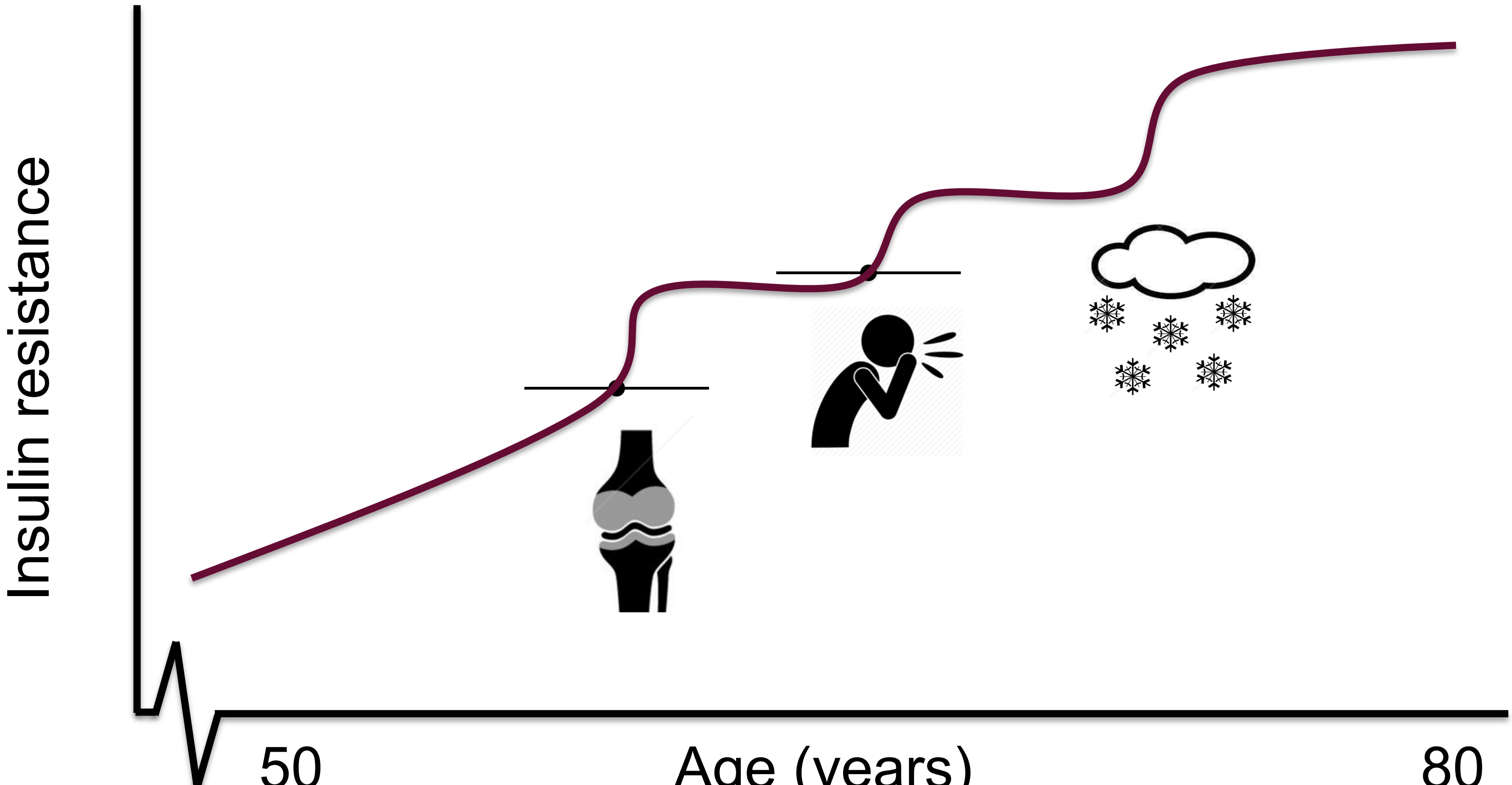
Oral glucose tolerance test



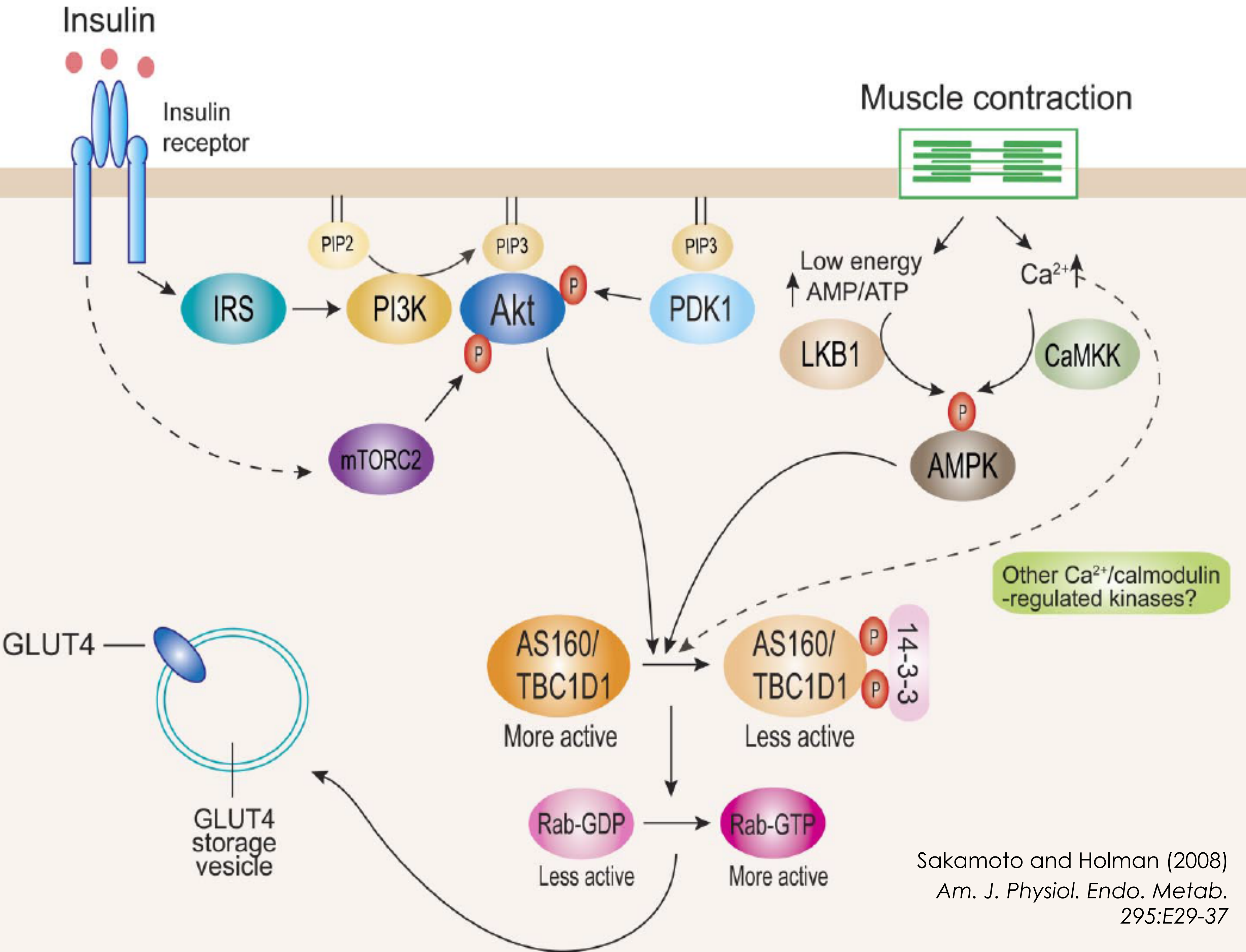
Oral glucose tolerance test response



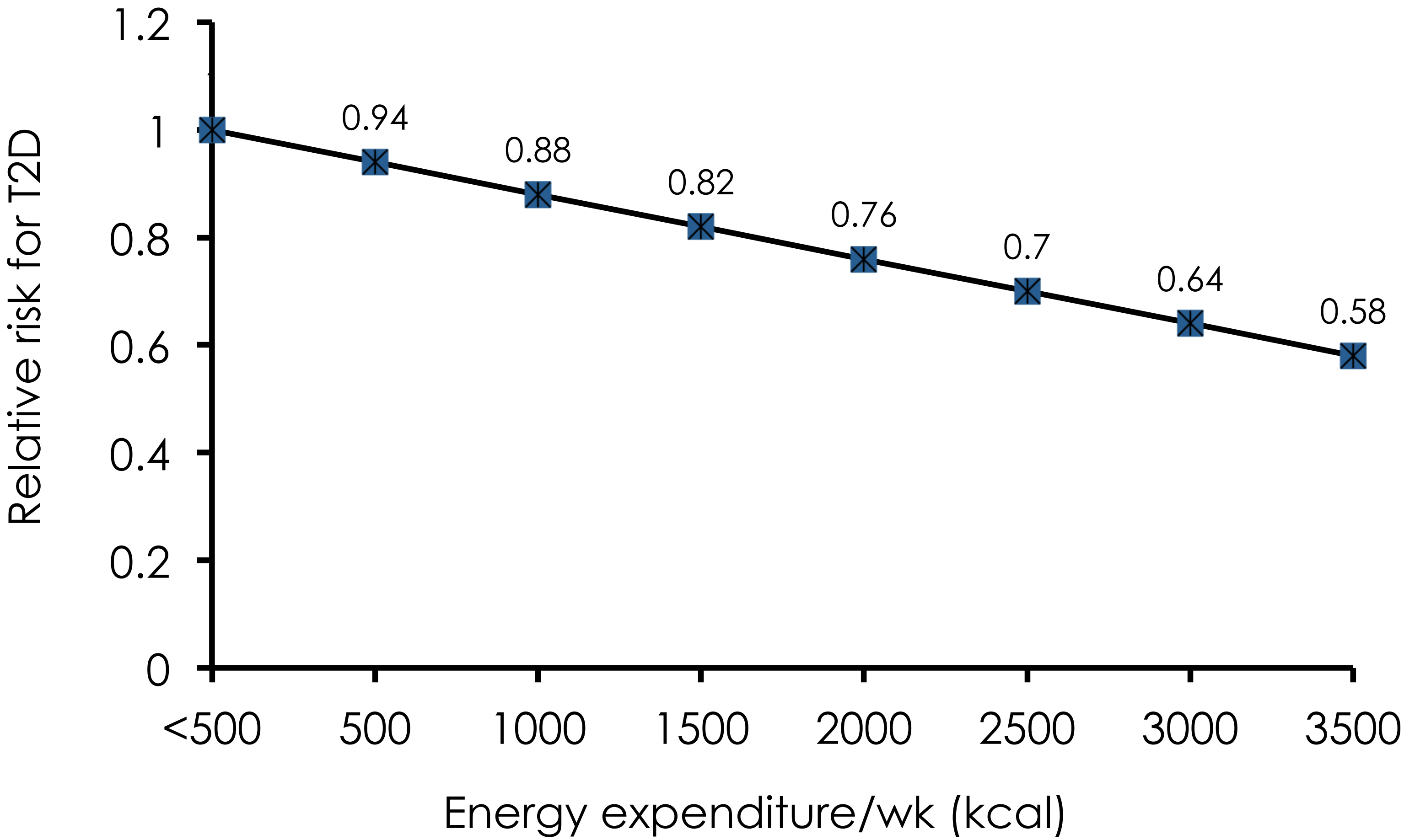
Its not just a catabolic crisis !



Exercise works !!

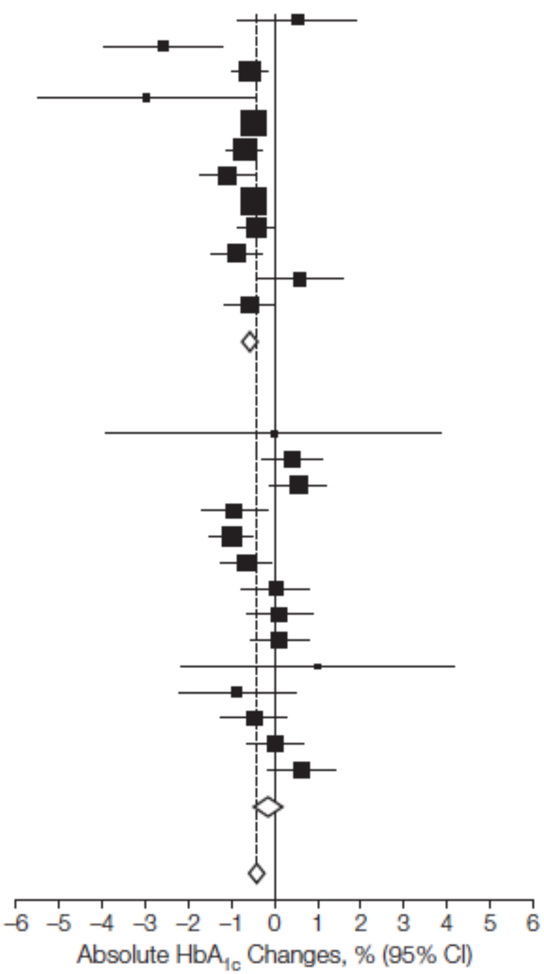


Sakamoto and Holman (2008)
Am. J. Physiol. Endo. Metab. *295:E29-37*



Helmrich, et al.,(1991) *N. Eng. J. Med. 18:147-152*

Source	No. of Patients: Intervention	No. of Patients: Control	HbA_{1c} Weighted Mean Difference, % (95% CI)	Weight, %
Physical activity advice with dietary cointervention				
Aas et al,[41] 2005	10	9	0.50 (−0.86 to 1.86)	1.18
Argurs-Collins et al,[42] 1997	32	32	−2.60 (−3.98 to −1.22)	1.15
Christian et al,[43] 2008	141	132	−0.60 (−1.00 to −0.20)	6.44
Dasgupta et al,[44] 2006	21	21	−3.00 (−5.51 to −0.49)	0.37
Di Loreto et al,[45] 2003	182	158	−0.50 (−0.62 to −0.38)	10.53
Hordern et al,[46] 2009	88	88	−0.70 (−1.08 to −0.32)	6.70
Kim et al,[47] 2006	32	10	−1.10 (−1.72 to −0.48)	4.04
Jakicac et al,[48] 2007	2486	2575	−0.50 (−0.56 to −0.44)	11.13
Mayer-Davis et al,[49] 2004	49	56	−0.44 (−0.87 to −0.01)	6.11
Ménard et al,[50] 2005	34	35	−0.90 (−1.49 to −0.31)	4.33
Vanninen et al,[51] 1992	38	40	0.57 (−0.43 to 1.57)	2.00
Wing et al,[52] 1998	13	15	−0.60 (−1.16 to −0.04)	4.62
All advice with dietary cointervention $I^2 = 57.5\%$; P for heterogeneity = .007			−0.58 (−0.74 to −0.43)	58.60
Physical activity advice alone				
Brun et al,[53] 2008	13	12	−0.04 (−3.93 to 3.85)	0.16
Cheung et al,[54] 2009	20	17	0.40 (−0.29 to −1.09)	3.49
Diedrich et al,[55] 2010	27	26	0.54 (−0.11 to 1.19)	3.82
Kim and Kang,[56] 2006[a]	22	23	−0.94 (−1.68 to −0.20)	3.19
Kim and Kang,[56] 2006[b]	28	23	−1.02 (−1.51 to −0.53)	5.28
Kirk et al,[57] 2003	26	31	−0.68 (−1.26 to −0.10)	4.40
Kirk et al,[58] 2009[c]	47	35	0.00 (−0.79 to 0.79)	2.88
Kirk et al,[58] 2009[d]	51	35	0.10 (−0.65 to 0.85)	3.13
Krousel-Wood et al,[59] 2008	37	39	0.10 (−0.56 to 0.76)	3.71
Leehey et al,[60] 2009	7	4	1.00 (−2.16 to 4.16)	0.24
Rönnemaa et al,[61] 1986	13	12	−0.90 (−2.25 to 0.45)	1.20
Samaras et al,[62] 1997	13	13	−0.49 (−1.24 to 0.26)	3.10
Tudor-Locke et al,[63] 2004	24	23	0.00 (−0.66 to 0.66)	3.72
van Rooijen et al,[64] 2004	75	74	0.62 (−0.14 to 1.38)	3.09
All advice alone $I^2 = 61.2\%$; P for heterogeneity = .001			−0.16 (−0.50 to 0.18)	41.40
Overall $I^2 = 62.9\%$; P for heterogeneity <.001			−0.43 (−0.59 to −0.28)	100.00



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

Diabetes prevention program

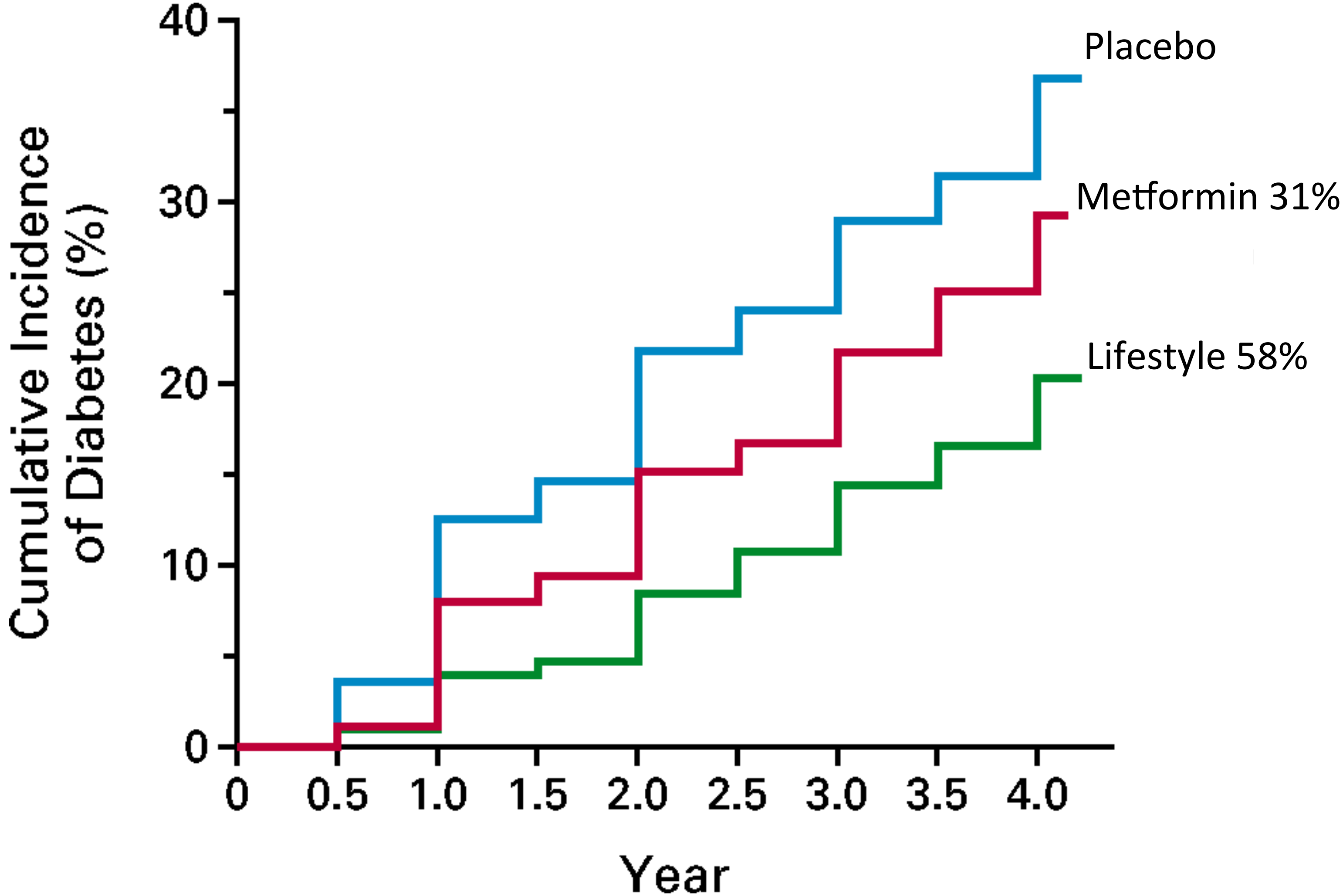
3234 non diabetics

1700 mg Metformin

150 min physical activity/wk + behavior modification

Placebo

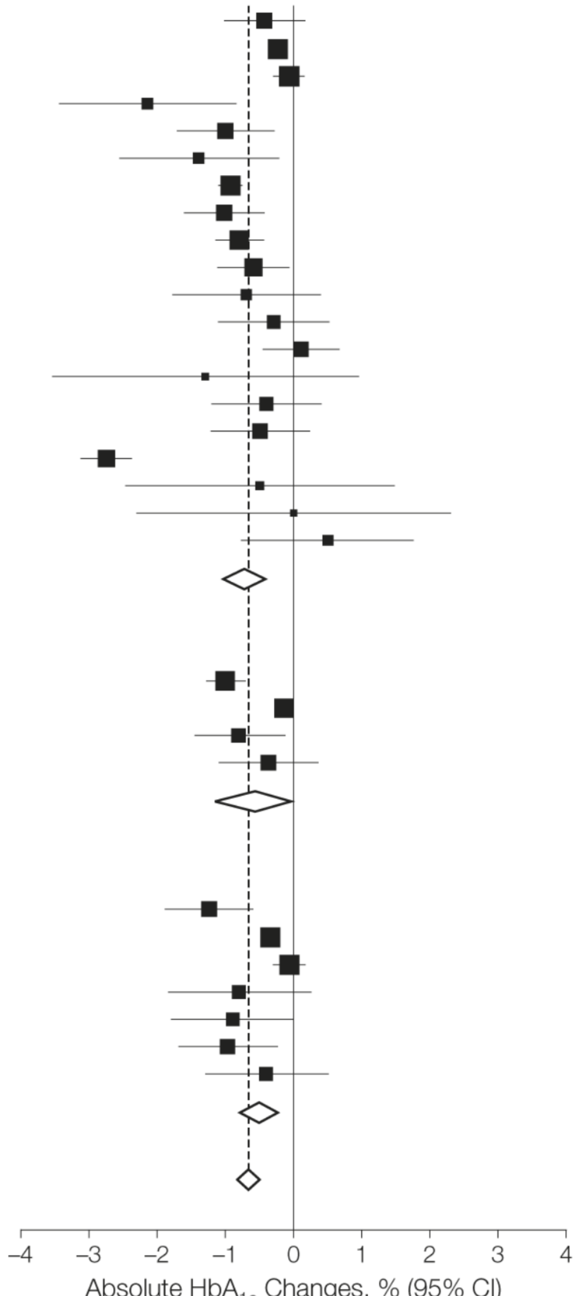
2.8 y follow-up



Diabetes Prevention Program Research Group (2002)
N. Eng. J. Med. 7:346:393-403

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

Source	No. of Patients: Intervention	No. of Patients: Control	HbA_{1c} Weighted Mean Difference, % (95% CI)	Weight, %
Aerobic training				
Bjørgaas et al,[20] 2005	11	11	−0.44 (−1.03 to 0.15)	3.46
Church et al,[8] 2010	72	41	−0.23 (−0.30 to −0.16)	5.77
Cuff et al,[21] 2003	9	9	−0.07 (−0.28 to 0.14)	5.37
Dela et al,[22] 2004	14	10	−2.14 (−3.43 to −0.86)	1.38
Giannopoulou et al,[23] 2005	11	11	−1.00 (−1.70 to −0.30)	2.96
Goldhaber-Fiebert et al,[24] 2003	33	28	−1.40 (−2.56 to −0.24)	1.61
Kadoglou et al,[25] 2007	29	27	−0.93 (−1.08 to −0.78)	5.57
Kadoglou et al,[26] 2007	28	26	−1.02 (−1.59 to −0.45)	3.55
Kadoglou et al,[27] 2010[a]	22	21	−0.80 (−1.15 to −0.45)	4.68
Kadoglou et al,[27] 2010[b]	23	23	−0.59 (−1.11 to −0.07)	3.81
Lambers et al,[28] 2008	18	11	−0.70 (−1.78 to 0.38)	1.78
Ligtenberg al,[29] 1997	25	26	−0.30 (−1.11 to 0.51)	2.57
Middlebrooke et al,[30] 2006	22	30	0.10 (−0.45 to −0.65)	3.64
Raz et al,[31] 1994	19	19	−0.30 (−3.53 to 0.93)	0.54
Ribeiro et al,[32] 2008	11	10	−0.40 (−1.19 to 0.39)	2.61
Sigal et al,[7] 2007	60	63	−0.50 (−1.22 to 0.22)	2.88
Sridhar et al,[33] 2010	55	50	−2.76 (−3.13 to −2.39)	4.60
Vancea et al,[34] 2009[c]	14	17	−0.50 (−2.47 to 1.47)	0.68
Vancea et al,[34] 2009[d]	9	17	0.00 (−2.30 to 2.30)	0.51
Verity and Ismail,[35] 1989	5	5	0.50 (−0.75 to 1.75)	1.43
All aerobic training I^2 = 92.8%; *P* for heterogeneity <.001			−0.73 (−1.06 to −0.40)	59.41
Resistance training				
Castaneda et al,[36] 2002	29	31	−1.00 (−1.27 to −0.73)	5.11
Church et al,[8] 2010	73	41	−0.15 (−0.22 to −0.08)	5.78
Dunstan et al,[37] 2002	16	13	−0.80 (−1.46 to −0.14)	3.17
Sigal et al,[7] 2007	64	63	−0.37 (−1.08 to 0.34)	2.92
All resistance training I^2 = 92.5%; *P* for heterogeneity <.001			−0.57 (−1.14 to −0.01)	16.68
Combined training				
Balducci et al,[38] 2004	51	53	−1.24 (−1.88 to 0.60)	3.24
Church et al,[8] 2010	76	41	−0.34 (−0.41 to −0.27)	5.77
Cuff et al,[26] 2003	10	9	−0.07 (−0.29 to 0.15)	5.31
Lambers et al,[28] 2008	17	11	−0.80 (−1.84 to 0.24)	1.86
Loimaala et al,[39] 2003	24	25	−0.90 (−1.80 to −0.00)	2.26
Sigal et al,[7] 2007	64	63	−0.97 (−1.69 to −0.25)	2.86
Tessier et al,[40] 2000	19	20	−0.40 (−1.29 to 0.49)	2.28
All combined training I^2 = 67.5%; *P* for heterogeneity = .005			−0.51 (−0.79 to −0.23)	23.61
Overall I^2 = 91.3%; *P* for heterogeneity <.001			−0.67 (−0.84 to −0.49)	100.00

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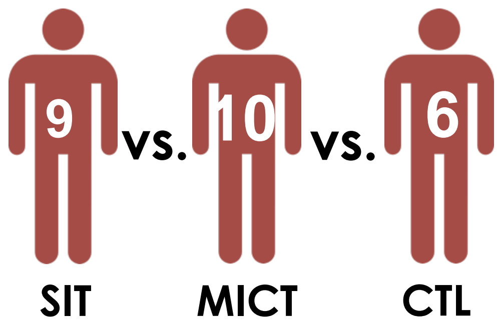
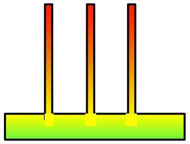
Villeneuve

Sprint interval training vs. continuous



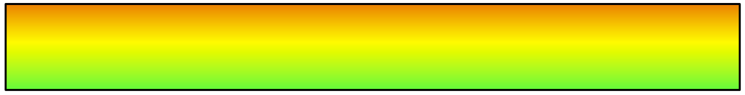
3x/wk, 12 wks training

SIT: 3 x 20 s sprints, 2 min recovery



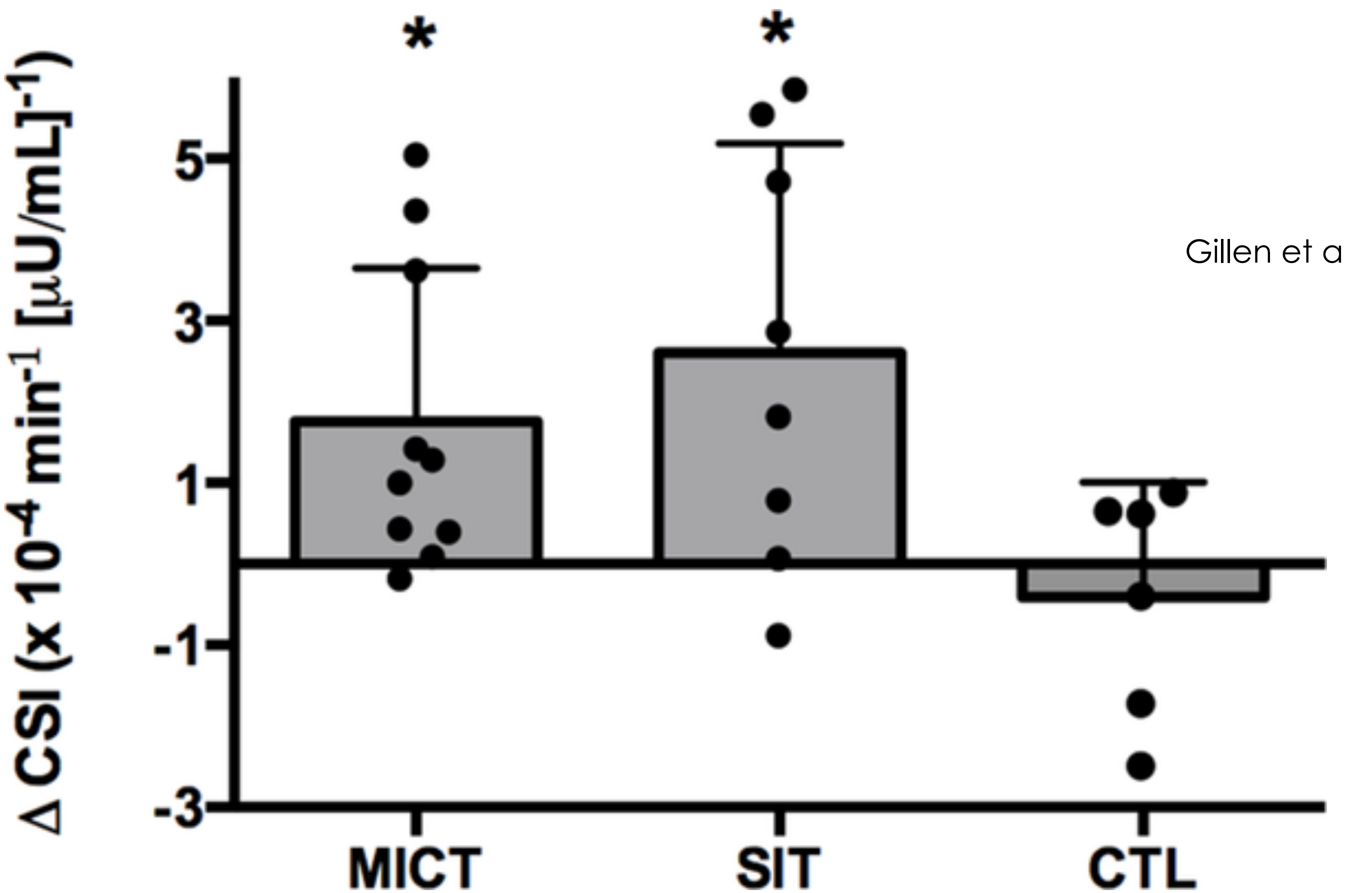
3 minutes of intense exercise within a 30 minute weekly time commitment

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



150 minutes of moderate-intensity continuous exercise per week

Sprint interval training vs. continuous

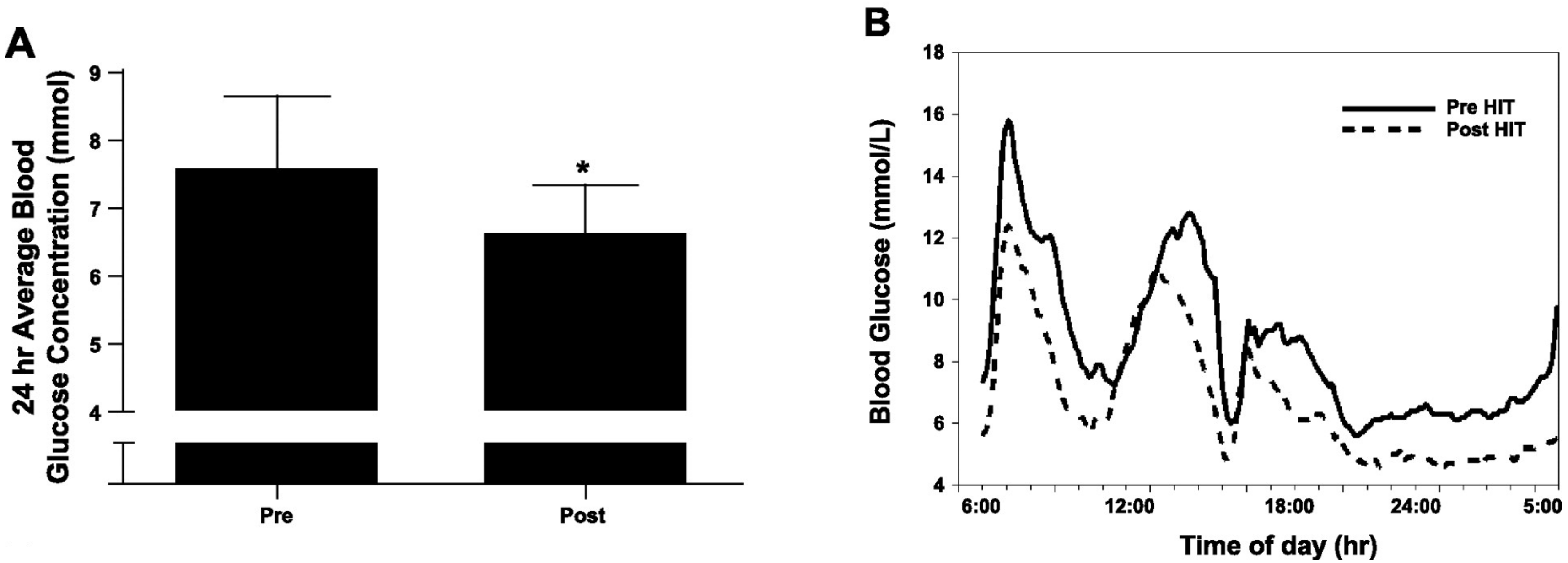


Gillen et al. (2016) PloS One. 11: e0154075.

Two weeks of HIIT reduces hyperglycaemia in Type 2 diabetics

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

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



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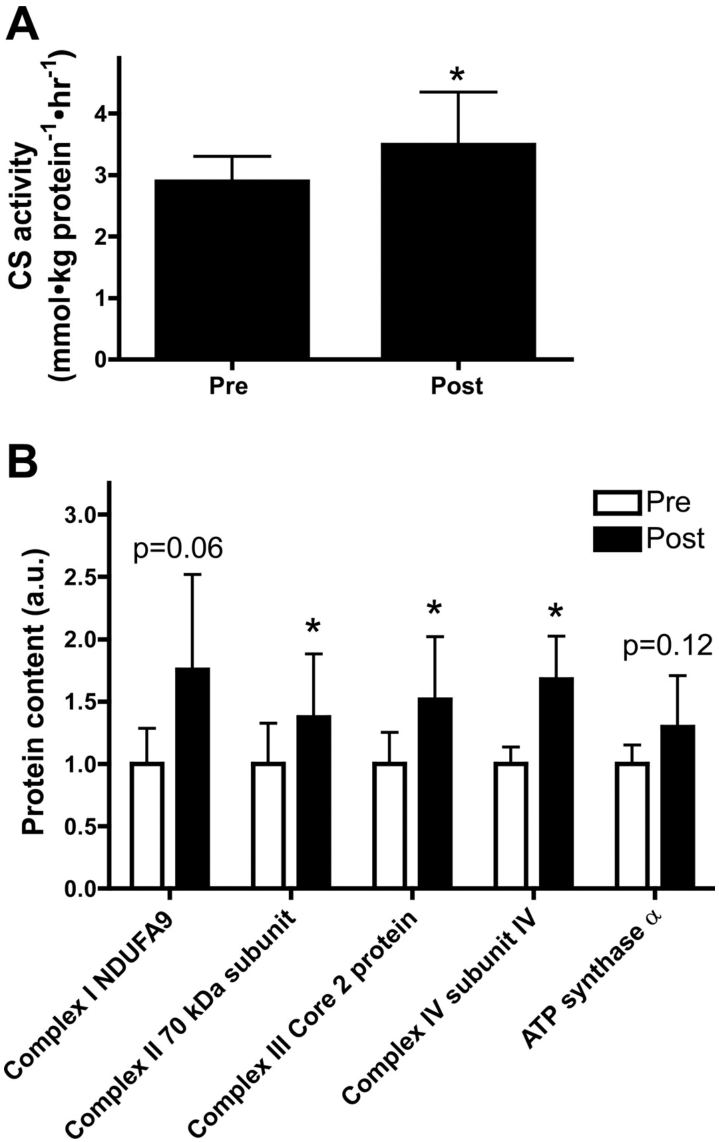
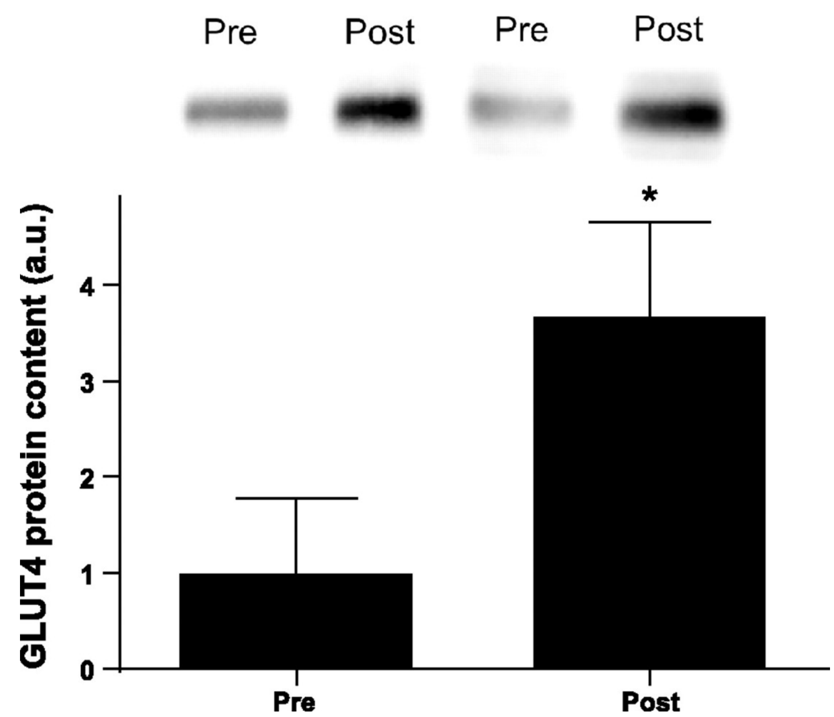
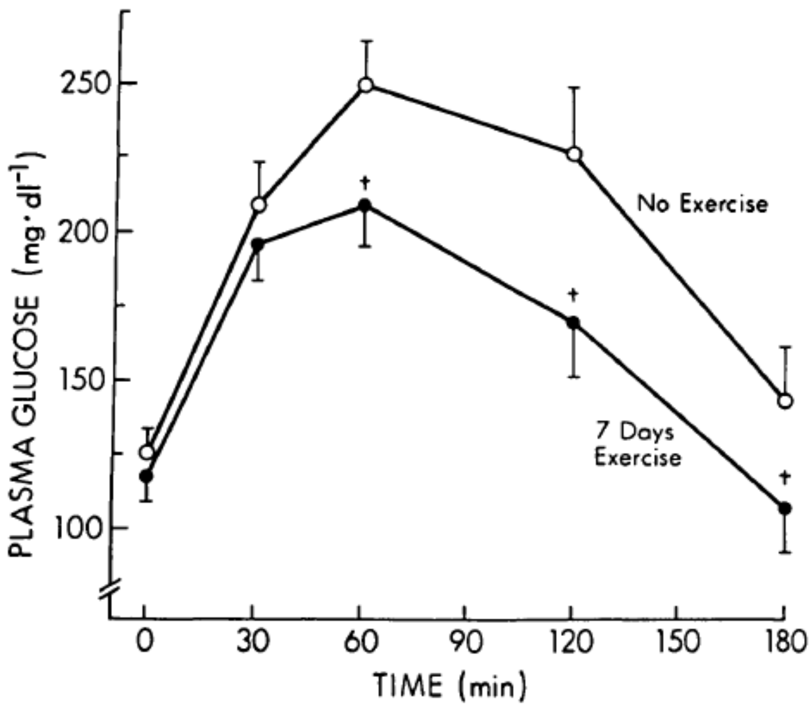

A
CS activity
(mmol•kg protein-1•hr-1)
0
1
2
3
4
*
Pre
Post
B
Protein content (a.u.)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Pre
Post
p=0.06
*
*
*
p=0.12
Complex I NDUFA9
Complex II 70 kDa subunit
Complex III Core 2 protein
Complex IV subunit IV
ATP synthase α

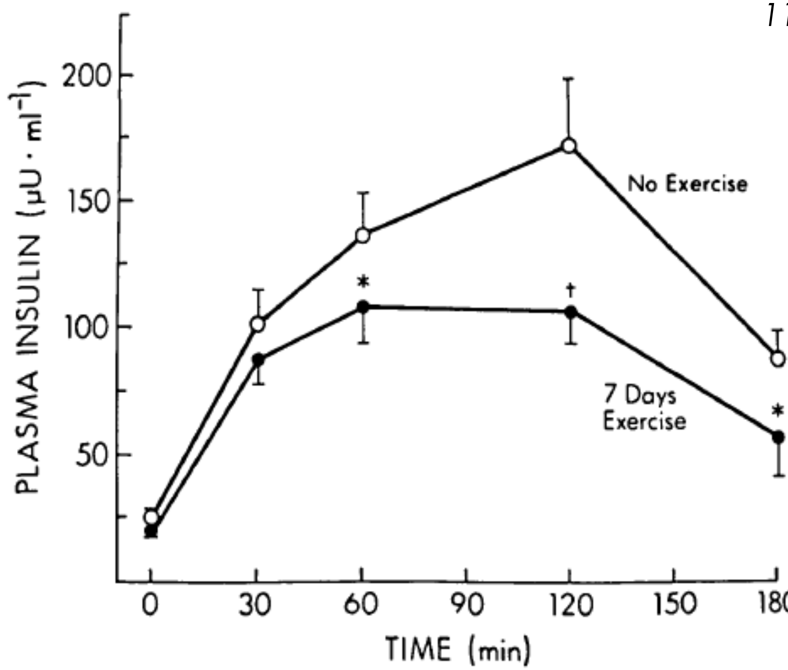

Pre
Post
Pre
Post
GLUT4 protein content (a.u.)
0
1
2
3
4
*
Pre
Post

Dr. John Holloszy, MD, PhD., 1980s

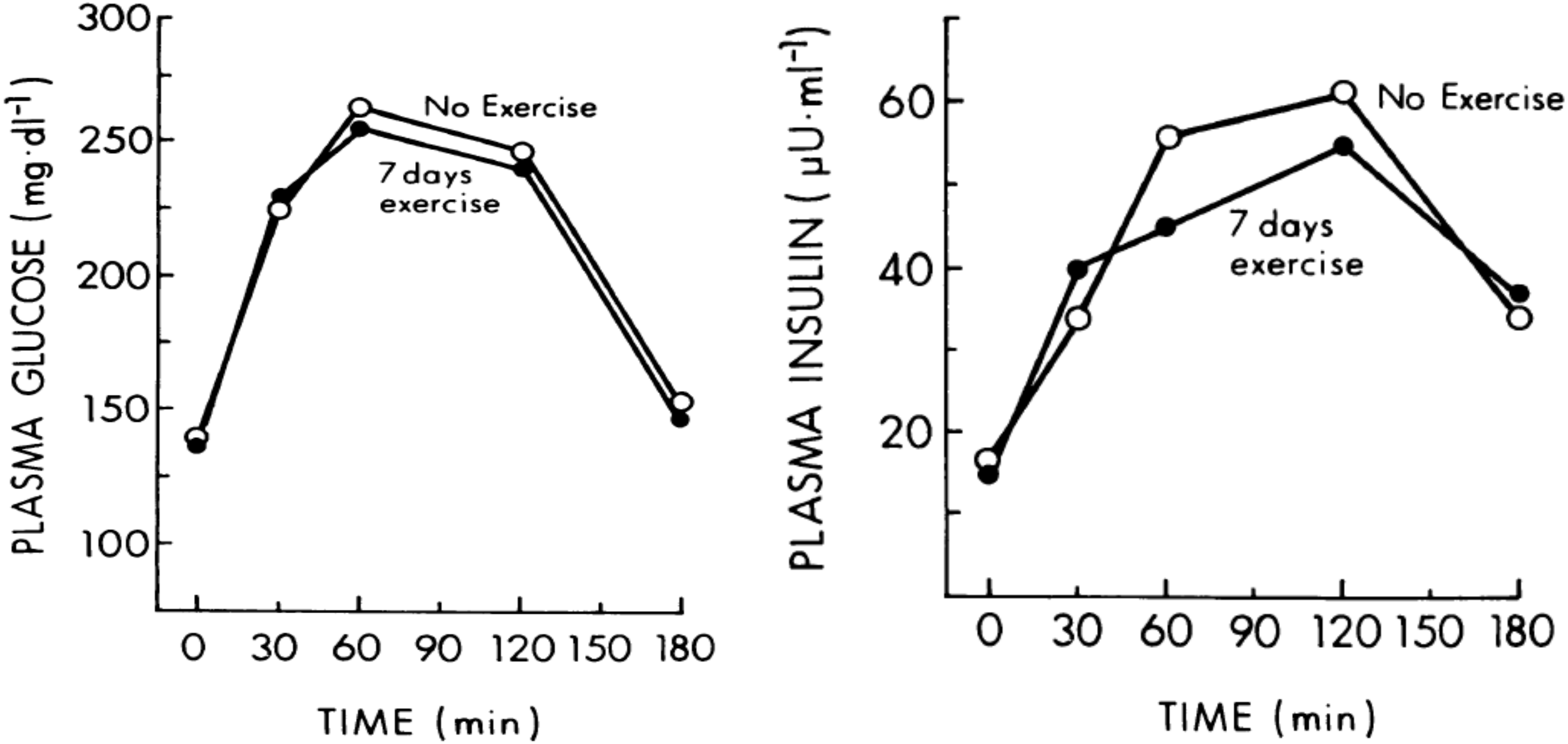
10 men (7 mild T2D; 3 impaired glucose tolerance)

Rogers et al., (1988) *Diabetes Care. 11:613-618.*



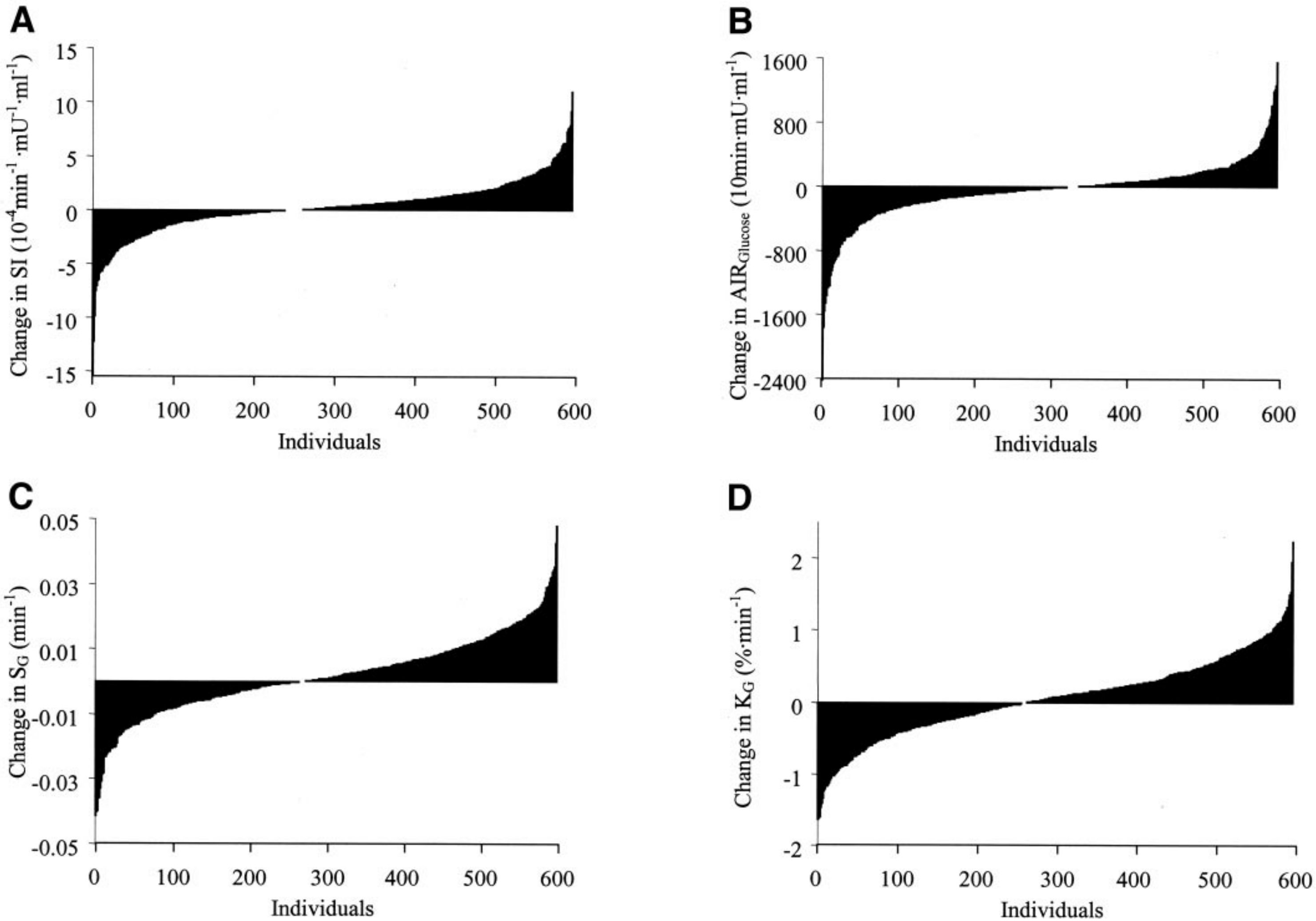


One size does not fit all



Canadian Diabetes Association

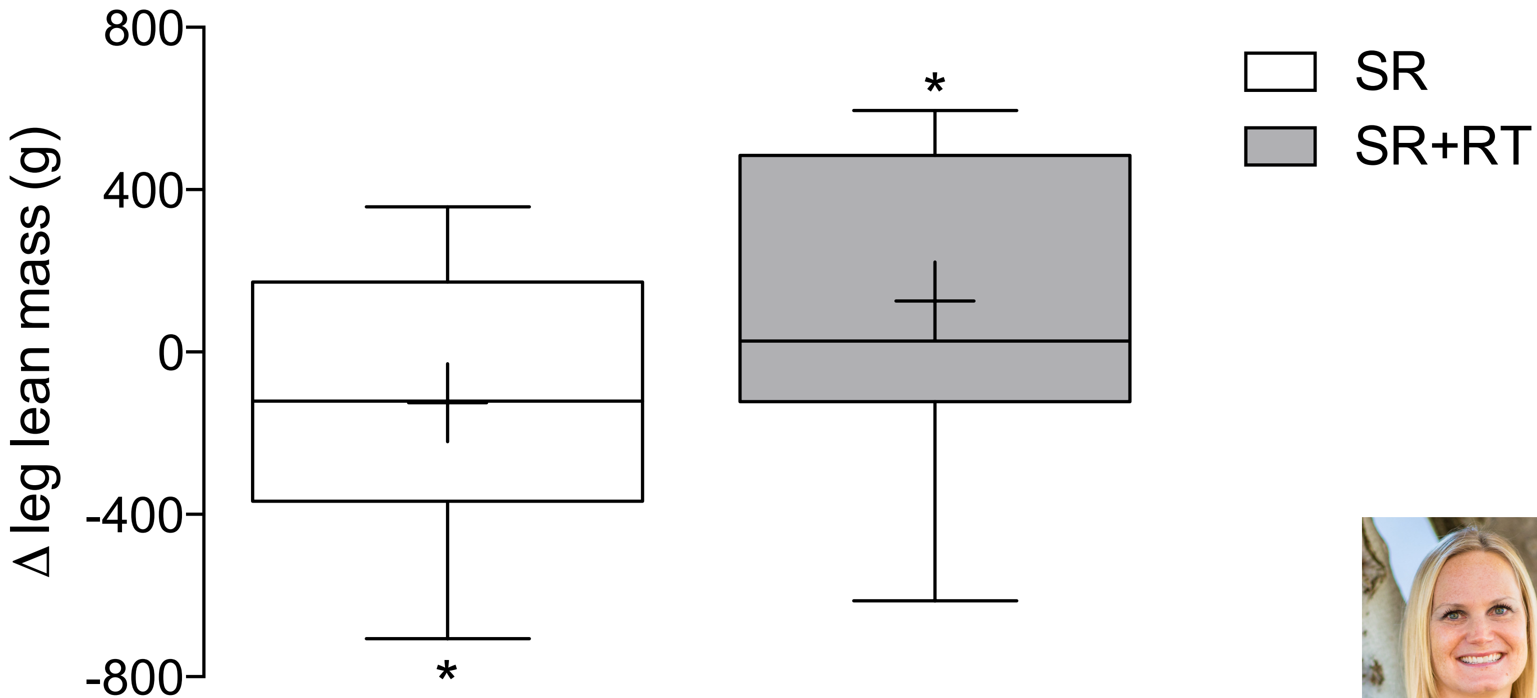
The HERITAGE family study



Boule et al. (2005) Diabetes Care. 28: 108-114.

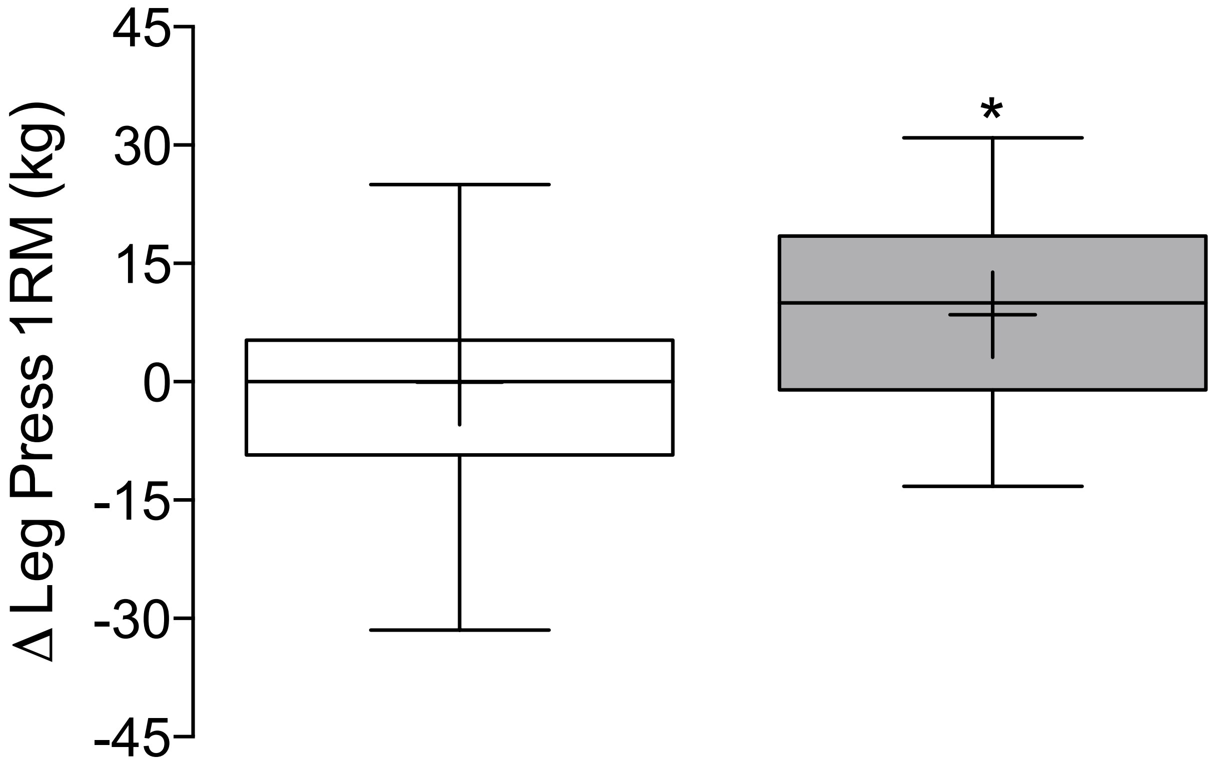
*‘Although the effects of structured regular exercise were highly variable, **there were improvements in virtually all IVGTT-derived variables**. In the absence of substantial weight loss, regular exercise is required for sustained improvements in glucose homeostasis’*

Resistance exercise attenuates atrophy



Devries et al. (2015)
Physiol. Rep. 3: e12493

Resistance exercise attenuates atrophy



Devries et al. (2015)
Physiol. Rep. 3: e12493

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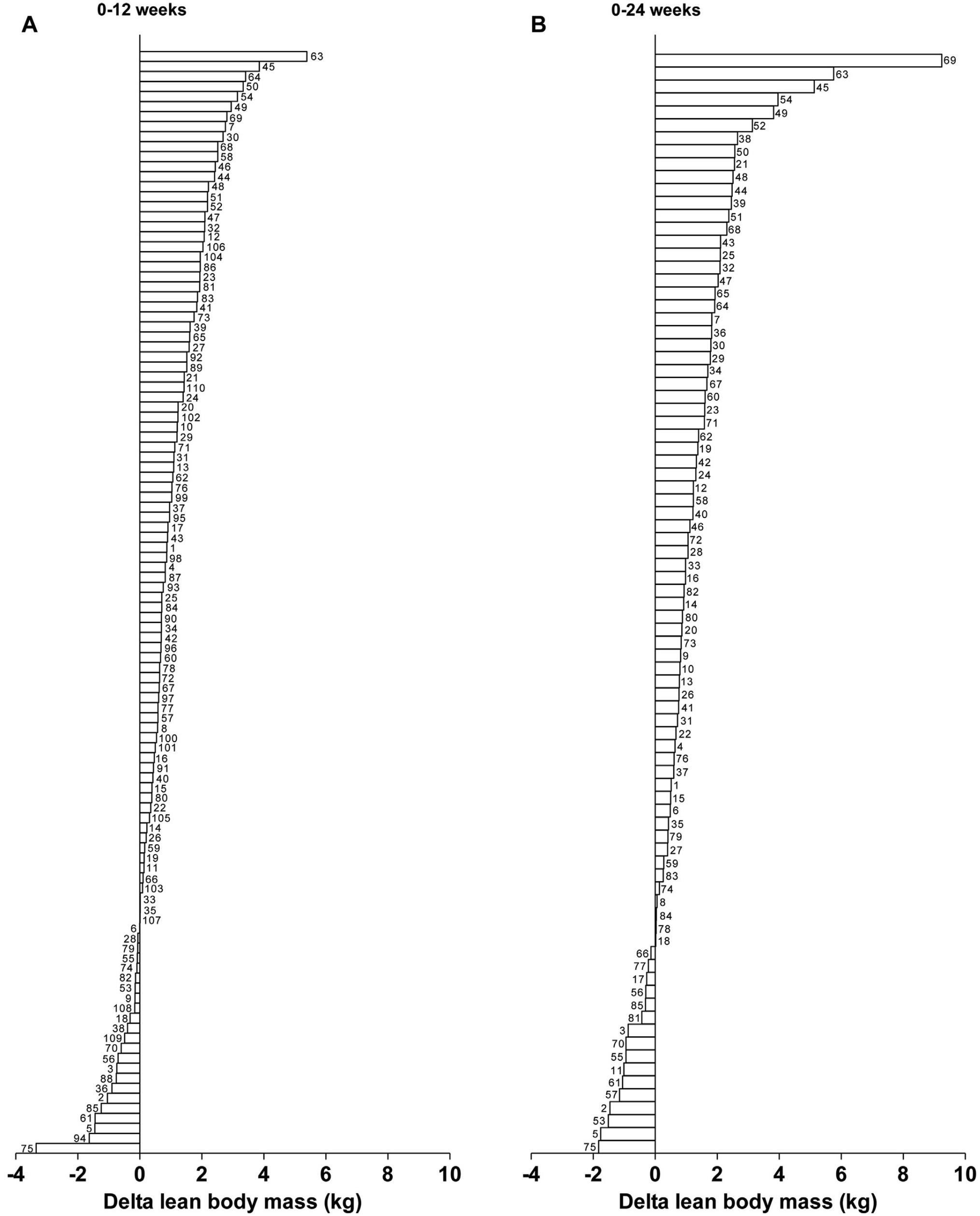
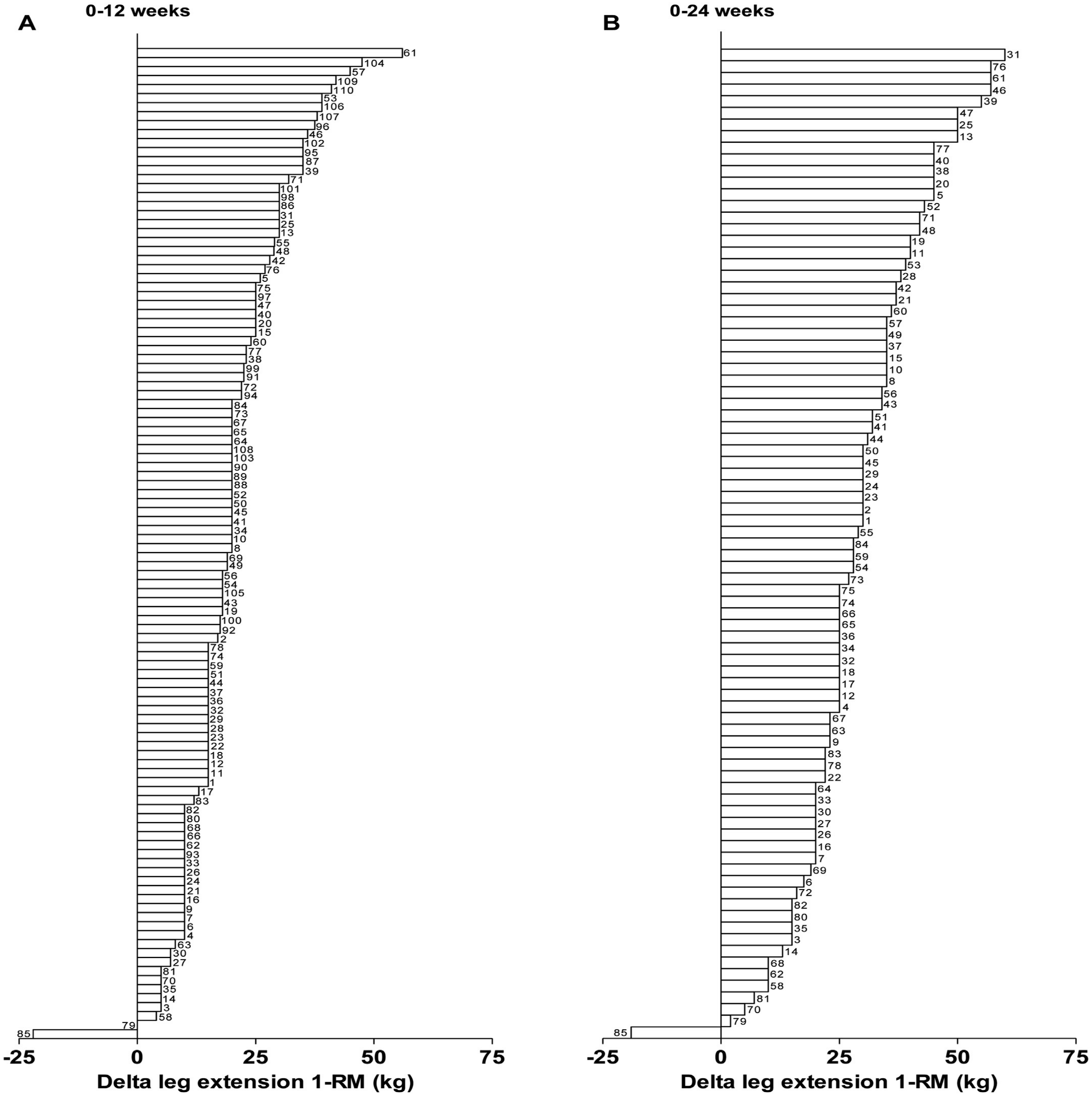


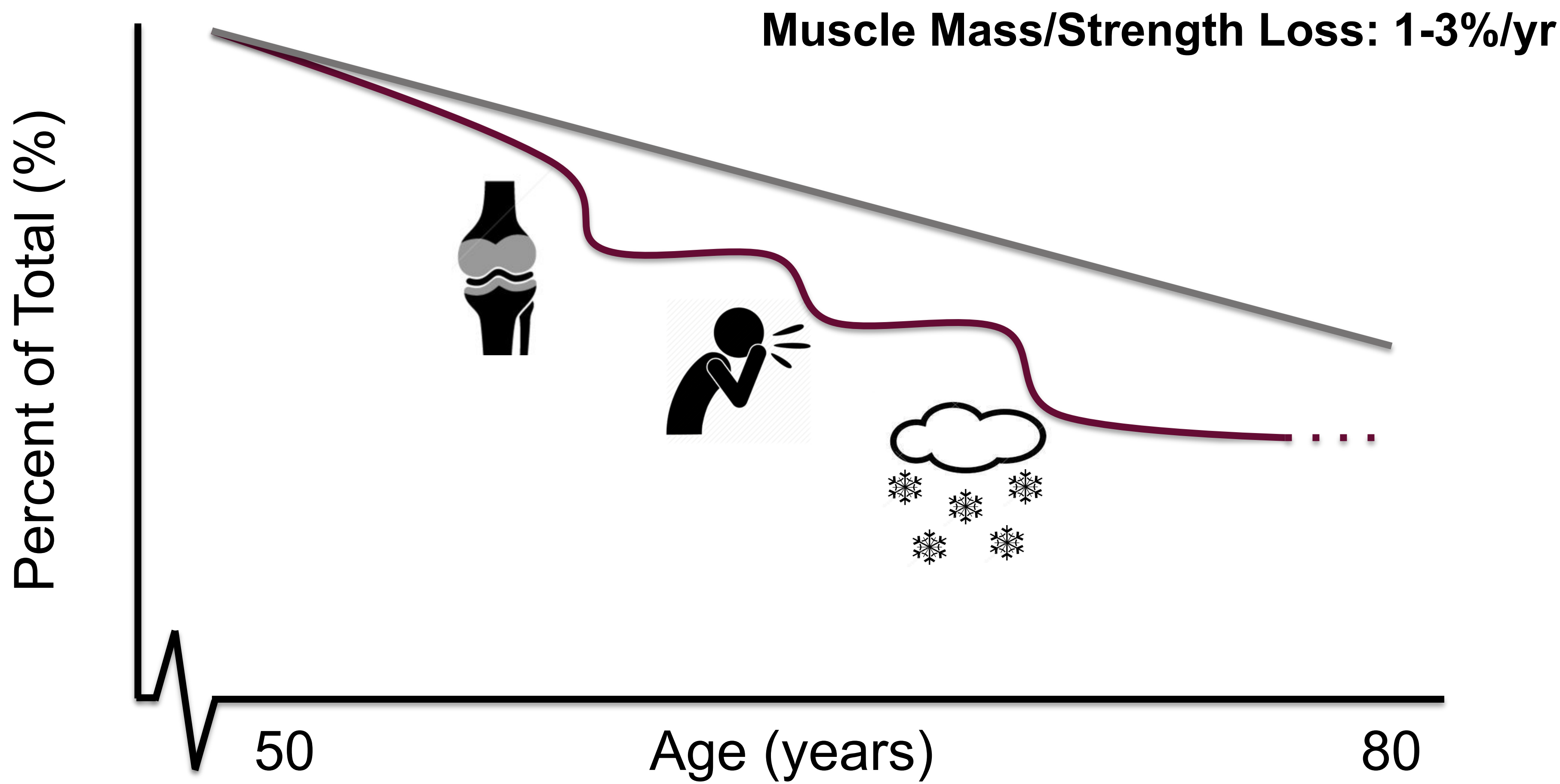
Churchward-Venne et al. (2015) JAMDA. 16: 400-411.

McMaster University



Chris McGlory, CDA, York University, 28th June 2016.

Physical inactivity accelerates sarcopenia



English and Paddon-Jones (2010)
Curr. Opin. Nutr. Metab. Care. 13:34-39

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

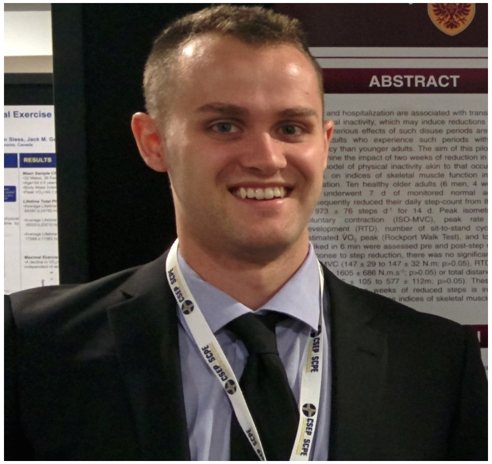
3 Physical activity and exercise are modifiable risk factors to improve skeletal muscle health

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

Canadian Diabetes Association

McMaster University

Phillips Laboratory

Thank You!